
NIH Request for Information:
Inviting Comments and Suggestions on a
Framework for the NIH-wide Strategic Plan

Analysis of Public Comments

October 2015

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Executive Summary

In response to legislation passed in December 2014, the National Institutes of Health (NIH) is developing a five-year NIH-wide Strategic Plan. With input from the Advisory Committee to the NIH Director (ACD) and representatives from the 27 NIH Institutes, Centers, and Offices (ICOs), senior leaders created a framework for the Strategic Plan. As part of the efforts to disseminate the draft framework and to solicit input from the public, NIH released a Request for Information (RFI): Inviting Comments and Suggestions on a Framework for the NIH-wide Strategic Plan ([NOT-OD-15-118](#)).

The RFI gathered input from the research community and other interested stakeholders on the potential benefits and challenges of the framework, compatibility with the NIH mission, cross-cutting research themes that should be included in the Strategic Plan, areas that are not applicable to the Strategic Plan, and emerging research needs. A web-based form for submitting comments was available from July 22, 2015 to August 16, 2015. During this period, NIH received 457 responsive submissions from a range of individuals and organizations.

The responses reflected a wide array of scientific perspectives and comments on NIH operations. While many respondents supported the framework and its compatibility with the NIH mission, the vast majority of comments suggested changes or additional areas to be included. From the analysis of the responses, several cross-cutting scientific areas and principles arose as being collectively significant. There was strong support for basic and applied sciences in broad terms, with many recommendations to explicitly emphasize translational research and behavioral and social sciences. A portion of responses advocated for increased research on specific diseases, while fostering interdisciplinary research and systems approaches also was encouraged. Furthermore, respondents noted emerging opportunities in data science and technologies that would serve to accelerate data collection and analysis. In addition to suggesting scientific themes for inclusion under the Areas of Opportunity, RFI respondents commented on the Unifying Principles sections. Partnerships with patients, communities, industry, and other federal agencies were supported for their potential to maximize resources and catalyze new discoveries. Finally, respondents expressed concerns about the biomedical workforce and encouraged efforts to support training, retention, and diversity.

Report on the Results of the RFI

Introduction

On December 16, 2014, Congress passed the “Consolidated and Further Continuing Appropriations Act, 2015” (P.L. 113-235). The Act directs National Institutes of Health (NIH) to submit an NIH-wide five-year Strategic Plan to Congress no later than one year following enactment. Additional, pending legislation in the 114th Congress outlines requirements for an NIH-wide Strategic Plan.

In order to fulfill the request from Congress and to advance its mission, NIH began the process of developing a five-year Strategic Plan. To inform the plan’s development, NIH formed an NIH-wide Strategic Plan Working Group composed of senior leadership and staff representing all 27 ICOs. The NIH Director, Dr. Francis Collins, and Principal Deputy Director, Dr. Lawrence Tabak, created a draft framework for the Strategic Plan with input from the Working Group and the Advisory Committee to the Director. The goal of the framework was to identify cross-cutting areas of research exemplifying the breadth of ICOs’ priorities and to outline a set of unifying principles to guide NIH in pursuit of its mission. The intent of the framework was to highlight major trans-NIH themes, not research opportunities for specific disease applications.

Throughout the process of creating the Strategic Plan, NIH leadership solicited feedback from the public and other stakeholders in order to identify emerging scientific opportunities and gather suggestions for how to improve the draft framework. NIH hosted a series of public webinars in August 2015 to provide opportunities for stakeholders to ask questions and offer their input. In addition, the framework for the Strategic Plan was presented at more than 20 meetings of the National Advisory Councils of the NIH ICOs, held in September and October 2015. Part of the efforts to disseminate the proposed framework and solicit input included a Request for Information (RFI): Inviting Comments and Suggestions on a Framework for the NIH-wide Strategic Plan ([NOT-OD-15-118](#)). Comments were accepted online from July 22, 2015 to August 16, 2015. NIH invited community feedback on several topic areas:

- Potential benefits, drawbacks/challenges, and areas of consideration for the current framework
- Compatibility of the framework with the broad scope of the NIH mission
- Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan
- Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine
- Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan
- Future opportunities or emerging research needs

Characteristics of Respondents:

NIH received 460 submissions to the RFI, including three that were left blank. Of the responsive submissions, 333 (73 percent) were submitted by individuals and 124 (27 percent) were submitted on behalf of organizations. Individuals who provided comments included 145 representatives from academic institutions, 41 from patient advocacy organizations or research foundations, 19 from professional societies or associations, 15 from private hospitals or companies, 12 from the biotechnology industry, 11 from government, and 90 private citizens. The organizations providing responses included 69 professional societies or associations, 44 patient advocacy organizations or

research foundations, six private hospitals or companies, and four academic institutions or groups. Some organizational responses were endorsed or signed by multiple people; in these cases, the group was counted as a single respondent.

Analysis of the Results:

RFI respondents were invited to give feedback on the six topic areas outlined above as freeform text comments. NIH staff analyzed the content of these responses using a standardized coding structure (See Table A1 in the Appendix for a description of the codes and sub-codes used in the analysis, along with sample responses). Codes were not mutually exclusive; response statements could be assigned to multiple codes as necessary. Some respondents provided narrative statements rather than responses to the individual RFI questions. The narrative content was coded according to the same structure as other responses.

Comments on the Framework and Compatibility with NIH Mission

While most respondents identified research areas or principles to be added to the Strategic Plan or given greater emphasis, there were 159 responses with declarative statements on the overall structure and purpose of the proposed framework. The majority of these comments (102) supported or endorsed the framework, stating that the proposal was “sound” and represented an appropriate breadth and balance of research that captures the current and future needs of NIH. The outlined Areas of Opportunity were thought to effectively foster cross-cutting themes and promote the inter-related nature of basic and applied research. Some respondents commented that the framework benefits from the absence of focus on specific diseases, explaining that this approach does not compete with the priorities of the ICOs and allows for flexibility. In contrast, several responses noted conceptual concerns with the framework, including that the proposal “largely continues the status quo” and lacks the innovation needed to improve NIH and its impact.

Nearly all of the responses (64 out of 68) on the compatibility of the framework with the broad scope of the NIH mission confirmed that the framework is consistent and aligned with the NIH mission. Very few responses (4) declared that the framework was incompatible with the NIH mission.

Suggestions and Comments Related to the Areas of Opportunity that Apply Across Biomedicine

There were numerous comments on the Areas of Opportunity that Apply Across Biomedicine, most of which suggested scientific areas to be included in the Strategic Plan or requested greater emphasis of existing pieces of the framework. The suggestions encompassed a wide spectrum of science, from basic, to translational and clinical research, and ranged from general fields (e.g. endocrinology and prevention research) to specific projects (e.g. Precision Medicine Initiative and immunotherapies for diabetes). Also, there were several comments indicating that the term “biomedicine” was limiting, as it may be construed to focus solely on biology and exclude psychological and social factors that impact health and disease.

Many respondents (90) made declarative statements applauding one or more of the Areas of Opportunity and mentioned support of the specific bullet points under each Area. For example,

respondents agreed that fundamental science is an essential priority, affirming that basic science is the foundation for progress and that discoveries often come from unexpected directions. Respondents also were “encouraged that the framework emphasizes the importance of research on prevention of disease” and were pleased with the focus on healthy individuals. Under the Advancing Treatments and Cures section, many comments supported the breakdown of traditional disease boundaries as an important approach to advancing research.

Basic science

As noted above, basic science was revealed to be a high priority for 114 respondents. Many of these responses recommended a greater emphasis on the role of basic research, in recognition that a long-term commitment to basic science is needed and that knowledge of basic life processes is key to understanding, treating, and preventing human disease. Other respondents provided suggestions of specific research topics to be included in the Strategic Plan. More than a quarter of these responses (35) encouraged a focus on basic research in cancer, such as mechanisms of tumor growth and immunotherapies, and some focused specifically on pediatric cancer. Other areas of basic science that were suggested in smaller numbers include neuroscience, immunology, basic mechanisms of chronic diseases, metabolic studies and endocrinology, and developmental biology (listed in order of frequency). Related to neuroscience, respondents noted there are many future opportunities in brain research that could lead to identification of common mechanisms, advances in diagnostics, and novel treatments for a variety of neurological conditions. In immunology, respondents highlighted emerging research on antimicrobial resistance and vaccine development, given recent outbreaks of infectious diseases in the United States and abroad. In addition, studies on genomics, aging, and intrinsically disordered proteins were mentioned as specific cross-cutting topics.

Translational Science

Translational research was a theme noted by many respondents (95) as needing explicit reference in the framework and requiring greater emphasis. Translational research was viewed as a critical component of the biomedical spectrum that increases the impact of science and leads to new innovations in clinical research and health care. More than one-third of these comments (40) focused on the science of disseminating and implementing best practices for treatment strategies and enhancing the adoption of these strategies into clinical practice. Another third of the comments (33) dealt with the translation from discoveries in preclinical studies to the development of new clinical studies and trials in humans. While some suggestions on the inclusion of translational research or dissemination and implementation science were general, many respondents identified specific challenges in translation that need to be addressed. These include the high failure rate of drugs when moving from the preclinical to the clinical stage and the need for improved predictive models to test for efficacy and toxicity. Reducing the time and cost of implementing new treatments and finding ways to scale-up implementation throughout clinical settings also were identified as important priorities. Finally, several respondents recommended that effective translation science requires strong partnerships between scientists and other groups, such as clinicians, patients, health care organizations, and industry.

Clinical Science, Prevention Research, and Population Health

Clinical science and specific clinical topics were featured in almost one-third of the RFI responses (138). Comments that were related to human subjects research on disease mechanisms and treatments predominantly focused on approaches and the conduct of clinical studies. For example, respondents encouraged NIH to emphasize patient-centered approaches and research on the whole person, which often encompasses multiple symptoms and comorbid diseases/disorders. The development of biomarkers, surrogate endpoints, and other clinical outcome measures to improve clinical study

efficiency also were suggested, as well as genetic testing to assess treatment efficacy or resistance. Some responses also proposed the use of novel methodologies in clinical trial designs and diagnostics.

A number of comments (43) concentrated on epidemiologic research, with several emphasizing the need to focus on pediatric diseases and increase the numbers of children participating in clinical studies. Research on risk factors and exposures during childhood to identify the developmental origins of adult health and disease was highlighted, as was conducting longitudinal studies across the lifespan. Respondents also noted the importance of increasing women and minority participation in clinical research.

Clinical outcomes and health services research were mentioned in 41 responses. There were many suggestions for the Strategic Plan to include a focus on quality of life, palliative care, and end-of-life care outcomes. Ensuring that advances in interventions and medical care are evidence-based was cited as an essential broad principle of clinical research.

While the focus on healthy individuals in the Health Promotion and Disease Prevention Area was supported, many respondents also endorsed the inclusion of population and public health concepts in the Plan. Several comments advocated for a greater focus on health promotion and wellness, not just treatment of disease. Specifically, research on physical activity in early life and adulthood, and lifestyle factors was highlighted as a possible means to facilitate population-based prevention efforts.

Behavioral and Social Science

Numerous comments (71) advised that behavioral and social science be explicitly referenced in the framework. Several of these suggestions were specific to basic, translational, or clinical research, while most comments were broader, such as the need to “recognize the impact of social, environmental, behavioral and economic conditions on disease causation and treatment”. Along with psychosocial and cultural factors, these elements fit under the umbrella concept of social determinants of health, which was cited as an important research need. These elements also were noted for their relevance to understanding and addressing health disparities. Additional comments supported the study of healthy behaviors and behavioral interventions.

Disease-Specific

Suggestions for increased emphasis on specific diseases or types of conditions were present in about one-third of the RFI responses (151). For example, some respondents cited the urgent need for new treatments in pediatric and other cancers. Other responses recommended greater support for research on mental illness in order to advance treatments with greater efficacy and fewer side effects. Wound healing, myalgic encephalomyelitis/chronic fatigue syndrome, and obesity, as well as chronic and rare diseases also were considered to be in need of more attention.

Additional Cross-Cutting Themes

The importance of interdisciplinary research was a common theme in the RFI (91 responses). A main aspect of these comments was to foster a collaborative environment among NIH ICOs to reduce barriers in cross-cutting areas of research. This type of collaboration was deemed necessary to advance research on diseases that fall within the missions of multiple ICOs, as well as to address diseases that are not assigned to an ICO. Other comments focused on promoting the development of interdisciplinary research teams, systems science, and research integration, which would leverage expertise from a range of scientific areas. In particular, physician scientists were noted as valuable members of interdisciplinary groups. Team-based approaches are needed to address comorbid diseases and identify mechanisms and

potential treatments applicable to multiple diseases. As one respondent noted, “AIDS research continues to lead to discoveries relevant to other infectious, malignant, neurologic, autoimmune, and metabolic diseases, as well as to the complex issues of aging and dementia.”

Promotion of big data and data science was emphasized in 50 responses. A common recommendation was to improve data sharing through the use of databases and registries, enabling more efficient research and faster discovery. Another suggestion was to enhance the use and development of computational analytics for large data sets, particularly when dealing with genomics and bioinformatics data. Respondents noted that improving data management and harmonization processes and encouraging use of electronic health records would lead to more effective decision support systems for the clinic. Comments related to big data largely overlapped with ideas about technologies and research methods, which were mentioned in 70 responses. Unique suggestions for technology and methods included enhancing the use of mobile applications and devices, or telemedicine, in order to remotely monitor patient outcomes. Leveraging social networks to accelerate dissemination of new therapies and behavior change was encouraged.

A number of other cross-cutting research topics were frequent among the RFI responses. Increased attention to health disparities was requested in 59 comments. Disparities can be influenced by a number of factors “including gender, race, ethnic, sexual orientation and socioeconomic imbalances”, and engaging communities is an important step to addressing these unequal burdens on health. Several respondents suggested that more attention be paid to the impacts of the environment and climate change on health (41 responses). The majority of comments related to animal and organismal models in research (48 responses) advocated for a decrease in the use of animals. Fewer numbers of comments were received on resources and infrastructure (33 responses), clinical practice or drug approval (25 responses), and health policy research (14 responses).

Suggestions and Comments Related to the Unifying Principles

Several responses in the RFI made declarative statements supporting the Unifying Principles and the sub-sections. In the Setting Priorities section, respondents applauded the focus on rare diseases, stating that “discoveries in areas of rare disease research are often beneficial to other areas of research, and contribute to a greater overall understanding of the human body.” Under the Enhancing Stewardship section, respondents generally were enthusiastic that the workforce pipeline and partnerships were included as priorities. For example, one respondent noted that “it is terribly important that the strategic plan shine a bright light on the need to attract new talent to this endeavor”.

Partnerships

In addition to supportive statements, respondents provided suggestions for details to be included in the Unifying Principles. One-fifth of the responses in the RFI (94) spoke to the necessity of partnerships and their benefits. Many comments noted that the “voice of the patient” was missing and needed to be represented by incorporating their experiences into research designs. Patient engagement serves to identify unmet medical needs and to facilitate the adoption of the most effective treatments in the real-world setting. Partnering with communities and the wider public aids the collection of data and allows for open science, which improves the impact of research and fosters “a stronger culture of sharing”. Partnerships with other federal agencies, biotechnology and pharmaceutical industries, and non-profit organizations also were encouraged in order to maximize resources and catalyze new discoveries.

Funding Mechanisms and Peer Review

Concerns or suggestions related to funding mechanisms were present in 84 responses. One-third of these (28) focused on the balance of investigator-initiated mechanisms versus targeted research approaches. Another third of these responses (30) concerned the need for early career and trainee funding support. In order to foster interdisciplinary research, respondents suggested that NIH create new funding mechanisms to promote collaborative research that crosses ICO boundaries. Furthermore, a number of responses (46) expressed concerns about the NIH peer review system. More specifically, the comments were related to the expertise of reviewers on study sections, the criteria upon which grant applications are judged, the length of the process, and transparency in funding decisions.

Workforce

Most of the comments about the biomedical workforce (72) were concerned with recruiting and retaining a new generation of researchers, as well as training at all career stages. Broadened training opportunities in interdisciplinary research, informatics, and technology were proposed, in addition to training for a variety of career paths. Some comments focused particularly on recruiting physician scientists. A number of respondents encouraged an increased emphasis on workforce diversity, citing that the workforce should be representative and encompass a broad range of perspectives.

Additional Topics

Suggestions related to disease burden and rigor and reproducibility were present in a modest number of responses. Of the comments regarding the use of disease burden in setting funding priorities (39 responses), many recommended that the definition of burden be expanded to include the impact of disease on the family and caregivers, quality of life, survival rates, severity of symptoms, and health care costs. A variety of suggestions for improving scientific rigor and reproducibility were given (36 responses), which included using more relevant disease models, using only well-characterized and validated techniques, and more thorough reporting of methods. Further, respondents encouraged strategies for data sharing among researchers to enhance openness and facilitate rigorous, reproducible results.

Additionally, there were several recommendations for fostering innovation (30 responses), such as encouraging the prioritization of high-risk, high-reward projects. Smaller numbers of comments suggested ways to reduce administrative burden (17 responses). Communication of scientific findings and health information with the general public in order to enhance education and health literacy was a priority in 43 responses. Finally, some respondents (21) commented on how the priorities in the Strategic Plan will be executed or how the Plan's performance will be evaluated.

Summary and Conclusions

The RFI responses provided numerous suggestions and commentary on the biomedical research enterprise for NIH to consider in the development of the NIH-wide Strategic Plan. The respondents represent a wide array of stakeholders from the general public and the scientific community, including large numbers of patient advocacy groups and professional associations. Many respondents endorsed the framework and the sub-bullets within each section and confirmed that the framework is aligned with the NIH mission. Feedback generally appeared to be driven towards optimizing the NIH research portfolio and its operations, with the ultimate goal of advancing human health and improving health outcomes.

Respondents were encouraged that basic science was a key priority within the Areas of Opportunity, as it was cited frequently for its importance as the foundation for medical progress. The application of science in regards to preventing and treating disease also was strongly supported in the RFI responses. However, an explicit mention of translational research in the framework was recommended, particularly with regard to dissemination and implementation science. In addition, respondents advocated for the inclusion of behavioral and social sciences, noting the importance of social determinants of health and disease.

Specific research topics and approaches to leverage emerging opportunities and enhance the impact of science were suggested for inclusion in the Strategic Plan. One-third of the RFI responses advocated for research on specific diseases, of which cancer was the most prominent. However, many respondents acknowledged that patients commonly have comorbidities and therefore, encouraged an emphasis on patient-centered approaches that account for multiple symptoms and conditions. On a related note, respondents urged NIH to develop new methods to foster interdisciplinary research and team science in order to facilitate the breakdown of disease boundaries. Mechanisms that allow for collaborations across ICOs were a common suggestion to better integrate various disciplines. In addition, respondents encouraged NIH to leverage new technologies and advances in data science to accelerate data collection, analysis, and sharing. Finally, health disparities were cited as an important topic needing greater emphasis in the Strategic Plan.

In addition to focusing on scientific areas of opportunity, RFI respondents offered comments and suggestions on the Unifying Principles sections of the framework, which describe the priorities for NIH operations and funding decisions. In particular, respondents supported the emphasis on partnerships and recommended increased collaboration with patients and communities, as well as industry and other federal agencies. The comments noted the many benefits of these types of partnerships, which include improving research design and data collection, leveraging resources, and increasing impact. Finally, many respondents expressed concerns about the future of the biomedical research workforce. Respondents suggested that NIH support broader training opportunities and improve recruitment of diverse researchers. In order to improve workforce retention, an increased focus on trainee and early career funding mechanisms was encouraged.

NIH appreciates the feedback received through this RFI and will consider the comments and suggestions in developing the NIH-wide Strategic Plan.

Acknowledgements

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Appendix

Figure A1. Framework

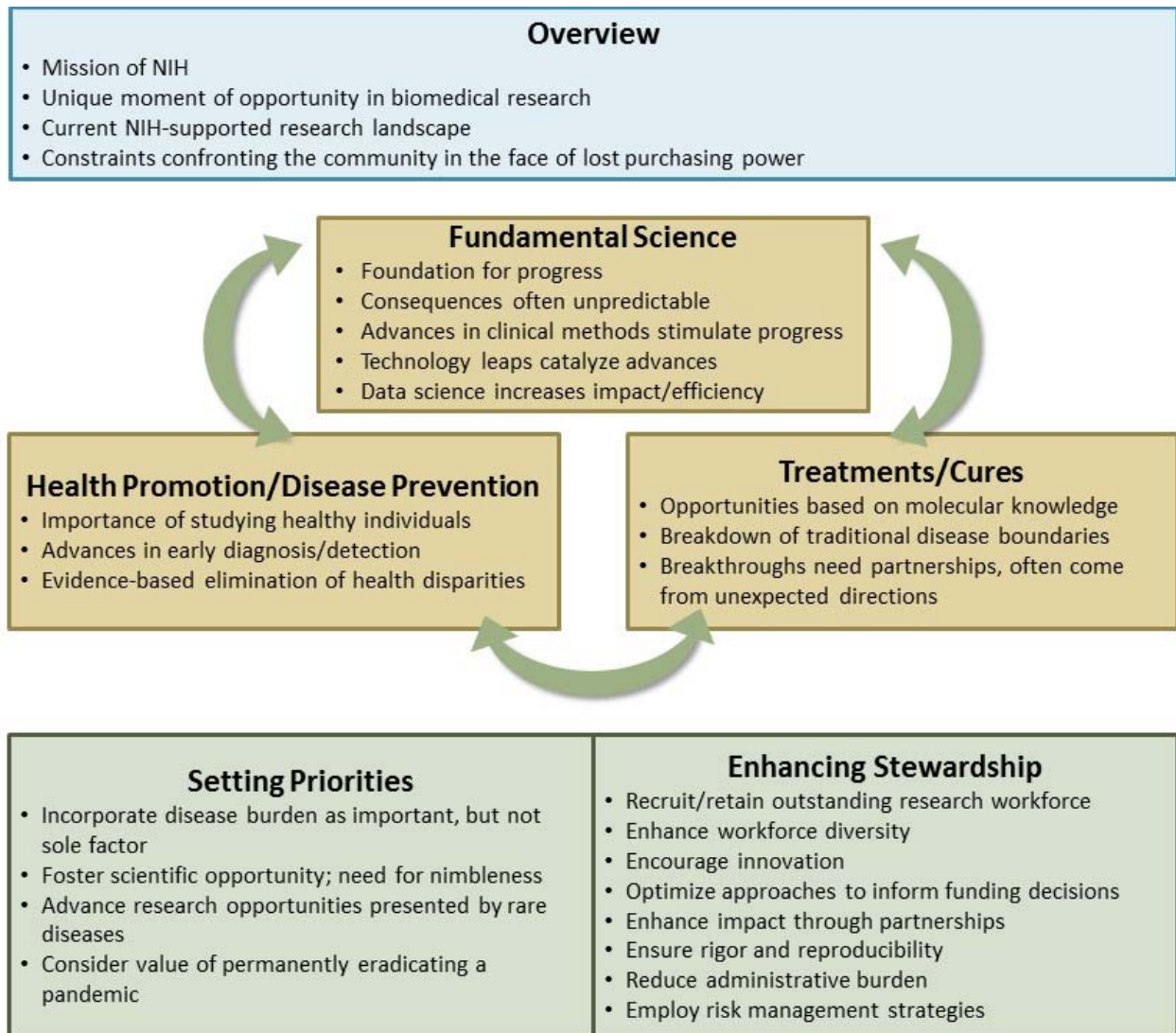


Table A1. Coding table and selected comments

The comments in the table below are taken directly from the RFI responses. Removed text is denoted by ellipses.

Primary Category	Code	Subcode	Selected Comment(s)
Feedback on the Whole Framework	General Comments	A1. Supportive Statement	supports the initial framework and approach from NIH. The benefits of the proposal are a clear delineation of overarching themes, underpinning the strong societal value of a leading national medical research program
			encouraged that the framework emphasizes the interrelated aspects of fundamental science, health promotion/disease prevention, and treatments/cures.
		A2. Conceptual Concern or Criticism	appears to largely continue the status quo in which almost all aspects of scientific inquiry are important
Compatibility with NIH Mission	Compatibility with NIH Mission	B1. Yes	The proposed framework provides the mechanism for achieving the mission and implementing the goals, and is thus in harmony with the broad mission
		B2. No	proposal appears inconsistent with NIH mission statement, focused solely on basic research, and not on the application of knowledge to enhance health
The 3 Areas of Opportunity that Apply Across Biomedicine: Suggestions and Comments	General Comments	C1. Supportive Statement	pleased to see that promoting fundamental science is first and foremost under areas of opportunities. As outside pressure is often focused on curing or treating a specific disease or condition, it is important for the NIH to clearly state this and explain that basic science is the basis for progress.
			Benefits include a scientific and data-based infrastructure, the inclusion of health promotion, disease prevention and healthy individuals
			in all medical disorders more broadly a "Breakdown of traditional disease boundaries" is essential.
	Basic Science	C2. Conceptual Concern or Criticism	I have difficulty with the term biomedicine which is defined as "a conceptual model of illness that excludes psychological and social factors and includes only biologic factors in an attempt to understand a person's medical illness or disorder."
			D1. Cancer
		D2. Immunology	Commit to understanding the basic biology of complex transmissible diseases, prepare by developing the vaccines and treatments, and be organized to allow for nimble reactions to new infectious threats.

		D3. Diabetes, Obesity, Metabolic, and Endocrine	Knowledge of the genetic factors of type 1 and type 2 diabetes, the complications of diabetes, and obesity at the most fundamental level may lead to discoveries producing improved disease prediction, prevention, treatment, and cures
		D4. Neuroscience	The study of plasticity of tissues, including nerve regeneration and brain remapping following spinal cord or brain injury, should be added to the areas of opportunity in the strategic plan.
		D5. Development	Mitochondria are central to apoptosis, responding to protein signals in the cell, releasing apoptotic proteins, and triggering the death of the cell. Apoptosis research may lead to new discoveries about cancer, embryonic development, and tissue atrophy.
			While a small fraction of the total burden of chronic disease can be attributed to a single gene, or a single environmental agent, or a single nutritional deficiency, the vast majority of human disease is attributable to a complicated interplay of all three.
		D7. Other Basic	We also encourage NIH to ensure that the strategic plan focuses appropriate attention on genomics research given the importance of this field to future gains in health and medicine
		I would recommend a focus in . . . the role played by intrinsically disordered proteins on human health. The extensive role of disordered regions in biological systems and their presence throughout proteomes has become apparent	
	Translational	E1. Applying Discoveries from Preclinical Studies to Human Studies	include a focus on putting significant resources into development of predictive human biology-based in vitro and computational methods . . . and organ-on-a-chip tests that more accurately predict human outcome and reduce clinical adverse events.
		E2. Enhancing the Adoption and Implementation of Best Practices	framework does not directly address NIH involvement in Implementation research. Today, there is an urgent need for smart and accelerated “implementation science” agendas across disease areas that lay out strategic plans for maximizing the impact of multiple new prevention and treatment interventions.
		E3. Other Translational	traditional translational model of the scientist and clinician partnerships needs to be augmented by new disciplines and interdisciplinary groups

	Clinical	F1. Human Subjects Research on Disease Mechanisms and Treatments	goals should be to increase the number of treatments, preventative measures, and cures for human diseases and decrease the number of diseases for which there are no diagnostic tests or biomarkers
			Much greater priority should be given to investigation of multisystem, multi-symptom diseases and syndromes. These present special opportunity for elucidation of, not just the specific subject conditions, but other diseases as well as the human ecosystem at large.
		F2. Epidemiology	we would urge that the strategic plan include a dedicated focus on pediatric priorities and issues to ensure the needs of children are given appropriate attention.
			Building on the importance of studying healthy individuals, NIH should support studying healthy groups and populations as entities to address broader health questions
		F3. Outcomes and Health Services Research	addressing the basic needs of patients with chronic diseases which limit mobility and access to health care, recreation, and a better quality of life is needed in the plan
	F6. Other Clinical	The second “area of opportunity” should be highlighted to promote the shift in focus at NIH to effectiveness of health care and evidence-based assessment of clinical care. Prevention, rather than disease management, should be a top priority.	
		there is insufficient attention to the evidence base for early physical activity in younger children (Pre-K -5th) in terms of impacts on risk for chronic disease development and behavioral issues	
	Behavioral and Social Science	G1. Behavioral and Social Science	include basic science of physical, social, economic environments since we know these can alter molecular risk for disease and affect disease progression and healing
			behavioral and social science research is cross-cutting and should be more explicitly stated throughout the plan.
Research on interventions that can either impact these social determinants at a population level, or moderate the impact of the social determinants on health outcomes is urgently needed.			

	Additional Cross-Cutting Themes	H1. Interdisciplinary Science	<p>Leveraging the expertise of multiple institutions and fostering a collaborative environment means that federal dollars will be more effective in bringing solutions to fruition.</p> <p>NIH should also increase its attention on interdisciplinary fields and activities that can most quickly capitalize on new findings, pathways, and understanding. In particular, innovations enabled with cross-cutting teams of researchers with a range of expertise and training, from traditional biological fields to applied engineering and development, can help speed innovation to the benefit of society.</p>
		J1. Big Data	<p>consider opportunities to ensure that data and information from supported studies and registries continue to be made available so that researchers can build off of these important efforts to further advance science as opportunities continue to emerge</p> <p>We have a new, pressing, growing and unmet national health need: the compilation, organization, homogenization and stewardship of the genetic sequencing data that is currently being obtained for research and clinical purposes.</p>
			J2. Health Policy
		J3. Environment	<p>another consideration would be to study the role of environment and manipulating environment to promote health and healthy behaviors.</p>
		J4. Animal Models and Other Organisms	<p>more emphasis should be placed on the development and use of human-relevant, non-animal alternatives</p>
		J5. Health Disparities	<p>Programs that support community-based, participatory research aimed at addressing health disparities must also be strategic priorities for the NIH</p>
		J6. Techniques, Methods, and Technologies	<p>Technologies incorporating telehealth capabilities and remote monitoring help patients remain proactive in their health management without burdening providers</p>
		J7. Resources and Infrastructure	<p>support the acquisition of research infrastructure, particularly shared core research technologies that are conducive to being used by multiple institutions and that are often cost prohibitive for a single entity to acquire.</p>
		J8. Clinical Practice and Drug Approval	<p>The clinical community needs protocols to allow for the administration of medications to which patients have previously had reactions.</p>

		J9. Other	NIH should incorporate its plans for the Precision Medicine Initiative into both this framework and the strategic plan. Given the Administrative and Congressional focus on and support for this initiative, NIH should address its plans for recruiting the one million American national research cohort and other activities that may occur over the next five years.
	Disease-specific	K1. Mental Illness	We need more research and options for newer, better, more effective medications with less severe side effects for the treatment of severe mental illness
		K2. ME/CFS/SEID	The Plan does not, at this time, adequately consider those diseases like ME/CFS which are multisystem and lack Institute affiliation
		K3. Cancer	there are many types of childhood cancer that do not even have basic understanding of the disease and the majority of childhood cancers continue to be treated with regimens that were developed in the 1950s, 60s and 70s. It's time that our nation's children with cancer and our world's cancer children be given the priority within the NIH strategic planning!
		K4. Wound Healing	knowledge of the pathophysiology, as well as molecular biology, of wounds and wound healing is still inadequate. Programs supporting research into the basic science of wounds needs to be supported, as do programs that promote development of new technologies
		K5. Other	There are over 7,000 rare diseases affecting more than 30 million Americans, and 95% of these diseases lack an FDA approved treatment. . . . we encourage this planning committee to include specific rare disease references in more of the Areas of Opportunity.
it is becoming increasingly possible to understand the factors that increase or decrease the risk of developing chronic disease, and therefore to prevent these diseases, or to ameliorate their effects in people who already have them.			

Unifying Principles: Suggestions and Comments	General Comments	L1. Supportive Statement	champions efforts to enhance stewardship, particularly in recruiting and retaining an outstanding workforce and encouraging innovation and new partnerships . . . It is also critical to continue to reduce administrative roadblocks and burden
		L2. Conceptual Concern or Criticism	Under Setting Priorities, we are not sure one could permanently eradicate a pandemic (an inspirational goal for sure); but rather continue to consider ways to limit the occurrence of a pandemic might be more realistic

	Disease Burden	M1. Disease Burden	we recommend expansion of the concept of “measures of disease burden” to include “assessment of patient-centered outcomes” to denote those outcomes that are deemed by patients that are important including disease response, survival, toxicity of treatment, functional status, and quality of life impact.
	Funding mechanisms	N1. Investigator-initiated and Targeted Mechanisms	Strengthen the support of investigator-initiated research, the proven way to explore the novel ideas that lead to the unpredictable fundamental discoveries
		N2. Early career and Trainee Funding	maintain a continuous stream of new investigators by facilitating the efforts of junior investigators in obtaining initial funding.
		N3. Other	It would be advantageous to generate new, discrete funding and review procedures for initiatives that cross the silos created by traditional institute boundaries. This has great potential to generate novel ideas to address complex biological problems
	Peer review	P1. Study Section	Scientific funding would be better spent by basic grassroots changes such as (1) improving the quality of scientists on review panels (use smart senior, even retired scientists more).
		P2. Review Criteria	Maintain and strengthen the integrity of the NIH peer review process to ensure that the most meritorious grants are funded without inappropriate external influences
		P3. Process	Steps should be taken to streamline the process of applying for and receiving NIH funding. More abbreviated timelines between application submissions and decisions would help applicants remain competitive in their respective fields.
	Workforce	R1. Recruiting and Training	the plan should emphasize and resource the effort to recruit high-quality new investigators and to incentivize high-performing investigators to stay in the field. Among the many ways to do so, we believe, will be to ensure that the NIH . . . provides adequate training and mentoring support.
			America’s future health and economic growth will depend on researchers who are well-trained to advance science and contribute to society in an array of diverse careers.
		R2. Diversity	ensure a first-rate, relevant, sustainable and diverse workforce into the future. With major demographic shifts upon us, the diversity component is absolutely integral in ensuring needed outreach and a steady, representative pipeline to move the next generation into biomedical research.

	Innovation	S1. Innovation	Innovative research: Establish flexible funding to support high-risk, high-reward science. This type of funding would provide margins for risk in a climate where conservative, incremental science seems to have a higher probability of funding given NIH budgetary constraints
	Partnerships	T1. Patients	Patients and caregivers have valuable information that can inform research design and priority setting. . . . Patients can contribute to hypothesis generation, selection of outcomes measures, and identification of treatment targets. NIH must come to terms with the role patients can play in biomedical research. Incorporating these views in a systematic way would strengthen NIH and its research, regardless of the disease or Institute involved.
		T2. Community and Public Engagement	maximizing community engagement in research through big data and other efforts to harvest information to advance biomedical research.
		T3. Federal Agencies	will require NIH to maintain a close awareness of how it overlaps with the missions of many federal health and science agencies. If this interdependence is embraced and multiple agencies engage together on the bigger picture, this could be an incredibly powerful catalyst for interdisciplinary discovery.
		T4. Industry	NIH should consider enhancing the support of collaboration between academic centers and industry to bring advances in diagnostic and treatment technologies to clinical practice.
		T5. Other	While improving chronic disease care will take time and require effective partnerships between health plans, drug manufacturers, providers, and patients, these investments will both improve outcomes and lower overall costs associated with chronic conditions
	Rigor and Reproducibility	U1. Methods and Reporting	enhancing the reproducibility of research findings, enhancing the predictivity of animal and in vitro models, . . . enhancing open data availability and data sharing, promoting rigorous controls in antibody-based methods
		U2. Data Sharing	Research on biomedical science knowledge sharing and uptake, including open science and electronic lab notebooks, and reproducibility of NIH-funded research should be a trans-NIH theme
	Administrative Burden	V1. Administrative Burden	In the interest of reducing administrative burden associated with research regulations, . . . encourages the NIH whenever possible to engage in efforts at harmonization and retrospective review of regulations to determine if they are leading to the desired outcome.

	Other	W1. Other	NIH has long recognized the central importance of human subjects protections, the ethical conduct of science, and scientific integrity in its stewardship of the research enterprise. . . we urge the NIH to carefully consider elevating ethics to a unifying element within its framework.
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Execution	Implementation or Evaluation of the Plan	X1. Implementation or Evaluation of the Plan	A “strategic plan” on the other hand is meant to be clear and concise. It sets goals, mobilizes resources (funding, manpower, etc.) to execute actions, and establishes performance measurements to gauge success.
	Communication with the Public	X2. Communication with the Public	Ensure that within the Plan’s Health Promotion/Disease Prevention area there is a strong focus on information dissemination to the public, promoting adequate health literacy and engagement with all stakeholders (including patients, researchers, healthcare providers). . . . Research is most valuable when it is accessible and easily understood and can be applied to inform future research and effective health decisions.

Request for Information (RFI): Inviting Comments and Suggestions on a Framework for the NIH-wide Strategic Plan

Notice Number:
NOT-OD-15-118

Key Dates

Release Date: July 22, 2015

Related Announcements

None

Issued by

National Institutes of Health ([NIH](#))

Purpose

This Notice is a time-sensitive Request for Information (RFI) inviting comments and suggestions on the framework for the NIH-wide Strategic Plan.

NOTE: It is important to read this entire RFI notice to ensure an adequate response is prepared and to have a full understanding of how your response will be utilized.

Background

In response to a request from the Congress, NIH is developing a 5-year NIH-wide Strategic Plan to advance its mission to support research in pursuit of fundamental knowledge about the nature and behavior of living systems, and the application of that knowledge to extend healthy life and reduce illness and disability. Senior leadership and staff from all 27 Institutes, Centers, and Offices (ICOs) are contributing to the proposed direction and content of the Strategic Plan, with input from the Advisory Committee to the Director, NIH. The framework below identifies crosscutting areas of research exemplifying the breadth of ICOs' priorities and aims to outline a set of unifying principles to guide NIH in pursuit of its mission. The goal of this larger NIH-wide strategic plan is not to outline the myriad of important research opportunities for specific disease applications (as that is covered in the strategic plans from each of the ICOs, which will be referenced appropriately), but to highlight major trans-NIH themes. The Strategic Plan is due to the Congress in late December 2015.

NIH-wide Strategic Plan Framework

Overview

This section will include a discussion on subjects such as the NIH mission, the status of and opportunities in biomedical research, the current NIH-supported research landscape (i.e., basic and applied research, extramural and intramural research, ICOs with their own strategic plans, Common Fund, challenges), and constraints confronting the community in the face of lost purchasing power

Areas of Opportunity that Apply Across Biomedicine

Promote Fundamental Science

- Basic science is the foundation for progress
- Consequences of basic science discoveries are often unpredictable
- Advances in clinical research methodologies stimulate scientific progress
- Leaps in technology often catalyze major scientific advances
- Data science increases the impact and efficiency of research

Improve Health Promotion and Disease Prevention

- Importance of studying healthy individuals
- Advances in early diagnosis/detection
- Evidence-based interventions to eliminate health disparities

Advance Treatments and Cures

- Unprecedented opportunities on the basis of molecular knowledge
- Breakdown of traditional disease boundaries
- Breakthroughs need partnerships and often come from unexpected directions

Unifying Principles

Set NIH Priorities – NIH sets priorities by incorporating measures of disease burden, understanding the need to foster scientific opportunity through nimble and adaptable methods, supporting opportunities presented by rare disease research, and considering the value of permanently eradicating a pandemic.

Enhance Stewardship – NIH enhances stewardship of the research enterprise by recruiting and retaining an outstanding biomedical research workforce, enhancing workforce diversity, encouraging innovation, optimizing approaches to guide how decisions are made, enhancing partnerships, promoting scientific rigor and reproducibility, reducing administrative burden, and employing risk management strategies in decision-making.

Information Requested

This RFI seeks input from stakeholders throughout the scientific research community and the general public regarding the above proposed framework for the NIH-wide Strategic Plan.

The NIH seeks comments on any or all of, but not limited to, the following topics:

- Potential benefits, drawbacks/challenges, and areas of consideration for the current framework
- Compatibility of the framework with the broad scope of the NIH mission
- Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan
- Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine
- Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan
- Future opportunities or emerging research needs

How to Submit a Response

All comments must be submitted electronically on the [submission website](http://grants.nih.gov/grants/rfi/rfi.cfm?ID=46) (<http://grants.nih.gov/grants/rfi/rfi.cfm?ID=46>).

Responses (no longer than 300 words in MS Word or pdf format) must be received by 11:59:59 pm (EST) on August 16, 2015. You will see an electronic confirmation acknowledging receipt of your response.

Responses to this RFI are voluntary. **Do not include any proprietary, classified, confidential, trade secret, or sensitive information in your response.** The responses will be reviewed by NIH staff, and individual feedback will not be provided to any responder. The Government will use the information submitted in response to this RFI at its discretion. The Government reserves the right to use any submitted information on public NIH websites, in reports, in summaries of the state of the science, in any possible resultant solicitation(s), grant(s), or cooperative agreement(s), or in the development of future funding opportunity announcements.

This RFI is for information and planning purposes only and shall not be construed as a solicitation, grant, or cooperative agreement, or as an obligation on the part of the Federal Government, the NIH, or individual NIH Institutes and Centers to provide support for any ideas identified in response to it. The Government will not pay for the preparation of any information submitted or for the Government's use of such information. No basis for claims against the U.S. Government shall arise as a result of a response to this request for information or from the Government's use of such information.

We look forward to your input and hope that you will share this RFI document with your colleagues.

Inquiries

Please direct all inquiries to:

Email: nihstrategicplan@od.nih.gov

RFI Responses¹

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The recent ability to identify, isolate, and/or engineer well defined cell populations to treat malignant, congenital, degenerative and other disorders represents an unparalleled opportunity to cure currently incurable diseases and to cure others with less toxicity than is possible with currently available therapies. Yet, the challenges imposed by extensive manufacturing and regulatory requirements for developing these cellular therapies means that the scientific and clinical development agenda is being driven by largely by pharmaceutical companies whose concern for profitability may not ensure that the most effective and cost-effective approaches are pursued. Support for effective infrastructures for multicenter clinical trials of cellular therapies by academic networks and facilitation of public/private partnerships to support such trials are essential. The NIH can and should provide a leadership role in both of these areas. Clinical networks such as the Blood and Marrow Transplant Clinical Trials Network and the National Clinical Trials Network should be fully supported. The costs of conducting these trials should be adequately assessed and reflected in reimbursement rates. The NIH should be an active partner in facilitating private/public sector collaborations and in negotiating with industry for trials to be run through NIH networks. Additionally, the NIH has a role in fostering inter-institutional cooperation for trials that cross traditional disease categories. Lack of inter-Institute collaboration leads to lost opportunities for rapid accrual, loss of efficiency in the trial development and implementation process and sometimes constitutes an insurmountable barrier to launching important interdisciplinary clinical studies.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

My comments relate to the lack of emphasis in the NIH framework on the relationships between ecological degradation and public health outcomes around the world (eg- see The Lancet: Whitmee, S. et al. 2015. "Safeguarding Human Health in the Anthropocene Epoch: Report of The Rockefeller

¹ Identifying information has been removed

Foundation—Lancet Commission on Planetary Health,” A Commission by The Lancet, July, 2015: 7-62. <http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2815%2960901-1/fulltext>). By most metrics, human health is better today than at any time in human history. Over the past several decades, life expectancy has soared from 48 in 1955 to 70 in 2012. In 1955 there were 21 million deaths in children under the age of five; by 1997 that number was more than halved to 10 million. These advances have occurred coincident with a vast degradation of nature’s ecological systems, again on a scale never seen in human history, leading to what some have termed the Ecological Paradox. Numerous global assessments from the GEO 4, to the Millennium Ecosystem Assessment, to the IPCC reports have warned that accelerating change to the structure and function of Earth’s natural systems represents a significant threat to global human health. And yet, global health has mainly improved as these changes have accelerated. How is this possible?

Compatibility of the framework with the broad scope of the NIH mission

The explanation is straightforward and sobering: we have been mortgaging the health of future generations in order to realize economic and development gains in the present. By mining nature’s resources at an unsustainable rate, global societies can flourish in the short term, but face significant health impacts from the degradation of nature’s life support systems over the longer term. It’s become undeniable that human activity is rapidly transforming most of Earth’s natural systems. The global health impacts of accelerating climatic disruption, land degradation, growing water scarcity, fisheries degradation, biodiversity loss, and pollution threaten the global health gains of the last several decades and are likely to represent the dominant global health threats of the next century. By altering the composition of the atmosphere, degrading arable lands faster than they can be replenished, overfishing, polluting, changing the chemistry and temperature of our oceans, withdrawing ground water faster than it can be recharged, and dramatically reducing the number and population size of species who co-inhabit the planet with us, we are putting the poor and future generations in harm’s way. It is striking that many assessments of future challenges for global health entirely overlook the potential for significant environmental changes to disrupt and potentially reverse the marked progress that has characterized recent human history. Current environmental trends indeed raise the grave prospect that many of the health gains we have recently experienced have been fueled by a pattern of resource use that is fundamentally unsustainable. It thus appears that these gains are built on shaky foundations, and that an urgent course correction is required, one that recognizes that the health of the environment and the health of humanity are inextricably linked.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

In short, much has been written about the social and economic determinants of health but all too often the need to address these determinants within finite environmental limits has been overlooked. Now is the time to transform the discipline of public health into one that integrates knowledge of the underpinning earth systems with understanding of the determinants of health and develops evidence-based, integrated policy solutions that address environmental sustainability together with human health and development goals. I have attached some illustrative citations relevant to the nascent field of Planetary Health, which I hope can be shared with those developing the NIH Strategic Plan Framework. Sarah Whitmee, Andy Haines, Chris Beyrer, Frederick Boltz, Anthony G Capon, Braulio Ferreira de Souza Dias, Alex Ezeh, Howard Frumkin, Peng Gong, Peter Head, Richard Horton, Georgina M Mace, Robert Marten, Samuel S Myers, Sania Nishtar, Steven A Osofsky, Subhrendu K Pattanayak, Montira J Pongsiri, Cristina Romanelli, Agnes Soucat, Jeanette Vega, Derek Yach. Safeguarding human health in the Anthropocene epoch: report of The Rockefeller Foundation—Lancet Commission on planetary health. The Lancet. 2015. S0140-6736(15)60901-1. <http://www.thelancet.com/journals/lancet/article/PIIS0140->

6736%2815%2960901-1/fulltext Samuel S. Myers, Lynne Gaffikin, Christopher D. Golden, Richard S. Ostfeld, Kent H. Redford, Taylor H. Ricketts, Will R. Turner, and Steven A. Osofsky. Human health impacts of ecosystem alteration. Proceedings of the National Academy of Science (2013). <http://www.pnas.org/content/110/47/18753.full> Patz, JA et al. Unhealthy landscapes: Policy recommendations on land use change and infectious disease emergence. Environ Health Perspect. 2004 Jul;112(10):1092-8. Matthew R Smith, PhD, Gitanjali M Singh, PhD, Prof Dariush Mozaffarian, MD, Dr Samuel S Myers, MD. Effects of decreases of animal pollinators on human nutrition and global health: a modelling analysis. The Lancet. 2015. 10.1016/S0140-6736(15)61085-6

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Samuel S Myers, MD, K Ryan Wessells, PhD, Itai Kloog, PhD, Antonella Zanobetti, PhD, Prof Joel Schwartz, PhD. Effect of increased concentrations of atmospheric carbon dioxide on the global threat of zinc deficiency: a modelling study. The Lancet Global Health. 2015. 10.1016/S2214-109X(15)00093-5 Marlier, Miriam E., DeFries, Ruth S., Kim, Patrick S., Koplitz, Shannon N., Jacob, Daniel J., Mickley, Loretta J., Margono, Belinda A., Myers, Samuel S. Regional air quality impacts of future fire emissions in Sumatra and Kalimantan. Environmental Research Letters. 2015. 10:054010 Ellis, A., Myers, S. S., Ricketts, T. A. Do pollinators contribute to nutritional health?. PLOS One. 2015. 10(1): e114805. doi:10.1371/journal.pone.0114805. Golden, C. D., L. C. H. Fernald, J. S. Brashares, B. J. R. Rasolofoniaina, and C. Kremen. 2011. Benefits of wildlife consumption to child nutrition in a biodiversity hotspot. Proceedings of the National Academy of Sciences, U.S.A. 108:19653-19656. Bausch et al. Public health impacts of ecosystem change in the Brazilian Amazon, Proceedings of the National Academy of Sciences 06/2015; 112(24):7414-9. DOI: 10.1073/pnas.1406495111 Kim, P. S., Jacob, D. J., Mickley, L., Koplitz, S., Marlier, M. E., DeFries, R., Myers, S. S., Chew, B. N., Mao, Y.H. Sensitivity of population smoke exposure to fire locations in Equatorial Asia. Atmospheric Environment. 2015. 102: 11-17. Increasing CO2 Threatens Human Nutrition. Nature (2014) Myers, S. S. and Bernstein, A. The coming health crisis. The Scientist: 2011. 25 (1); 32-37. (2011)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

I am delighted that the NIH are taking this overarching view of the priorities for future research. This review is timely and highly relevant. The post genomic era of medical/biomedical research presents many opportunities for concerted, collaborative investigations, often driven by new technology as well as enabling new technology developments. The goal of course must be to improve the health outcomes of all. I would recommend a focus in analytical methodology, and also in the understanding of the role played by intrinsically disordered proteins on human health. The extensive role of disordered regions in biological systems and their presence throughout proteomes has become apparent only in the last 15 years, after work by Uversky, Dunker, and others. Prior to this, functional characterisation was centred on structured, folded proteins. Methods for probing the role of protein disorder in function are in their infancy, but simply if a single conformation cannot be visualised then application of the existing

structure/function paradigm fails.

Compatibility of the framework with the broad scope of the NIH mission

Both the fundamental concept of functional disorder that is the prime role of IDPs and the alternation of this 'normal' function in many disease states place IDP research as of critical importance. In particular IDPs are strongly implicated in Cancer, neurodegenerative disease, and diabetes. This is an area that the NIH would be advised to consider as able to have fundamental and translatable impact.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

no comment

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Again I highlight the need for analytical science and the investigation of conformationally dynamic systems here, significant challenge areas with the potential to further our understanding of cellular processes and disease. The need to develop new analytical approaches is critical, part of the reason we do not understand IDPs is due to the inadequacies of classical structural biology methods to reveal the disorder function relationship.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

New strategies for drug discovery New methods to understand the behaviours of IDPs in cells/disease

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The exponential amount of data generated by the " OMIC" researches, and the phenomenal evolution within the Bio-medical informatics has forged an emerging frontier in healthcare called Population Health. The data generated should be harnessed, stored safely to provide a knowledge base and retrieved as needed in a timely manner to make inferences about diseases and management. The current architectural designs of the infrastructure used by most of the large and small health organizations do not meet the sophistication needed to enable " interoperability and transparency " at intra-organizational and inter- organizational levels due to semantic encoding differences. This is due stringent standards guidelines not being set up.

Compatibility of the framework with the broad scope of the NIH mission

To enhance the concept of interoperability and transparency, the current infrastructure has to be updated with new architectural designs with specified standards to facilitate semantic encoding which will enable timely exchange of data within and between health organizations in a safe and regulated environment.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Use digital appliances to provide sensory data transmission from patients to health care providers, data

centers and machines for distance monitoring. Egs Telehealth.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

For education and to improve health care literacy state of the consumers , and empower them to make better informed decisions about their own health care in collaboration with the healthcare providers.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

The study of Geo-spatial distribution of disease within the community in relationship to their social economic status.

Future opportunities or emerging research needs

Pharmo- genomics for drug repurposing. Epi- genetics to study the non -coding part of the RNA.. How the process impacts the phenotypical expression in relation to environment and behavior. Data safety. Data storage and retrieval of large amounts of data. Formulate new semantic encoding methodology to promote interoperability

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

There is a misperception that pediatric cancer has been largely solved and cured. Nothing could be farther from the truth: · Fact: Pediatric cancer is the #1 disease killer of children. · Fact: Only about one third of children diagnosed with cancer go on to lead long, healthy lives after treatment. · Fact: Though our society is witnessing a scientific revolution in cancer treatments, this revolution has not reached children with cancer. · Fact: Of the approximately 900 drugs in the cancer pipeline, only a handful are in clinical trials for children. · Fact: When a company discontinues research of a drug for an adult cancer, there is rarely a chance to continue developing that drug for kids.

Compatibility of the framework with the broad scope of the NIH mission

Childhood cancer is a core mission of the NCI. Areas of research investment that are highly valued by society such as children should be prioritized by the NIH. In addition, areas of research that are overlooked by the private sector should be addressed by the NIH.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

1. Improve the NIH Study Section Program by Establishing that Pediatric Experts Serve At Least on an Ad Hoc Basis When Study Sections Review Pediatric Grant Applications. Pursuant to Congressional report language in the NIH appropriations bills over the past NIH study sections reviewing pediatric cancer grant applications should have at least two pediatric cancer Grant Reviewers who are permanent members, or ad hoc members serving solely to review the pediatric applications. 2. Establish a Pathways to Pediatric Care The FDA, NIH and CDC in concert with outside medical experts, pharmaceutical executives and advocates should identify high priority gaps, places where pediatric medical options lag behind adult options, and create task forces to develop strategies for making pediatric medical care as good as adult medicine. 3. Require Children and Young Teens To Be Included On Adult Trials When Medically Possible Children and young teens are often excluded from trials solely because they are not yet 18. In many cases, there is no medical or scientific justification for this age cut off. A 1998 NIH regulation, "NIH Policy and Guidelines on the Inclusion of Children As Participants In Research Involving

Human Subjects” provides that the NIH promote the inclusion of children and teens on clinical trials. (see <http://grants.nih.gov/grants/guide/notice-files/not98-024.html>). The NIH should enforce this regulation. In addition, a NCI initiative to ensure that all contracts between the NCI and companies providing clinical supply for research include a provision addressing access of the drug by Children’s Oncology Group for a pediatric trial. 4. Fund a Pediatric Cancer Survivorship Program 5. Fund the Children's Oncology Group Match Trial 6. Create Specialized Programs of Research Excellence (SPORE) Grants for Kids

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The proposed Strategic Plan Framework ignores large scale biophysical changes (global environmental changes, including climate change, land system change, freshwater use, and ocean acidification) that are beginning to affect human health and well-being. Understanding and addressing the adverse health consequences associated with global environmental change, and the projected risks under a changing climate, cut across NIH Institutes and Centers. The NIH Strategic Plan Framework is an important opportunity for NIH to promote the basic science to understand the environmental drivers of climate-sensitive health outcomes, promote modeling how climate and development choices could alter future health burdens (including the magnitude and pattern of projected changes), determine the likely effectiveness of adaptation and mitigation options to reduce projected burdens, and estimate the health co-benefits of adaptation and mitigation policies and programs implemented outside the health sector. This increased understanding would provide an evidence base for improving health promotion and disease prevention. Incorporating global environmental change, specifically climate change into the Strategic Plan Framework also would support the President’s Executive Order issued in 2013 on Preparing the United States for the Impacts of Climate Change. The Executive Order acknowledged that climate change is already affecting public health across the Nation, with the impacts often most significant for poor and marginalized communities. Twenty years of national and international scientific assessments provide increasingly robust evidence of impacts, with projections indicating that profound health risks could arise as the climate continues to change. Effective and efficient adaptation can reduce much but not all of those risks. Therefore, the President directed the National Government to undertake efforts to reduce risks through deliberate preparation, including risk-informed decision making tools and preparedness planning. Agencies are tasked with providing information, data, and tools for climate change preparedness and resilience. This is NIH's opportunity to support the President in improving public health.

Compatibility of the framework with the broad scope of the NIH mission

The Strategic Plan Framework focuses on a narrow perspective of the scope of the NIH mission: to

promote the biomedical research enterprise. The health of many Americans are already being affected by the consequences of changing weather patterns, including increases in the frequency, intensity, and duration of extreme weather events, with changes in the magnitude and pattern of climate-sensitive health outcomes. Building on the relatively limited knowledge base about current and projected risks, and the opportunities for proactively and efficiently managing those risks, would generate the insights needed to protect the health of all Americans from most of the impacts of climate change. Doing so would engage across NIH Institutes and Centers, providing a unifying theme to help integrate data and research into a richer and more nuanced understanding of how to increase health resilience to climate change.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Please see previous comments on global environmental change as a key emerging research need; the importance of understanding the health risks of these changes will only increase over the coming decades. Failing to address these issues now will mean public health and health care will not have the knowledge, data, and tools necessary to manage the challenges as they are needed.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The "Unique moment of opportunity in biomedical research" that the framework refers to has a range of flavors, many of which revolve around the digital transformation that our society is currently undergoing, and research with it. While the framework specifically refers to "[u]nprecedented opportunities on the basis of molecular knowledge", the digital transformation is affecting all of the Areas of Opportunity, along with every major aspect of how research is being planned, performed, disseminated, administered, evaluated, funded and reused. This should be reflected in the Strategic Plan, both in that elements of the plan cover strategies to manage those changes, and in that elements of the strategy remain valid despite the changes. One way to approach this would be an emphasis on sharing more of the research process rather than just the outcomes (be they narratives, data, code, materials or other resources), and engaging the relevant communities - intra- and extramural researchers as well as patients, physicians, citizen scientists or the wider public - much earlier than is typical today, so as to pave the way for breakthroughs to actually "come from unexpected directions", as stipulated under "Advance Treatments and Cures". Potentially, this might even mean to involve these communities already during the planning stage of research projects, in the drafting of proposals, or in the process of funding decisions. Such an emphasis on open science would further help to "[e]nsure rigor and reproducibility", an important topic that is currently buried as the 6th bullet point in the 6th and last part ("Enhancing Stewardship") of the framework — I think it should have a higher visibility,

perhaps as part of the "Fundamental Science" part.

Compatibility of the framework with the broad scope of the NIH mission

The digital transformation affects key components of the NIH mission, providing new opportunities "to foster fundamental creative discoveries, innovative research strategies, and their applications as a basis for ultimately protecting and improving health" and "to exemplify and promote the highest level of scientific integrity, public accountability, and social responsibility in the conduct of science" as well as for "conducting and supporting research [...] in directing programs for the collection, dissemination, and exchange of information in medicine and health, including the development and support of medical libraries and the training of medical librarians and other health information specialists." An emphasis on openness throughout the research cycle, as outlined above, would certainly help advance NIH in these directions.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

The report on the strategic vision for the National Library of Medicine recommends that NLM should * "be a leader and innovator in open science efforts worldwide" * "lead efforts to support and catalyze open science, data sharing, and research reproducibility, striving to promote the concept that biomedical information and its transparent analysis are public" * and, in particular, "lead efforts to promulgate and implement best practices in open source, open science, standards, and data harmonization, forming partnerships across communities, stakeholder organizations, agencies, and countries" as well as "be an active participant in the design and oversight of programs that incentivize and celebrate the open sharing of data and resources." While I fully support these recommendations, I think it makes sense to expand the idea of leadership in open science beyond NLM and across all of NIH.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

What I am missing here is an item on open science under "Promote Fundamental Science" (perhaps "Open science increases the impact and efficiency of research", i.e. analogous to its data science item) as well as the notions of sustainable infrastructure and of crowdsourcing beyond current standards. The latter two points do not neatly fit into any of the three main Areas of Opportunity, as they extend across all of them. Infrastructure is necessary for progress in any of the areas listed, but sustainability is an issue here, especially in light of a continuously evolving and increasingly international and networked research landscape. As for crowdsourcing, many research databases are curated by a community rather than individuals or labs, and via citizen science, the public gets more and more involved in how research is being conducted. In addition to that, patient-led innovation can complement innovation led by researchers, physicians, companies or others, and the optimal parameters for that interplay have yet to be explored. The recent BD2K RFA on Crowdsourcing and Interactive Digital Media is an important step along these lines, and the Precision Medicine Initiative lends particular weight to such approaches.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

I do not see any components of the proposed framework that would not be applicable to an NIH-wide Strategic Plan.

Future opportunities or emerging research needs

One aspect of the digital transformation that I haven't yet touched upon in my response is that of new pathways to discovery, which may involve data management plans, social media, robot scientists or

many other components that have not traditionally been part of the research process. Finding ways to experiment with such pathways will likely be beneficial for navigating NIH through those next five years. On a practical note, I would welcome it if such RFIs would provide an option to make submissions public, so that everyone interested could share in their thoughts and engage with them more directly than will be possible through the upcoming report that will summarize the submissions. Mine is available via <https://github.com/. . . /datascience/blob/master/nih-strategic-plan.md> .

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The . . . funds childhood cancer research, to cure all pediatric cancers and improve the quality of life for patients and survivors. Due to the smaller (as compared to adults) patient population, significant progress has been limited to a handful of more than 100 diseases. Success in one disease (ALL) has skewed results and have been permitted to misrepresent the true status of research into most pediatric cancers. Cancers in adults are not grouped together as "adult cancers" so results for a single specific diseases such as breast or prostate cancer do not skew results for all adult patients. Each disease is a special area of focus. By the age of 45, 90% of survivors will live with a life-long, late effect, 2/3 of them, life-threatening. This creates a tremendous burden on the health care system and other institutes/centers/ICOs. Historically, the childhood cancer community was fragmented, and while some independent operators remain, the community is increasingly coalescing behind a roundtable process and a prioritized list of needs (developed in 2014 and 2015) which represents the principal concerns of patient advocates. A similar effort has been initiated in the physician-scientist realm. For the first time, we have the opportunity to align the entire research, healthcare and patient universe in a strategic, focused and needs-based strategic plan to make real progress. With the vastly improved collaboration and the greater mass communication resources in the community, we are poised to be a true partner to the NIH/NCI for perhaps the first time.

Compatibility of the framework with the broad scope of the NIH mission

In 14 years of visits to Capitol Hill I have encountered confusion as to the true mission of the NIH/NCI. Some believe the NIH role is basic science exclusively, some say translational science and others a combination of these and more. The true role must be clarified. We recognize research progress in the future will be less derived from where in the body cancer occurs, than what genetic markers were triggered and which common pathways exist with seemingly unrelated cancers. Most of the public is incredulous that approximately 4% of the NCI budget is invested in pediatric research annually. We understand this number is misleading as it does not mean a full 96% is invested in adult research, programs and infrastructure to support both patient populations is significant. A full 60% of research funding for adult cancers is provided by the pharmaceutical industry, with less than 1% of pediatric funding coming from this source. My own organization, . . . , and yet we are 1/10th the size of any of the large national cancer organizations which focus primarily on adult research. I will not advocate to do less for adult patients, but trends in research, advanced technologies and this strategic planning process indisputably present a historic opportunity to advance initiatives that all patients to benefit, and to design studies where pediatric specialists are involved from the concept stage and where children's needs are considered and prioritized equally when NIH/NCI begin a new endeavor.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Children with cancer who are fortunate to survive, face a life time of late effects including but not limited to dental disorders, cognitive impairment, sensory loss, stunted growth, infertility, heart disease,

secondary and tertiary cancers and more. Each Institute of Health should desire reduced toxicity for medical treatments for young developing bodies, and all efforts should be made to allow children with cancer to benefit from work being done across the institutes. The reality today is families perceive, correctly or not, but perception is reality to them), that children are a low priority at the NCI. Many believe the NCI would prefer children with cancer have their needs addressed by rare disease branches, while the rare disease community believes the NCI should be responsible for children with cancer. The net-effect is fighting the #1 disease killer of our children, our future, appears to be a hot potato. It is doubtful pediatricians would be asked to represent adult patient concerns and research needs, yet adult oncologists frequently presume to understand children's unique needs, and many believe that the NCI is slow to recognize these unique needs, or does so in corrective fashion after decisions have been made to benefit adults which adversely impact children.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

NIH funds projects in the developing world, where significant pediatric cancer patients exist. Our early-phase exploration/discussions with pharmaceutical and biotech companies suggests great opportunities exist to build public/private/corporate partnerships which will allow more pediatric patients to participate in and benefit from clinical trials and other research. This will enable studies aimed at all pediatric diseases, especially the rarer ones, to accrue more patients, accelerating research progress. This should be a priority.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

Not being a scientist, I would prefer to defer to NIH experts and those in the biotech/biomed fields as well as academic physician-scientists who best understand where opportunities for collaboration lie. However, in an age of austerity, collaboration between experts and institutions, as well as the charitable sector, should be encouraged and "rewarded" so greater progress can be made and finite resources may be maximized.

Future opportunities or emerging research needs

Pediatric cancer research is a challenging specialty to recruit for, given the scarcity of funding as compared to other specialties. 10 years ago a US shortage of pediatric oncologists was predicted within 10-15 years - essentially now. Supporting young scientists will attract greater numbers to careers in medical research and will help every disease/discipline. Retaining this generation of scientists, not losing them to China and India and other countries which are proactively investing in research, should be a priority and for the NIH. NIH resources are finite, so priority should be given for those fields, such as pediatric oncology, where funding is more scarce than in fields where more ample resources exist. My organization continually works to ensure we are not replicating investments already made elsewhere. Our supporters expect us to do this, and similarly, the American taxpayer expects the NIH to do the same. The patient advocate community across most disease disciplines believes the NIH is taking fewer risks and is investing more in "sure thing" research. If it's so safe, is it really the best investment when lives are at stake? To significantly move the needle in terms of patient outcomes, NIH should set aside more dollars for high-risk, high-reward research. Again, not being a scientist, for more in this area, I defer to medical experts. However, my organization, as well as the . . . , in which we play a leadership role, and many others are eager to work with the NIH/NCI to thoughtfully consider all opportunities and find winning solutions for all concerned parties - especially patients. We look forward to participating in further dialogue!

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The general outline of the NIH-wide Strategic Plan Framework is both reasonable and effective. An opportunity for accelerated and elevated progress lies in how NIH supports its high and special areas of research priority. For instance, there is great excitement and anticipation in research, clinical, and allied health professional communities about the recent addition of physical activity research to the NIH Common Fund. Specifically, the NIH Common Fund launched a research program on the Molecular Transducers of Physical Activity in Humans. This will be the largest targeted NIH investment of funds, focused on the mechanisms of how physical activity improves health and prevents disease. Complementing this major commitment, NIH should consider additional steps to make this even more transformational, such as infrastructure adjustments that will support the progress of physical activity research (such as an office and director of physical activity as exists for nutrition). As just one other example of how NIH could implement a comprehensive approach to supporting all areas of high priority research, the NIH National Center for Advancing Translational Sciences or NCATS could do far more on the behavioral aspects and dimensions of scientific discoveries, in this case, especially as relates to physical activity. Approaching physical activity in the same fashion as a pharmaceutical or surgical intervention from a comparative effectiveness standpoint for patient and public health. Engage all aspects of NIH, including organization and infrastructure, to support high priority research areas, such as physical activity.

Compatibility of the framework with the broad scope of the NIH mission

The Framework is compatible and consistent with the broad NIH mission. A high priority should be placed on the opportunity of "Improve Health Promotion and Disease Prevention." The . . . member of FASEB. When there is a need to underscore the role of NIH in impacting gains in patient and public health, the strongest case for NIH is never made given the lack of emphasis on science-based approaches to lifestyle behavior change for disease prevention and health promotion. With the announcement of physical activity research being added to the NIH Common Fund NIH Director Francis Collins said, "This program will lay the foundation for our understanding of how physical activity affects the human body, and ultimately, advance our understanding of how activity improves and preserves health. Armed with this knowledge, researchers and clinicians may one day be able to define optimal physical activity recommendations for people at various stages of life, as well as develop precisely targeted regimens for individuals with particular health needs." The . . . , in vigorously applauding the decision of Director Collins, also feels that more can and should be done now by NIH as to the power of physical activity to improve health outcomes and prevent and manage disease.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

To mention just one additional concept about the acute opportunities that exist for physical activity research and its translation into prevention and treatment strategies. . . . a program called Exercise Is Medicine. This is now a global health initiative, and is an excellent model of a translational science and research and evidence based endeavor to change both healthcare professional and patient behavior to improve health and reduce disease in clinical settings. This is a cross-cutting example that could benefit and inform various ICO strategic plans.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

In regard to "evidence-based interventions to eliminate health disparities," it is essential that gains in knowledge about physical activity and health and disease be focused on reducing health disparities and promoting health equity. The . . . has several efforts underway to ensure that is addressed. NIH should be intentional about this as well.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

None at this time.

Future opportunities or emerging research needs

Nothing in addition to what has already been mentioned.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

Under the current organization of the agency, the proposed framework for the NIH-wide Strategic Plan is appropriate.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Stagnant/declining budgets are detrimental to the health of our citizens, pushing important discoveries further from reach. Additionally, such insufficient budgets as the NIH has been dealt over the past decade negatively impact the nation's economy, slowing economic growth and providing the opportunity for other countries to edge closer to leading the world in biomedical research. A strategic plan will be most effective if coupled with needed funding increases. Perhaps the plan can include some broad examples of what NIH may not be able to support under current budget constraints, ala the MIT report "The Future Postposed." (See http://dc.mit.edu/sites/default/files/innovation_deficit/Future%20Postponed.pdf) Maintaining the best biomedical research enterprise in the world requires not only robust funding, but also strong, sound scientific guidance to determine which fields, ideas and proposals are most promising and worthy of support. Additionally, with an understandable concern over and impatience about the "valley of death," from policy-makers, patients and other stakeholders, sustained efforts to bridge basic research discoveries over to treatments and cures will continue to be necessary.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

U.S. biomedical research workforce challenges are significant and NIH's leadership and guidance will be necessary to ensure a first-rate, relevant, sustainable and diverse workforce into the future. With major

demographic shifts upon us, the diversity component is absolutely integral in ensuring needed outreach and a steady, representative pipeline to move the next generation into biomedical research.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Certainly basic science research sponsored by NIH will continue to underpin future advances in healthcare and medicine. To fully deliver on the potential of this work, NIH should also increase its attention on interdisciplinary fields and activities that can most quickly capitalize on new findings, pathways, and understanding. In particular, innovations enabled with cross-cutting teams of researchers with a range of expertise and training, from traditional biological fields to applied engineering and development, can help speed innovation to the benefit of society. Given constrained budgets, creation and leveraging of programs that encourage public-private partnerships earlier in the riskier developmental stages of new drugs, techniques, protocols, and healthcare technologies can help NIH catalyze a new era of innovation. This approach promises to be more efficient with taxpayer dollars while also being more efficient in improving the health and well-being of the public. There is no reason to keep science, clinical practice, and engineering separate in this pursuit, and more collaboration between NIH and other government agencies, foundations, and companies can help provide the right environment for the next decades of healthcare advances. Numerous partnerships already exist based in a number of different government funding agencies in other areas, such as manufacturing and computing, for example, and these can be used as exemplars and a source of best practices for NIH moving forward. These examples also highlight the need for investment in education and training programs at scale so that new communities of innovators can grow. New joint programs between NIH and NSF, for example, can help reduce the undue burden on truly interdisciplinary researchers and scientists to make their work “less science-y” or “less engineering-like” in order to meet the criteria of funding programs designed for separate, stove-piped, less efficient support of groundbreaking work.

Compatibility of the framework with the broad scope of the NIH mission

The framework is generally compatible with the broad goals of the NIH, but the plan could multiply its reach and impact if more interdisciplinary programs and deeper public-private partnerships could be established and supported as well. Additionally, more comprehensive support for career management and growth programs into a range of non-traditional fields for the ever-increasing number of postdoctoral researchers would help attract a more diverse set of individuals to health- and medicine-related fields.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

A structure that recognizes and can act on cross-cutting synergies (in disease centers, technology development, medical simulation, etc.) that are created and/or exist in NIH-sponsored programs can result in cost savings on numerous levels, thereby “doing more with less” while also spurring economic growth and supporting long-term workforce development. Aging-related interdisciplinary research and development, for instance, can be leveraged across numerous dimensions of NIH-sponsored projects, resulting in more holistic understanding and treatment of a range of diseases and conditions.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Maintaining artificial boundaries that separate biology, healthcare-, and disease-related research from engineering research does a disservice to those conducting the research as well as to the public who

expects a return on the government's investment in these activities. While those boundaries may have made sense decades ago, now they can stifle creativity, prevent good ideas from being pursued, and result in inefficient use of both time and resources. NIH has the opportunity to create and support new paradigms for discovery that combine these disciplines early, in both the education and research arenas, so that cross-cutting languages and cultures emerge in the healthcare community. In particular, expanding capabilities enabled by big data can help to revolutionize healthcare, but only if a community of clinicians, researchers, and educators first come to consensus on ways in which to best leverage this emerging capability. Without close and constant dialogue and collaboration, this consensus may never emerge, or may emerge more slowly than it should. NIH has the ability to set the course for these conversations through significant commitment and investment now.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

N/A

Future opportunities or emerging research needs

In order to train and grow a truly interdisciplinary workforce around health, wellness, disease, and treatment, members of this next generation workforce must have viable and rewarding career paths at all levels, from baccalaureates to doctorates and beyond. By establishing interdisciplinary programs for research and development that include fields not traditionally encompassed by NIH funding, the available career paths for these new graduates will also become more diverse and more attractive to a greater percentage of the population. Investment in programs that do more to integrate public policy with science and technology, for instance, can help to develop advocates and experts that can formulate and influence ideas and initiatives that can lead to major healthcare breakthroughs. Integration of new technologies with innovations in medical simulation and training, in medical schools as well as for continuing education for healthcare professionals, must be strongly encouraged in order for the practice of medicine to advance at the pace of change driven by research advances. NIH must lead in these critical workforce development issues.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

In my experience, research areas supported by the NIH has been shifting from best possible science to science claiming to have the most translational ability. It is clear that NIH stakeholders and public in general want more of basic scientific discoveries to be implemented in better therapies, and to shorten the time between a discovery and application in clinic. However, scientific experience suggests that many of the translational studies often fail to achieve the promise indicated initially. I would like to suggest that the new NIH strategic plan more strongly emphasizes importance of basic research and downplays the necessity of most applications being "translational".

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity

that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Basic Science is the foundation for progress – The . . . supports this area of opportunity. Basic science can have a powerful impact across a wide array of conditions and can be especially impactful for rare and understudied conditions. Growing the basic science knowledge base is essential for moving all areas of research forward. It is clear that many basic physiological functions, such as cerebrospinal fluid regulation and movement, are still poorly understood but would benefit many conditions including hydrocephalus, infantile macrocephaly, and arachnoid and gliependymal cysts, among others. Advances in early diagnosis/detection – . . . supports this area of opportunity. Advances in early diagnosis and detection hold the potential to dramatically decrease disease burden over a lifetime. This is especially true for conditions that are often under- or misdiagnosed, such as Normal Pressure Hydrocephalus. By improving the sensitivity and specificity of early diagnostic testing, appropriate medical treatments can be utilized to hopefully arrest or slow down disease progression. Breakdown of traditional disease boundaries – . . . supports this area of opportunity but sees significant challenges. Historically, researchers have been isolated in the silos of specific diseases and disciplines. The development of a Neuroscience discipline sought to break some of these barriers, but it is clear that more needs to be done. If successful, however, rare and understudied conditions have a lot to gain – especially hydrocephalus which cuts across conditions to include mechanisms of traumatic brain injury, preterm birth, infection, cortical development, and even cancer metastasis. Consequences of basic science discoveries are often unpredictable – . . . believes that this area of opportunity is redundant and not actionable. This area appears to overlap with the areas of opportunity: Basic Science is the foundation for progress and Breakdown of traditional disease boundaries.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Strengthen the public health impact of NIH supported research – The NIH National Institute of Mental Health (NIMH) incorporated this concept in the NIMH Strategic Plan. This objective aims to “bring the knowledge and findings derived from the previous Strategic Objectives to practice, to improve the reach and quality of existing services, and to develop novel evidence-based services.” . . . believes that this strategic objective incorporates the area of opportunity, Evidence-based elimination of health disparities, but is broader, more cross cutting, and is aligned with the NIH mission

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Shared databases and biorepositories accelerate research progress – . . . believes the NIH should consider including this area of opportunity in the NIH-wide Strategic Plan. Shared databases and biorepositories can greatly accelerate research by centralizing information and by providing high-quality specimens in sufficient quantities to conduct well designed studies. Over the next five years, it will be important for NIH to continue to support existing and develop new shared resources. Chronic disease monitoring – . . . believes the NIH should consider including this area of opportunity in the NIH-wide Strategic Plan. In agreement with the 21st Century Cures Act, section 1122, National Neurological Diseases Surveillance System, . . . supports the systematic surveillance of neurological diseases. Insights garnered through epidemiological and longitudinal surveillance studies will provide a detailed picture of disease burden across a lifetime, identify unknown risk factors and health disparities, and provide the data necessary to develop valid outcome measures.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Areas of consideration: The continued focus on basic sciences in the plan is commendable as it forms the foundation of future healthcare and policy. To realize the benefits of massive investments and advances in the biologic sciences, however, a complementary focus on translational sciences is needed. In particular, the traditional translational model of the scientist and clinician partnerships needs to be augmented by new disciplines and interdisciplinary groups that have traditionally translated scientific advances to human benefit. For example, electrical engineers have translated advances in physics to usher in the modern computer age, chemical engineers revolutionized society by translating polymer chemistry to products. The area we need to focus on is to develop engineers that translate biologic advances to similarly benefit society.

Compatibility of the framework with the broad scope of the NIH mission

The framework is quite compatible but can possibly include NIH partnerships with other agencies, especially in areas not directly related to patient care.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

While the NCI plan offers a comprehensive plan against cancer, some concepts are cross-cutting across NIH given the intersection of this major disease with the topics of many other institutes. For example, aging-related disease and cancer share many of the basic process breakdowns, needs for diagnoses and scale of problem. Survivors (numbering more than 14 million in the US alone) share many issues that affect organs, diseases and topics from other institutes. A focus on cancer (and other diseases broadly) has a set of unique issues that cut across ICs and needs to be handled at the NIH level. A concept to focus on cross-cutting needs of survivors with a focus on technologies to assist them in productive lives is needed.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity

that Apply Across Biomedicine

Infusing engineering approaches: Going beyond such successful programs as Physical Sciences in Oncology and in nanotechnology, physical sciences and engineering are cross-cutting themes that should be included. The concept of engineering analysis, from uncovering details of biologic processes to handling big data to finding optimal health solutions, spans the breadth of the NIH enterprise. Furthermore, it is the need of the day to deliver better healthcare at lower cost and larger scale. These conditions and public health needs are precisely the ones where engineering can provide solutions with analytical, design, manufacturing and simulation capabilities. We suggest the formation of “engineering health” centers in the vein of a cancer, neuroscience or diabetes center, but with a cross-cutting mission to apply common engineering principles across the human lifespan.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

Training the next generation – at even earlier stage.... It is widely recognized that a barrier to public health advances today is the silo-ing of knowledge into disciplines. For many public health concerns like cancer, furthermore, the focus in education comes at the graduate level. Integration of public health topics in the undergraduate curriculum of traditional disciplines is a tremendous opportunity to tap an under-utilized pool to make health advances, boost the quality of undergraduate education, increase the quality of the pipeline to graduate and medical schools, and educate the public of tomorrow on the broader importance of health research. In particular, inclusion of public health in engineering is an opportunity that goes beyond any one topic or the narrow pedagogical definition of the departments of Bio(medical)engineering. New training programs that focus on both traditional diversity in terms of ethnicity and race should be increased to include diversity of ideas from undergraduate backgrounds that are traditionally less represented, but nevertheless very important, for public health such as engineering. Healthcare Simulation Simulation can help manage physician education and patient roles in a rapidly changing biomedical practice, provide better quality and continuing education in initial training and provide an effective means of translation. From molecular systems to complex surgeries, simulation infrastructure needs to be built in the context of tremendous advances in computing, virtual reality and modeling. The opportunity is to use these modern scientific tools to address the need that will arise to design, test and deliver better care practices in the context of scientific advances.

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

As the leading sponsor of research in the US and worldwide, the NIH has long recognized the central importance of human subjects protections, the ethical conduct of science, and scientific integrity in its stewardship of the research enterprise. With its encouragement, ethics has become an integral component of scientific design, the training of scientists, grant and contract review, and the sharing and dissemination of research results. . . . respectfully suggests that the NIH build on this history by ensuring that its new strategic plan emphasizes the centrality that ethics plays in the research enterprise. Specifically, we urge the NIH to carefully consider elevating ethics to a unifying element within its framework. For . . . complete comments on this matter, please see the attached file. Respectfully submitted on behalf of the . . .

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Given the brain science, genetic and epigenetic research around addiction, substance abuse and understanding emerging drug issues with specific substances such as marijuana, the framework appears to be flexible to include substance use prevention is necessary for overall health.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Missing is the evidence based interventions that support population based prevention. It appears that all of the areas are primarily focused on an individual approach.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

It is critically important that the NIH-wide Strategic Plan framework continue to support basic

fundamental research, since that opens substantial doors to new discoveries and often serves as the basis for more applied discoveries. A critical aspect of NIH focus should be on the biomedical workforce, as projections show that trained investigators entering research careers is declining. Most critical are funding mechanisms aimed at new faculty, where paylines should be somewhat more flexible. This is a group of very talented young investigators who are particularly disadvantaged by the current funding climate. One aspect that should be emphasized in the new NIH-wide strategic plan is communication of research findings to the public. It needs to be the responsibility of each investigator to actively and broadly communicate the implications of their results, in terms that can be easily related to the general public (but not overstated). NIH should focus additional resources on core facilities and shared resources, to allow universities and research institutes to be at the cutting edge of technology, with resources devoted to both the purchase and maintenance of such equipment.

Compatibility of the framework with the broad scope of the NIH mission

NIH needs to support a broad portfolio of research, including basic science, mechanism-based studies, clinical studies, technology advancement and data science. It is important that the NIH portfolio of projects remain flexible to allow an evolution of funding priorities as global health challenges develop. For example, new programs can be created that explicitly target large societal challenges, such as treatment-resistant infectious diseases. The Ebola outbreak in west Africa serves as a stark example of the need for programs aimed at minimizing the risk of potential pandemics in emerging countries. Substantial emphasis should be placed on disease prevention rather than just disease treatment.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

It is critical that work be supported that crosses NIH center and institutes and that is NIH-wide. New programs should be created that explicitly encourage and target broadly cross-disciplinary approaches to understanding fundamental biological and biomedical processes, e.g., medicine-engineering, medicine-behavioral science and medicine–public health. NIH could partner with other funding agencies to support targeted programs and leverage funding streams, such as has been done with the National Multiple Sclerosis Society and NINDS.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Global Health

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

The overall research process is being re-envisioned in innovation districts across the country. These approaches employ design thinking and view research more broadly as concept creation through commercialization. NIH should be aware of these initiatives and support appropriate parts of the research development process.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Our son, . . . , was diagnosed with childhood acute lymphocytic leukemia at age 4 in 1998. A high WBC

count placed him in the high-risk group with the CCG-1961 protocol, and as a slow early responder was given cranial radiation. He did very well and his oncologists had high hopes for him living to be a grandpa. Thankfully, the leukemia never returned. But 10 years later . . . developed glioblastoma, a secondary cancer caused by the radiation treatment, and died a year and a half later in 2009, at age 15. Although childhood cancer is considered rare, in . . . Kindergarten class of 20, three children were cancer survivors, and two of them have died of secondary cancers as a late effect of their treatment. Sadly, our pediatric oncologists say that research for better treatments has not progressed fast enough, and they continue to use outdated treatments. Cancer is still the #1 disease killer of our children in this country, and the way things are going is NOT working! There is unique opportunity during this time of new discovery and technology. What is learned from breakthroughs in childhood cancer research will facilitate advances in understanding adult cancers and other diseases. Because childhood cancer does not get much attention in the private sector/pharmaceutical companies, research is dependent on charities and the NCI. Young scientists have told us there is not enough funding to support entering the field of childhood cancer research. Our government has a moral imperative to improve the chances of survival and quality of life for all children in the present and the future. Five-year survival is NOT an acceptable goal for our children, who should be able to look forward to a lifetime, without disability or death from a secondary cancer and other late effects from toxic treatments.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

While the . . . sets the standards for nursing care of people with complex, life-threatening needs then educates and credentials nurses to provide that care, as the . . . our members' empirical experience confirms that most critically ill patients require care for conditions that would be infrequent or even absent if these patients were healthy to begin with. Unfortunately, the NIH framework maintains a narrow focus that equates disease prevention with health promotion while critical illness and injury and their aftermath continue to consume the lion's share of dollars allocated to acute care. Even where the framework addresses disease prevention, it does not appear to recognize the impact of social, environmental, behavioral and economic conditions on disease causation and treatment. It is generally when these factors intersect that a person requires critical care, something that areas of study such as

epigenetics is showing. And the inability to recover from critically illness or injury is often because of factors such as discharge to unsafe places, low literacy and limited essential resources. The framework does not display the integration required to catapult science forward and continues to foster a siloed approach that does not compel integration across institutes and researchers. The NIH strategic goals should integrate biomedical, economic, racial and other similar factors in such a way that the very thought of considering them separately would be unfathomable. In a similar way, the goal should engage the widest range of health professionals and scientists in true collaboration across the entire enterprise, not leave it to chance. Specific gaps and recommendations to strengthen the plan and its relevance to current population needs are identified in the comments below.

Compatibility of the framework with the broad scope of the NIH mission

The NIH's mission is described as seeking "fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability." One might describe this as the application of knowledge to care for vulnerable people in vulnerable families in vulnerable communities with the ultimate goal of reducing vulnerabilities at all cost and seeking to eliminate them wherever possible. Yet, as noted in the previous comment, the framework appears to maintain a limited focus on basic science and the search for treatments and cures. Where the framework does address health, it appears to equate health promotion with disease prevention. While both are key, they are not interchangeable and conflating them will continue the current trajectory where the pursuit of health is secondary to the treatment of disease.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

- Focus on palliative care and end-of-life across all ICOs - Interprofessional partnerships and collaboration across ICOs that is intentional and not left to chance - Collaboration across governmental agencies, external organizations (eg, payors, healthcare systems, local communities), academic institutions and institutional review boards - Bidirectional partnerships with patients, families, communities and businesses

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

[refers to NIH Strategic Framework graphic (Aug 2015)] Overview - Bullet 2: "biomedical and behavioral research" Fundamental Science - Continuous, noninvasive, multi-parameter monitoring that captures integrated patient changes over time with minimal impedance of mobility. - Such monitoring technology could help understand among healthy individuals the trajectory of physio-bio-chemical parameters over time Promotion/Prevention Add: Partner with individuals, families and communities to improve health and reduce risk Add: Patient activation in self-care and global health and communication Change Bullet3 to: "Achieve health equity" and reflect the impact on health outcomes of unequal treatment to factors including gender, race, ethnic, sexual orientation and socioeconomic imbalances Add: Emergency preparedness including nurses' role to align with global acknowledgement that emergency preparedness is important to decrease healthcare inequities among people displaced by climate change. Add: Injury prevention across the lifespan and life situations Add: Advances in primordial prevention, reduction of risk, early diagnosis/detection Treatments/Cures Add: Identify and validate common biomarkers for common pathophysiology underlying multiple diseases (eg, neutrophils, oxidative stress, etc.) based on the premise that a grandmother root exists for branches of disorders that share a basic commonality such as inflammation. Add: Support for people to live successfully with chronic conditions and disability Add: Patient-centered interventions Add: Cost-effective, evidence-based self-management strategies for chronic conditions Add: Focused evaluation of the impact of research findings to reduce

the missteps and unintended consequences of research utilization Priorities Add to Bullet1: “social determinants of health” Stewardship Add: Develop resiliency among healthcare providers in all areas Add: Support balance between innovation and steady methodical progress to build science in an area while speeding the pace of knowledge generation and dissemination Add: Reduce administrative burden while maintaining accountability (eg, IT advances have maintained accountability but significantly increased administrative burdens) Add: Peer reviewer training Add: Develop evidence-based assessments

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

Areas of opportunity that are not applicable to an NIH-wide strategic plan can best be identified once the identified gaps have been narrowed or eliminated and a resource-allocation decisions need to be made within the context of a balanced plan.

Future opportunities or emerging research needs

- Clearer alignment between the public’s priorities for health-related research and the NIH’s strategic direction - Impact of expanded use of informatics, technology and decides by the widest range of healthcare providers and consumers

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Childhood cancer is the number one non-communicable disease (NCD) killer of children in the world globally, regardless of whether they live in a developed or developing country. In spite of this devastating loss of life of our world's children, childhood cancer is the poor forgotten, highly underfunded research focus within the NIH and NCI. In addition, virtually all survivors of childhood cancer will face late effects from their disease and treatment. One quarter of survivors will face late effects that are categorized as severe to life threatening. These include cardiac and lung damage, secondary cancers (often treatment induced), endocrine dysfunction, cognitive deficit to name a few. In the 1980s, childhood cancer received close to 20% of the NCI clinical budget. Today, that budget has been reduced to less than 4% of the NCI budget. As a result, there are many types of childhood cancer that do not even have basic understanding of the disease and the majority of childhood cancers continue to be treated with regimens that were developed in the 1950s, 60s and 70s. It's time that our nation's children with cancer and our world's cancer children be given the priority within the NIH strategic planning!

Compatibility of the framework with the broad scope of the NIH mission

There are many types of childhood cancer for which there is little to no understanding of the molecular basis of the disease. Cancers such as acute myelogenous leukemia, diffuse intrinsic pontine glioma, small cell hepatoblastoma, Ewings sarcoma, rhabdosarcoma, osteosarcoma hold a poor prognosis for long term survival. Many of the residual types of childhood cancer do not have cell lines produced or available for research. This makes it impossible to discover the unique mutation that leads to these often lethal forms of childhood cancer. Funding for the NIH to build live tissue repository, expanding the COG biorepository and creating cell lines of residual types of childhood cancer will enable the NIH to treat children on an individual basis. This precision medicine approach to treating disease is will within the scope and goals of the NIH and the NCI and there are no patients more worthy than our nations' future - i.e., children with cancer.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

After the creation of cell lines for the residual types of childhood cancer, there needs to be increased partnerships with industry so that the NIH is given access to potential curative drugs. Drug screens need to be an integral part of funding childhood cancer within the NIH.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

The NCI is often regarded as the sole funding institution for childhood cancer. Sadly, cancer takes more lives of America's children than any other disease, yet the Institute for Child Health and Development (NICHD) funds little to no childhood cancer research. Research needs to include psychosocial impact of disease, long term patient outcomes research (funding to non-profit organizations such as the American Childhood Cancer Organization) that has a huge grassroots patient and parent base, as well as impacts on the disease within the school setting through studies looking at bullying of childhood cancer survivors etc. Funding for childhood cancer needs to extend beyond the boundaries of the NCI.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

The World Health Organization via the World Health Assembly held the first side meeting on childhood cancer during the May 68th WHA hearings in Geneva Switzerland. As a result, the WHO is taking an increased interest in access to essential medicines and care for children with cancer globally. America needs to take a leading focus on childhood cancer so that we can be seen by the WHO and PAHO (in America) as a leader in this global child health burden. The WHO has recognized that childhood cancer is the number one NCD killer of the world children and as such there is a huge need to cut across the biomedicine boundaries to identify the molecular fingerprints of childhood cancers so that children can receive targeted therapy and not solely toxic chemotherapy.

Future opportunities or emerging research needs

The development of childhood cancer treatments in the 1950s and 1960s including multi-drug cocktails led to successful treatments of adult cancers. In the USA, the Food and Drug Administration ("FDA") has approved 109 new drugs to treat adult cancers since 1990. In sharp contrast during the same time period, only 2 drugs have been approved by the FDA to exclusively treat childhood cancer. This weak record of drug development for pediatric cancers underscores a huge gap and highlights the fact that children continue to be treated with drugs primarily developed in the 1950s-70s and with drugs that were developed to treat the many adult types of cancer that children simply don't get such as breast, prostate, lung and colon cancer. Research has shown that childhood cancers are biologically distinct from adult cancers, resulting in a need for drugs to be developed that are specific to children's treatment needs. (<http://www.medilexicon.com/drugs-list/cancer.php>). There is a huge emerging research need to develop drugs to treat the many types of childhood cancer and this has to be a huge focus of the NIH because history has shown that it will not be the focus of industry. Childhood cancer MUST be a huge focus of the NIH 5 year strategic plan!

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Given the new environment under Accountable Care Act, NIH research results and recommendations of its Strategic Plan should be framed in the context of health outcomes and reduced costs. Consistent with NIH Unifying Principles of Setting Priorities and Enhancing Stewardship, it greatly benefits the NIH to

partner with Federally Qualified Health Centers (FQHCs) and the National Association of Community Health Centers (NACHC). The July 2015, NACHC Fact Sheet #0815 (http://www.nachc.com/client/documents/Cost%20Effectiveness_FS_2015.pdf), well documents the cost effective, quality care that is provided to over 23 million Americans, by over 1,300 FQHCs, in every US state and territory, through over 9,000 delivery sites. Areas for consideration for the current framework include NIH priorities that impact the largest populations experiencing health disparities and inequities, greatly characterized by the 23 million patients FQHCs presently serve as part of the US health care safety net. Partnering with FQHCs brings the potential to represent all parts of the country and US territories, sub-populations (Rural, Urban, Farmworker, Homeless, Public Housing residents, and LGBT, etc.), and their access to interventions via NIH translational research and trans-NIH initiatives. Communication to develop additional partnering relationships among FQHCs and the NIH can be accomplished through contacting NACHC, state Primary Care Associations (PCAs) and Health Center Controlled Networks (HCCNs).

Compatibility of the framework with the broad scope of the NIH mission

Judging by the information provided through the RFI and additional detail gathered through the NIH-wide Strategic Plan Webinar and Q&A segment, it appears that the presented NIH framework is compatible with the broad scope of its mission.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

- Costs for implementation and cost savings as part of research
- Address genetics and areas of the country especially considering safety net populations.
- Health costs, considering aspects of prevention and cost savings
- Consider Co-morbidities especially with behavioral health, trauma based care, evidence based interventions and cost savings
- Look at population health, systems of care and develop a body of evidence to address this in a scientific manner (which would include metrics for care coordination)
- Conduct evidence based studies on the impact, costs and health outcomes of National Metrics (i.e. NQF 18 for Million Hearts), the HIV continuum of care, etc.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Under the sub-category of Advance Treatments and Cures under the heading of Areas of Opportunity that Apply Across Biomedicine, Webinar Q&A discussion included consideration of the Social Determinants of Health (SDH) as drivers of health disparities. NACHC, in collaboration with FQHCs in multiple states, are now studying these upstream socio-economic factors (NACHC PRAPARE Project) that strongly affect our understanding of disease processes and boundaries and greatly expands the traditional scientific medical model approach. Inclusion of initiatives such as the recently released NIH FOA NIMHD trans-disciplinary Collaborative Centers for Health Disparities Research Focused on Precision Medicine (U54) begins to address the disproportionate share of chronic diseases and adverse health conditions FQHC minority populations face. It is important that FQHCs be strongly considered for inclusion as consortium partners in regional coalitions.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

None noted.

Future opportunities or emerging research needs

- Systems approach to improving health outcomes
- Documenting the costs of “health”
- As discussed

in the Q&A on the webinar, providing a low-barrier grant process would help to advance translational clinical research in the FQHC arena and for others. • Patient Centered/Patient Informed research can be a game changer in the ACA environment. Partnerships with patients and patient-centered organizations are important to performance-driven, patient-experience sensitive, initiatives to advance the overall quality and cost of population health. Since FQHC governing boards (over 1,300 in 2015) are made up of 51% or more active health center patients, FQHCs offer a source for rich input from patient stakeholder groups. NACHC organizes and staffs a national Consumer Board Member Committee that meets biannually to receive frontline input from a diverse group of patients (geographic, socio-economic, and population specific; such as farmworker, homeless, public housing, LGBT and HIV/AIDs communities).

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

As a community of primarily basic researchers that relies heavily on NIH support, the . . . supports the framework for the strategic plan as it is currently structured and is particularly pleased to see that promoting fundamental science is first and foremost under areas of opportunities. As outside pressure is often focused on curing or treating a specific disease or condition, it is important for the NIH to clearly state this and explain that basic science is the basis for progress. The . . . also appreciates that the framework highlights the need to work across boundaries, recognizes that research findings are unpredictable, and notes that as NIH considers investments in research and potential treatments/cures, it must think beyond the boundaries of a specific disease. A benefit of the way the current framework is structured is that the plan is placed in the context of the NIH mission. However, this mission has been constrained by financial shortfalls and lost purchasing power, restricting the progress of research that would benefit all stakeholders. NIH must continue to inform Congress and the public of the consequences of funding restrictions that reduce research opportunities. Another benefit is that the plan clearly demonstrates the strong ties between basic research, finding new treatments, and promoting health. One challenge raised by the framework is that even though it indicates the need to break down traditional disease boundaries, many institutes are dedicated to specific disease areas included in their mission statements, and NIH's Research Portfolio Online Reporting Tools (RePORT) tie funding to specific diseases.

Compatibility of the framework with the broad scope of the NIH mission

The Framework rightfully leaves open room for unexpected opportunities, which is especially important in such a tight fiscal environment. It also specifically notes the need to support a diverse workforce and to support rare diseases, areas that could easily fall by the wayside given the vast demands placed on the Institutes for its resources. As a federally-funded entity, NIH is the critical organization in supporting both of these endeavors, and both are critical to our country's health and economic well-being.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

The NIGMS Strategic plan specifically recommits itself to investigator-initiated research and to finding ways to rebalance the portfolio in support of that type of research. These initiatives should be applied across the NIH. As noted by the framework, the impacts of basic science discoveries are unpredictable. NIH needs to ensure that ICs commit to supporting and fostering these discoveries. The NIGMS plan also commits to continued open communication of the Institute with its external stakeholders regarding NIGMS programs, processes and policies. NIH should also commit to open communication with these audiences, as well as across ICs as it moves forward with implementation of the new strategic plan.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Basic research requires a stable workforce, stable funding, and the intellectual space for creativity, which the NIH needs to explicitly support. The framework can encompass these fundamental requirements for research. However, innovative technology and instrumentation is also a requirement for research progress, and the plan does not incorporate a mechanism to financially support instrumentation development or instrument acquisition. An opportunity should be reserved for such ventures.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

With the loss of NCRR, it is important that NIH include as part of its mission the need to support research infrastructure and instrumentation development. While the framework mentions, "Leaps in technology often catalyze major scientific advances," it does not clearly include the need for NIH to make sure that support for the technology and instrumentation is necessary for those developments to take place. Funding for postdoctoral and predoctoral training is an important component of workforce diversity and stability, and the NIH needs to decide and communicate what its policies and commitments will be in this area moving forward.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Not nearly enough funding is given in the area of pediatric cancer research. Currently, the NCI only allocates 4% of the budget towards pediatric cancer research yet it remains the #1 leading disease cause of death for children in the United States. More children die each year from some sort of pediatric cancer than AIDS, asthma, diabetes, congenital abnormalities, or cystic fibrosis combined. Worldwide over 175,000 children are diagnosed each year not to mention the children who are not newly diagnosed and continue to battle each an every year.

Compatibility of the framework with the broad scope of the NIH mission

Only three new drugs have been created specifically for pediatric cancer in the past 20 years. This is unacceptable. One of the goals of the NIH is to have creative discoveries and innovative research strategies, but there is nothing innovative nor creative about only 3 drugs over a span of 20 years. The next goal is to help in the nation's ability to prevent disease but nothing is being done to help with early detection of easily diagnosed pediatric cancers. Third is to ensure a continued high return on the public investment in research. The children who are now being diagnosed and treated for cancer may never be able to invest in society because the NCI will not invest funds for better treatment options. The last goal speaks of public accountability, scientific integrity, and social responsibility. Does this just apply to the adult population because at this point our children are not receiving the same playing field to fight pediatric cancers? What about that shows integrity, accountability, or social responsibility and to whom?

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

We need research that specifically targets each of the 12 most common types of pediatric cancer to find a cure as well as better treatments.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Not only is there a need for more research for a cure or at least drugs that allow kids to "live" with cancer but consideration also needs to be given to the long term side effects of those who do survive.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

It is well documented that many large programs of international renown suffer from management systems that do not expedite implementation and results. Increased research costs and complexity, shortage of high quality information systems, increased regulatory burdens, and low participant enrollment and retention have made it difficult to operationalize studies with high quality and efficiency. Projects have been stalled by the inability to harness stakeholder input and energy into a focused decision and resultant actions. Moreover, a lack of on-demand access to program performance information and people responsible for using it makes it challenging to manage schedule, cost, and risk. Taking these factors into account it is understandable that vendors and investigators are challenged to develop teams with the required domain expertise, understanding of the scientific process, and experience to manage large-scale studies. Therefore, we recommend that NIH consider incorporating best practices in scientific management – from acquisition to partner management to efficient decision making and dissemination of findings – into soon to be launched large-scale biomedical research. This can ensure that great science is efficient and effective. Incorporating scope, requirements, schedule, financial, quality, stakeholder, communications, and risk management from proposal development, through acquisition and program execution will ensure greater control of study assets and ensure timely high quality research. Adding this focus to the current framework is an area of to ensure that NIH remains the international leader in life sciences research and sets the standard for rigor and integrity.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

In an era of budget uncertainty, it is important that NIH identify and implement effective and responsible infrastructure elements to support the stewardship of public funds. This may include methods to assure data quality, efficient collection and processing of large volumes of data, and timely dissemination of scientific findings. Based on our experience in population-based prevention and early detection, with a focus on eliminating health disparities, we believe the government will need to attend to a number of significant issues. First, new approaches are needed to deal with the declining cooperation, response, and retention rates in health studies, regardless of mode. This will be particularly relevant as NIH increases the focus on healthy populations. While traditional recruitment methods, such as the use of registries for unhealthy individuals, are often used, this is not viable for healthy individuals.

Therefore, novel approaches to assembling a sample of healthy individuals through web panels and non-probability sampling should be investigated. This would affect studies across NIH. Secondly, integrating epidemiological and observational methods with clinical trials investigations may also provide new approaches to increase sample and explore research questions that have remained unanswered.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

The development of ECHO, Precision Medicine Initiative, and the BD2K programs share the anticipated goals of the framework to expand extant data use, increase power, and allow previously unanswered questions to be addressed. As NIH moves towards operationalizing these studies it will have to determine how to account for varying protocols, populations, designs, and epochs when integrating data together. Data integration will be affected by different instrument wording, response options, and measures; facets of statistical and operational design; and weighting procedures. To undertake the challenge of such data integration, with the scientific rigor that NIH requires, new research should be conducted in the area of data harmonization (DH). DH is a set of standardized data management and statistical procedures to achieve comparability of measures over time and across studies. Research on DH should investigate flexible methods to accommodate all data types with the primary goal of providing a robust and efficient solution for attaining data comparability. DH research should consider six primary areas: 1) efficient methods for indexing and aggregating data, documentation, and metadata across all studies of interest; 2) automatic comparisons of study metadata to assess similarities and differences between data items for recoding efficiency; 3) standardized procedures for data recoding; 4) determine how to adjust for different study design, post-stratification, and re-weighting; 5) appropriate production and public use file formats to ensure open access to data and reproducibility, 6) robust disclosure review methods to protect the identity of study participants. Research in these six areas will NIH with effective methods for DH and high quality data.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

To help advance the mission of the National Institutes of Health (NIH), The . . . recommends that the NIH-wide Strategic Plan place a priority on stimulating and supporting trans-NIH initiatives developed by the NIH Geroscience Interest Group. Understanding the basic cellular and molecular underpinnings of aging as a principal risk factor for chronic disease has the potential for slowing the appearance and progression of not one, but most age-related chronic diseases all at once. This could have a major impact not only on the health of the U.S. population, but also the growing federal health expenditures spent on age-related chronic diseases. It is an approach that is unmatched by any other. Biomedical gerontology has been hindered by the bias against cross-disciplinary work both in the academy and by declining research dollars. Measures to counteract that trend, such as by setting aside substantial funds for cross-institute grants—particularly for those involving the National Institute on Aging and the many institutes whose main focus is on an age-related disease—would help break down the traditional silos and promote synergy and potential cost savings between disparate research communities. This is vital

for progress on addressing age-related chronic diseases that currently account for more than 75 percent of Medicare and other federal health expenditures. We are close to major breakthroughs. Stimulating and supporting research collaborations among NIH institutes and centers would position NIH to accelerate the scientific discoveries that could have a major impact on the nation's health and economy.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The . . . appreciates the opportunity to provide comments on the framework for the National Institutes of Health Strategic Plan. . . . Many of our members are NIH funded investigators who conduct research on "cross-cutting" questions that address the boundaries of disease areas and the interfaces between institutes. For example, endocrine scientists are working to understand the relationships between organs and organ systems, and how disrupted hormonal systems and signaling networks contribute to disease. The . . . is encouraged that the framework emphasizes the interrelated aspects of fundamental science, health promotion/disease prevention, and treatments/cures. We assert that endocrine systems and hormonal status are central to all three of these themes, and should therefore be explicitly incorporated into the plan. Research on hormones and endocrine science is uniquely cross-cutting; according to a recent survey, at least 18 different NIH Institutes and Centers fund . . . research programs. However, we are concerned that the lack of a strategic focus on endocrinology creates barriers to the integration of endocrinology into NIH programs and initiatives. For example, study sections and review groups may not appreciate how endocrinology and hormone health is related to cancer. We anticipate that an emphasis on endocrinology in the NIH-wide strategic plan will help highlight the importance of hormones and hormonal systems to the broader biomedical research community.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

The . . . is also encouraged that the framework emphasizes the importance of research on prevention of disease. We hope that the strategic plan will acknowledge the importance of environmental health and reducing chemical exposures to prevent disease. We know that exposure to endocrine disrupting chemicals contributes to increased risk for diseases such as breast cancer, obesity, and diabetes. However, more research is needed to understand the fundamental links between exposures and human clinical endpoints. We believe that a strategic focus on early life exposures and developmental origins of health and disease could prove transformative in efforts to prevent disease.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

These comments are from . . . on the proposed NIH Strategic Five-Year Plan. Public Comment Opportunities and Response Times: We hope there will be other times in the near future when the public, advocates for diseases, and associations representing patients with diseases can respond to the NIH Strategic Plan. The amount of time given for these first responses is far too short with far too little information offered by the NIH to present the best informed of responses. It is not enough to have a few audio webinars and some other cursory information given to the public on what might be a major change in direction for the NIH. ME/CFS within NIH Currently: Myalgic encephalomyelitis/chronic fatigue syndrome is a "...serious, chronic, complex multisystem disease that frequently and dramatically limits the activities of afflicted patients." (Institute of Medicine, "Beyond Myalgic Encephalomyelitis/Chronic Fatigue Syndrome," February 2015.) It affects up to 2.5 million people in the United States alone, most undiagnosed. It is undiagnosed because there is so little medical education about it in medical schools that most physicians cannot accurately diagnose it or think it is psychological, not physiological, in nature. ME/CFS is undiagnosed because it is 233rd on the NIH disease-funding list and has received only \$2.50 per patient per year during the last 20 years for research. HIV/AIDS, affecting fewer than one million patients in the U.S., receives \$2500 from the NIH per patient per year – 1000 times more. Yet ME/CFS is a catastrophic disease for those who contract it, ruining lives, and often taking lives. Higher rates of cancer, heart disease, and suicides among those with ME/CFS than in the general population have been documented. It costs the economy an estimated \$17-24 billion per year.

Compatibility of the framework with the broad scope of the NIH mission

Because ME/CFS is a multisystem disease, it currently is not assigned to an Institute. It had been part of NIAIDS until 2000 when it was removed from this Institute and moved to the Office of Research on Women's Health. However, it is not a woman's disease, any more than Multiple Sclerosis is a woman's disease, simply because more women than men suffer from it; an estimated 25% of patients are men. The ORWH has no budget to fund research for this illness. The NIH created a Trans-NIH Working Group the purpose of which is to promote research, but for all practical purposes it has done almost nothing to help patients. It is not made up of experts in this field, and some are not well informed about the

disease. In spite of 30 years of research studies to the contrary, some Trans-NIH Working Group members have been steadfast in their belief that ME/CFS is a psychological disorder. The Group has turned down funding to highly qualified and expert ME/CFS researchers. While rejecting grant applications from well respected ME/CFS researchers, the Trans-NIH Working Group contends that there are not enough good projects to fund.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

ME/CFS' Likely Position Within the New Strategic Plan: Under the NIH New Strategic Plan (latest iteration), this neglect will continue. The Plan does not, at this time, adequately consider those diseases like ME/CFS which are multisystem and lack Institute affiliation. There are few diseases that fit this category which have so many patients – 2 ½ million people is far more than have HIV/AIDS in the U.S. Yet, a person is far better off having MS or HIV/AIDS than having ME/CFS. As Dr. Nancy Klimas has famously said, "I split my clinical time between the two illnesses [HIV and AIDS], and I can tell you, if I had to choose between the two illnesses in 2009, I would rather have HIV...." The billions spent on HIV/AIDS have paid off handsomely in extending and greatly improving life for those with HIV or AIDS. Yet there are more than double the number of those who have ME/CFS than who have HIV/AIDS but who have no representation in the NIH. ME/CFS has not been included in the Global Burden of Disease study, yet the disease burden of ME/CFS is enormous on patients and caregivers, almost beyond comprehending unless one knows someone with this disease. Since "incorporating disease burden" is one of the NIH priorities of this plan, ME/CFS should come to the forefront in the planning process as a disease that NIH should study with far more commitment and resources.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

A question was asked at the August 14, 2015, audio webinar about this type of disease, i.e., one not under an NIH Institute umbrella and how such a disease would fit into the framework of the Strategic Plan. The answer from Dr. Lawrence A. Tabak, Principal Deputy Director, NIH, was that a framework will be put in place to provide the wherewithal to provide the Trans-NIH approach [for such diseases]; it will be more process than any special condition or disease would have if they were located in an Institute. Also, he said that the final funding decisions will be made by the Institutes and Centers. Therefore, if a disease is not housed within an Institute, it will get a "process," not a focused plan with funding. Therefore, ME/CFS, in spite of its numbers of sufferers, will remain with essentially no funding and no medical champions within the NIH under the new Strategic Plan. There have been NIH ME/CFS workshops and reports, and reports and workshops, but little funding for research into causes, markers, population studies, and treatments. Because no Institute "owns" ME/CFS, there is no commitment or power to push for any of these types of research. There is no evidence to suggest that a Trans-NIH Workgroup approach for ME/CFS under the new Strategic Plan be any improvement or that it would move the science forward. ME/CFS needs to be taken out of the ORWH and put into an Institute, most logically the NINDS. ME/CFS is not an orphan disease; it has too many patients to be deemed as such. It is, however, treated like an orphan within the structure of the NIH. The . . . urges the NIH to give it a real home in an Institute and fund research for it in accordance with its burden on the patients,

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

We see tremendous potential benefits. Challenges foreseen: 1) accelerating ongoing change in internal NIH culture required to cut across ICO lines and form effectively harmonized -- even integrated -- NIH-wide operational plan. This is essential, e.g., in maximizing benefit of the framework's first Area of Opportunity -- "Promote Fundamental Science." Clearly, basic science cannot be confined within artificial boundaries of organ systems or individual IOCs; the strategic plan should include mechanisms for accelerating current trans-NIH efforts such as those in the Neurosciences Blueprint, muscular dystrophy coordinating committee and mitochondrial research and for taking full advantage of additional opportunities for trans-NIH extramural and intramural research collaboration; 2) framework recognizes the essential nature of partnership and collaboration ("Medical science is a team sport." Dr. Tabak). Nowhere is this more evident and nowhere is public-private partnership with full range of NIH stakeholders more essential than in translational and clinical research. Neither the NIH, nor industry, nor academia nor patient advocacy groups can, alone, accomplish the translational and clinical research required to treat diseases. All these stakeholders must be fully involved. Despite various NIH approaches to its participation in these essential partnerships, the greatest impediments have been the slow pace of NIH decision making regarding its commitment and inflexibility in responding to evolving requirements during execution. Many patient groups are devoting much time and resources to partnering with industry and academic partners to conduct translational and clinical research. These partnerships frequently decide they simply cannot wait for the time required to secure NIH participation. We strongly urge that the strategic plan include new mechanisms for significantly accelerating the review, decision and commitment timelines for public-private partnerships and for increasing flexibility in responding to inevitable changes in data-driven programmatic requirements; 3) Resources - NIH needs more. We continue to work hard to help secure them.

Compatibility of the framework with the broad scope of the NIH mission

Seems completely compatible to us.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

As noted above, current crosscutting programs such as the Blueprint for Neuroscience Research should be continued and enhanced. A number of NCATS programs (e.g., TRND and BrIDGs) should also be included and enhanced.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

We applaud the focus on the importance of crosscutting, NIH-wide opportunities and on collaboration and partnership. We would like to call special attention to several important opportunities not specifically mentioned in the current framework: 1) NIH collaboration with the FDA -- We suggest the strategic plan highlight the importance of the NIH-FDA collaboration and outline efforts to broaden and deepen that collaboration. We are frequently faced with FDA issues in which greater NIH involvement could have had very beneficial impact -- for example, development of biomarkers, clinical endpoints, more robust pre-clinical data, better clinical trial design, clinical trial training, and better FDA understanding of specific diseases; 2) Greater collaboration among ICOs re translational and clinical sciences -- Most ICOs have their own translational and clinical programs. We see a great opportunity to

develop more concerted effort across these separate programs. Convening the leadership of these multiple programs on a regular, NIH-wide basis would seem to have great potential benefit. Also, our view is that the NIH center tasked with Advancing Translational Sciences (NCATS) could be very helpful in this regard; 3) greater collaboration among the NIH-funded extramural institutions in translational and clinical research. For example, the CTSA provide a great opportunity. The strategic plan should include mechanisms for achieving the CTSA program's potential by developing it as a fully collaborative network rather than 62 competing sites. Our view is that this will require strong NIH leadership reinforced by greatly increased NIH prerogative regarding the individual CTSA budgets so as to identify and support truly innovative and collaborative projects.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

We do not see any.

Future opportunities or emerging research needs

We applaud the inclusion in "Unifying Principles," "Setting NIH Priorities" of "supporting opportunities presented by rare disease research" as well as the strong statement that "Breakthroughs need partnerships and often come from unexpected directions." We have heard Dr. Collins say, "It is often the insights that come from the rare diseases that teach us something about more common ones." We believe that this principle will be borne out in most of the NIH-wide crosscutting efforts currently under way and those to be added in the strategic plan. Also in regard to rare diseases, the strategic plan should outline a bright future for the Office of Rare Disease Research (NCATS). We also applaud inclusion under "Enhancing Stewardship," that "NIH enhances stewardship of the research enterprise by recruiting and retaining an outstanding biomedical research workforce." We are all together in facing this crucial challenge and believe it is terribly important that the strategic plan shine a bright light on the need to attract new talent to this endeavor, and to provide the support and incentives required to retain and develop that talent. So, the plan should emphasize and resource the effort to recruit high-quality new investigators and to incentivize high-performing investigators to stay in the field. Among the many ways to do so, we believe, will be to ensure that the NIH funds sufficient blue-sky, high risk/high reward research and provides adequate training and mentoring support.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Please consider the number of years lost when measuring the incidence and relevance of childhood cancer. Our children deserve more than 3.8% of the NIH budget for cancer research. There are thousands of us bereaved parents fighting relentlessly for cures for childhood cancer. Several types of childhood cancer are only funded by the efforts of those who have lost children to the rarest childhood cancers. No family should have to personally feel obligated to find cures for a national problem. Please, please help by allocating more funds to develop new drugs for childhood cancers. Childhood cancer is only rare until someone you love is diagnosed. Please help.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Childhood cancer.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

Addressing Public Health and Chemical Exposures: An Action Agenda National Conversation on Public Health and Chemical Exposures Leadership Council, June 2011 Executive Summary (excerpt) Achieve a More Complete Scientific Understanding of Chemicals and Their Health Effects Protecting the public from harmful chemical exposures requires continuous improvement in knowledge and understanding of chemical toxicity, modes of action, sources of exposures, and potential adverse health effects. Despite significant research efforts to date, the United States continues to lack critical information in key areas including: 1) health effects of chemicals, including low-dose, multiple, and cumulative exposures; 2) individual susceptibility/intolerance including, but not limited to, the interplay between genes and environment; 3) community vulnerability and disproportionate effects from past exposures; and 4) effectiveness of interventions to protect public health. Progress can be made by developing and using novel, validated analytical tools to more quickly evaluate chemical hazards, filling critical data gaps to prioritize chemicals for further assessment, and developing tools for characterizing chemical exposures across product life cycles and human life stages. Advances in chemical hazard testing, as suggested in the 2007 National Academy of Sciences' report Toxicity Testing in the 21st Century , are needed to support preventive decision making. Data gaps must be filled quickly to allow federal agencies to identify chemicals posing the greatest potential hazards. Additional exposure assessment protocols and tools should be developed to understand and predict when and where exposures occur along chemical product and process life cycles and across human life stages. Public health professionals in all sectors

need better access to existing information across multiple databases, improved understanding of variations in individual susceptibility/intolerance to chemical exposures, and understanding of how gene-environment interactions relate to chemical exposures. Potential links between indoor air quality and fetal and human development should be evaluated, and better scientific methods should be developed for investigating the

Future opportunities or emerging research needs

. . . Millions of Americans experience severe and debilitating multi-system reactions and intolerances to a panoply of chemicals, over-the-counter and prescription medications, alcoholic and caffeinated beverages, and numerous other substances and products. Approximately 15-30% of Americans report adverse reactions to particular chemical exposures. Those disabled by chemical sensitivities or chemical intolerances (CS/CI) may be as high as 6% of the population. There is a need for population-based studies among exposed individuals using a validated questionnaire; for research on the mechanism by which people develop these sensitivities or intolerances following chemical exposures; for the creation of an interdisciplinary group to develop and implement research on CS/CI, and for the construction and staffing of an Environmental Medical Unit (EMU), a hospital-based research facility, as recommended by multiple professional and scientific meetings and supported by Congress. The Scientific Understanding Work Group, part of the CDC's National Conversation on Public Health and Chemical Exposures, is the most recent work group report to make detailed research recommendations to investigate individual susceptibility including the use of an Environmental Medical Unit (See Recommendation 7): http://www.resolv.org/site-nationalconversation/files/2011/02/Scientific_Understanding_Final_Report.pdf.) Clinical investigation of chemical intolerance using an EMU would permit examination of populations affected by toxicant-induced intolerances to determine the biomarkers and mechanisms by which to identify individual susceptibility so as to avoid placing such individuals in hazardous situations, detect affected individuals early in their illness, and provide prompt intervention.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The . . . appreciates the opportunity to comment on the framework for the NIH-wide Strategic Plan in the attached letter, which is summarized below. The . . . fully supports the NIH's proposed framework and agrees that an agency-wide plan cannot provide an exhaustive overview of the myriad scientific directions and questions supported by NIH funding. The . . . believes that the current framework of the plan outlining the three Areas of Opportunity captures the most pressing and emerging opportunities in biomedical research for the NIH. We support a Strategic Plan that can be updated or revised as needed to fit the goals and unpredictable nature of scientific research, particularly when attempting to bring together diverse disciplines in the biomedical, social, behavioral or other sciences. The . . . has also long supported building an evidence base to eliminate health disparities and would like to stress that such development involves a systems approach across the Areas of Opportunity to understand the causes of inequity at individual, community, and societal levels, and the interactions between those causes. The . . . encourages the NIH to develop a Strategic Plan that complements the plans and research goals of other agencies in the Department of Health and Human Services and to explore opportunities for collaboration where possible. The . . . strongly favors the inclusion of goals to enhance the stewardship of the research enterprise and believes the conduct of research and development of the biomedical workforce are critical factors to the NIH successfully carrying out its mission. Specifically, we encourage: the continued development of initiatives that support a diverse workforce; efforts at harmonization and retrospective review of regulations to reduce administrative burden; the promotion of research rigor

and reproducibility; and an emphasis on the value of research partnerships.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Please allocate more funding for research towards childhood cancer. Children deserve hope and treatment that works effectively, without harming their young bodies. The current treatment is out dated and extremely harmful.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

All diseases must be accounted for and have an appropriate home within NIH so they don't fall between the cracks. The current decision-making process and framework doesn't accommodate nor insure this will happen. The NIH organ or medical specialty centric "silo" framework leaves multi-system diseases such as ME/CFS at risk of exclusion from any and all "silo" umbrella entities, and consequently excluding them from each silo's priorities, strategic plans and therefore denied NIH research dollars for years or decades. This exclusion problem carries over into current NIH-wide or cross-cutting endeavors such as Bid Data and "burden of disease" reporting and is likely to carry over into this new endeavor unless the process is corrected. For example: ME/CFS is excluded from by Big Data, because it's not under the purview of any of the participating NIH entities. Although "NIH sets priorities by incorporating measures of disease burden", some diseases are not included in the "disease burden" report. How can NIH evaluate if the disease burden rises to a priority? Currently, excluded multi-system diseases need a proper home, with a "whole-disease" center and "whole-disease" expertise to coordinate research across NIH. A "whole disease" knowledge base, for a multi-system disease will maximize cost effectiveness and research efficiency while best advancing disease knowledge.

Compatibility of the framework with the broad scope of the NIH mission

All diseases must be accounted for and have an appropriate home within NIH so they don't fall between the cracks. The current decision-making process and framework doesn't accommodate nor insure this will happen. ME/CFS is an excellent example.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Multi-system diseases, such as ME/CFS, are ideal choices for NIH cross-cutting efforts. It provides an opportunity to address diseases that do not fit into and are not represented in individual Institutes or Centers.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

- Replication and validation of important research on specific diseases will allow advancement in disease knowledge, which can lead to next steps and next steps. Without funding from NIH, much important research goes un-validated and stops progress in disease understanding. Import disease advances should never be lost due to a lack of replication funding. This is important for ME/CFS

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The proposed framework is an excellent start to advance the mission of the NIH. However, to fully leverage the power of a trans-NIH strategy, we recommend that proposed framework also include a focus on the reduction of and management of pain. Recent estimates suggest that pain costs the United States over \$800 million dollars per year. Given the increasing rise in opioid prescriptions for pain and the corresponding increased risk of opioid abuse, it is abundantly clear that existing treatments (e.g.,

opioids) are unable to address the full extent of the problem. Complementary and integrative health therapies combined with a thoughtful utilization of routine pain approaches have the potential to play a vital role in addressing the pain of Americans. Additional research is needed that utilizes varied study designs including typical randomized clinical trials, pragmatic trials, cluster randomized trials, practice-based research and observational studies.

Compatibility of the framework with the broad scope of the NIH mission

The proposed framework is consistent with the NIH mission.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

The ability to leverage to the full power of the NIH lies in its ability to develop and implement cross-NIH collaborative strategies. As noted previously, one area of utmost concern for millions of Americans lies in the reduction and management of pain. Pain is not just a concern for patients served by the research conducted by the NHLBI, NIAMS, NICHHD, NIMH, NIDDK, NIA or the other exceptional institutes of the NIH. Rather, pain is a cross-cutting concern for all institutes, centers and office of the NIH. One such center that has the capacity to bridge the various patient populations served by the entire NIH is the NCCIH. By its very nature, the NCCIH serves many different patient populations and also has a research portfolio that contains numerous innovative methods to improve pain management. New initiatives to support the development of complementary and integrative health approaches along with routine pain management strategies across a trans-NIH platform could play a major role advancing the health of Americans.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Since pain is a significant factor impacting the health, productivity, and quality of American's lives, we advocate a trans-NIH focus on understanding how innovative pain management strategies can be developed, evaluated and deployed across the wide ranging American health system. A trans-NIH focus on innovative pain reduction and management strategies would be a cornerstone to Improving Health Promotion, and Advancing Treatment and Cures. Finally, such a strategy would position the NIH to understand how an innovative pain strategy would impact the utilization of healthcare by Americans. Given the Supreme Court's upholding of the Affordable Care Act this summer, a trans-NIH initiative on innovative pain reduction and management approaches could include assessment of models that are both cost-effective and cost-avoidant.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

The proposed components of the Areas of Opportunity are applicable to an NIH-wide Strategic Plan.

Future opportunities or emerging research needs

Complementary and integrative treatment approaches, combined with a thoughtful utilization of routine strategies for treating pain have the potential to play a vital role in addressing the pain experienced by so many Americans, including the underserved. Additional research is needed that includes both complementary and integrative, and conventional medicine. These studies should utilize varied study designs including typical randomized controlled trials, pragmatic trials, cluster randomized trials, practice-based research and observational studies.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The Framework laudably emphasizes “promoting scientific rigor and reproducibility” and “employing risk management strategies in decision-making.” To this end, all NIH projects involving animals should be carefully reviewed to assess whether data gleaned from those studies can be reliably translated to humans. A 2014 review paper published in the BMJ (1) concluded, “if research conducted on animals continues to be unable to reasonably predict what can be expected in humans, the public’s continuing endorsement and funding of preclinical animal research seems misplaced.” Indeed, the scrutiny brought by NIH (2) and the Institute of Medicine (IOM) (3) to the scientific necessity of chimpanzee experiments revealed that chimpanzee use has been “largely unnecessary” and has “rarely accelerated new discoveries or the advancement of human health for infectious diseases.” Applying similar consideration to all areas of experimental use of animals would help bolster NIH’s mission to “ensure a continued high return on the public investment in research” and “exemplify and promote the highest level of scientific integrity, public accountability, and social responsibility.” Other systematic reviews have similarly documented the inapplicability of data from nonhuman animals for numerous areas of investigation into human disease—prompting recommendations that systematic reviews be conducted before approval is granted for animal use (4, 5). Indeed, the Netherlands requires a systematic review as part of grant applications (6). We urge NIH to consider implementing a similar approach to promote high-quality science while reducing waste; and to undertake its own reviews—as it has already done with regard to chimpanzee use—to inform strategic and cost-effective decisions about its project areas. 1. P. Pound, M. Bracken, BMJ doi: 10.1136/bmj.g3387 (2014) 2. NIH (2013): http://dpcpsi.nih.gov/council/pdf/FNL_Report_WG_Chimpanzees.pdf 3. Institute of Medicine (2011): http://www.nap.edu/catalog.php?record_id=13257 4. J. Bailey, ATLA 42, PMID:25413291 (2014) 5. A.Z. Akhtar et al, Rev Neurosci. 19, PMID:18561820 (2008) 6. M. Leenaars et al, ALTEX 32, PMID:25863034 (2015)

Compatibility of the framework with the broad scope of the NIH mission

We are encouraged to see the inclusion of disease prevention, human-based studies, clinical research methodologies, and data science in the Framework and, given the documented failure of animal models of human disease, are confident that these human-relevant avenues will yield findings that will “enhance health, lengthen life, and reduce illness and disability,” in accordance with NIH’s mission. To this end, we would encourage NIH to direct greater funding into nonanimal research methods—for both its intramural and extramural programs. We also agree with emphasis in the Framework on the importance of basic science discoveries. - While basic science studies using animals may be beneficial for the species being studied—in veterinary medicine, for example—benefits are unlikely when translating from one species to another. We therefore caution that reliance on animals to model human disease is not a cost-effective approach to promoting human health. - Moreover, we note that data obtained through animal experiments can only be substantiated with clinical studies. It would be prudent to forego animal experiments in favor of modern nonanimal technologies—using these more reliable methodologies prior to clinical tests. Furthermore, while “social responsibility” is central to NIH’s mission, we note the growing concern regarding the use of nonhuman primates in experimentation. As reflected in language included by Congress in the NIH’s budget bill for FY16 (1), there is considerable interest from Congress, researchers and animal advocates in applying greater ethical scrutiny to the use of nonhuman primates in NIH-funded experiments. Recent cases highlighting the need for this enhanced review include controversy surrounding NIH’s maternal deprivation experiments on infant monkeys at a Poolesville, MD laboratory (2) and abuses documented at NIH primate supplier Primate Products.(3) 1. <http://appropriations.house.gov/uploadedfiles/hrpt-114-hr-fy2016-laborhhsed.pdf> 2. <http://www.scientificamerican.com/article/cruel-experiments-on-infant-monkeys-still-happen-all-the->

time-that-needs-to-stop/ 3. <http://www.scrippsmedia.com/fox4now/news/Congress-wants-Primate-Products-probe-310747421.html>

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Several landmark studies have revealed critical differences in the manifestation of disease in humans and nonhumans. For example, a 2013 NIH-funded study used genomic analysis to determine that the genomic response of mice to inflammatory conditions has nearly no correlation to the genomic response in humans (1). In an excellent blog on the troubling findings of this paper, NIH Director Francis Collins wrote: “[W]hen it comes to molecules designed to target a sepsis-like condition, 150 drugs that successfully treated this condition in mice later failed in human clinical trials—a heartbreaking loss of decades of research and billions of dollars.” Dr. Collins added: “The NIH plans to commit \$70 million over the next five years to develop ‘tissue chips’—miniature 3-D organs made with living human cells—to help predict drug safety and efficacy.” (2) Investment in human-based (and therefore, human-relevant) technologies is absolutely critical in promoting NIH’s mission. We applaud NIH’s allocation of resources to these methodologies—and encourage increased funding of such human-based technologies, as even \$70 million pales in comparison to the 47% of the NIH’s \$30B budget currently allocated to projects involving experiments on animals, known to have an overwhelmingly low return on investment. Similarly, a 2006 NIH-funded study used confocal microscopy and multiple immunofluorescence to elucidate significant differences in the physiological and structural characteristics of pancreatic islet cells in humans and mice (3). The researchers concluded that “the composition of a human islet is so different than that of the rodent model, it is no longer relevant for human studies.” (4) We urge NIH to apply the insights of such breakthrough studies to funding decisions, rejecting projects where findings from the animal model will not be relevant to humans. 1. J. Seok et al, PNAS 110 (2013) 2. F. Collins, 2013: <http://directorsblog.nih.gov/2013/02/19/of-mice-men-and-medicine/> 3. O. Cabrera et al, PNAS 103 (2006) 4. <http://www.diabetesresearch.org/page.aspx?pid=409>

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

We agree with the unifying principle that the NIH should promote “scientific rigor and reproducibility.” To this end, we urge NIH to not only encourage uniform and robust reporting standards, such as those defined in the ARRIVE guidelines (1), but to require adherence to such guidelines in publications of NIH-supported studies. While poor experimental design and lack of transparent reporting are widely acknowledged as contributing to the failure to animal-based studies to translate to humans (2, 3), NIH is not presently safeguarding the public funds that it allocates to animal experiments by requiring, at the very least, clear communication in published studies of the study design, experimental procedures, animal housing and husbandry, statistical methods used, and the like. While many prominent journals have endorsed the ARRIVE guidelines (4), it is easily demonstrated through a simple perusal of articles in these very journals that the guidelines are not being implemented (5). As a result, comparisons of studies are substantially hindered and unnecessary studies are conducted. The ARRIVE guidelines were developed in consultation with the scientific community; but in order for the guidelines to fulfill their objective, funding agencies must develop policies requiring their use in the reporting of studies. While mandating the use of robust reporting standards, such as ARRIVE, will help address some concerns pertaining to scientific rigor and reproducibility, for the reasons noted in other sections of these comments, we strongly recommend that NIH direct greater funding into nonanimal research methods. 1. C. Kilkenny et al, PLoS Biol. 8, e1000412 (2010) 2. C.R. Hooijmans, M. Ritskes-Hoitinga, PLoS Med 10, e1001482 (2013) 3. S.C. Landis et al, Nature 490, doi:10.1038/nature11556 (2012) 4. NC3Rs, <https://www.nc3rs.org.uk/arrive-animal-research-reporting-vivo-experiments#journals> 5. D. Baker et al,

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

As noted in an earlier section of these comments, the scrutiny brought by NIH and the IOM to the issue of chimpanzee use in behavioral and biomedical research—revealing that such use was “largely unnecessary” (1) and “rarely accelerated new discoveries or the advancement of human health for infectious diseases” (2)—underscores limitations in the current system of oversight of experiments on animals. Both the NIH and IOM reports highlighted that harmful intramural and extramural experiments on chimpanzees continued to be approved, funded, and conducted for years despite there being superior alternatives in virtually every area where chimpanzees were being used invasively. It is clear that the system of oversight prevented adequate evaluation of the ethical concerns and scientific merits of projects involving chimpanzees. This same problem of impoverished review processes currently exists in the oversight of experiments involving other animals—resulting in the approval, funding, and execution of harmful experiments on animals where other methods might have been used. We recommend the inclusion of independent bioethicists in reviews of all intramural programs of animal experimentation—to ensure compatibility with NIH’s mission to promote the “highest level of scientific integrity, public accountability, and social responsibility in the conduct of science.” And, we reiterate our earlier recommendation that NIH undertake evaluations of the scientific necessity of all areas of experimental use of animals—to help inform the agency’s funding of intramural and extramural projects. Lastly, in light of the concerns raised in the earlier sections on the failure of experiments on animals to reliably translate to humans, we strongly recommend that NIH prioritize the funding of human-relevant technologies and research methodologies over animal-based studies. And we respectfully request that NIH allocate greater funds toward the development and implementation of nonanimal methodologies. 1. NIH (2013):

http://dpcpsi.nih.gov/council/pdf/FNL_Report_WG_Chimpanzees.pdf 2. Institute of Medicine (2011): http://www.nap.edu/catalog.php?record_id=13257

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The . . . is supportive of efforts that will truly improve research discovery and patient care; we do have a concern with the lack of emphasis on reducing the use, and need, of animal models within NIH’s strategic plan. It is the NIH’s mission to “seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability,” and we believe that some of the research being done on animal models may have been misleading due to the lack of translation to human or the lack of reproducibility. There are currently 7000 known human diseases, but only 500 have treatments, which is partially due to the lack of clinical translation from animals to humans. The failure rate of drugs in clinical trials exceeds 90%, despite promising results from animal studies, and it requires an average of 13 years of testing and more than 1 billion dollars to see a drug become available to patients. Furthermore, according to a recent Bernstein report, over the past 60 years, drug approval rates have declined rapidly despite the large increase in investment. The number of new drugs approved per billion US dollars spent on R&D has halved roughly every 9 years since 1950, falling around 80-fold in inflation-adjusted terms. It is instrumental for the NIH, if we want to increase the amount of knowledge that can be translated to human, to address these

issues by being extremely critical of the value/lack of value of animal studies. One of the NIH's priorities should be to facilitate and finance the development and use of innovative human-specific tools and technologies as well as to require that animal models be used as a last resort.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

The continued emphasis on animal models engineered in attempts to replicate the human disease has been shown frequently to be unsatisfactory and can often fail and mislead research. We have seen a growing literature criticizing animal disease models and we would like to strongly encourage the NIH to invest in the development and use of new technologies in order to accelerate the understanding of diseases and identify new targets. Investment in additional animal models, as well as continued investment in existing animal models, is unlikely to result in the kind of progress needed to overhaul medical science. A recent publication by Langley highlighted the importance of utilizing existing, as well as developing and using new, tools in the field of Alzheimer's disease research. Several other publications, in the fields of (e.g. in asthma, stroke, Huntington's disease, sepsis, inflammatory disorders, autism, burns and trauma), have shown growing issues of reproducibility and relevance of the use of animal models. Investments in alternatives have led to the development of new technologies, such as the MIMIC system (Modular Immune In vitro Construct), which enables scientists at Sanofi Pasteur to test vaccines and drugs in an artificial human immune system. The NIH, the Food and Drug Administration (FDA) and DARPA (Defense Advanced Research Projects Agency) awarded Harvard's Wyss Institute a grant to develop organs-on-chips to study complex human physiology outside the body. This project holds great promise, including for personalized medicine and development of cures for rare diseases. We recommend to the NIH to act rapidly by making sure that funding is allocated to research based on human-biology models as well as the gathering of human information from research, including biomarkers and clinical trials, such as translational research that the National Center for Advancing Translational Sciences (NCATS) has been tasked

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

We strongly believe that the NIH should capitalize on all existing knowledge. The NIH should facilitate the collection of all existing information into a common database in a way that facilitates use of this information in disease research, for example by populating a "knowledgebase" of biological of inter-related pathways and diseases analogous to the Adverse Outcome Pathway concept that is revolutionizing chemical safety testing. The US Environmental Protection Agency, the European Commission's Joint Research Centre, and the Organization for Economic Cooperation and Development are working jointly on such a knowledgebase for toxicological applications. A similar approach for medical research is fundamental to maximally leveraging existing information to broaden our understanding of diseases, identify new targets and overall advance medical science. The NIH has initiated such effort through the Big Data to Knowledge (BD2K) and would greatly benefit from collaborating with the US EPA and the Europeans counterparts already working on such efforts.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

To facilitate the dissemination of information on available non-animal methods we encourage the NIH to create a webpage which would list the technologies available within NIH but also new technologies used by external labs financed by NIH. Some research areas that NIH could focus on, is the development of new tools to study neurodegenerative diseases. This is an area where NIH could work in partnership with the Department of Defense to create new models to study diseases such as PTSD, ALS, Alzheimer, Parkinson or addictions. Those models could also be developed to study neurodevelopmental diseases and disorders such as autism. Amyotrophic lateral sclerosis (ALS) research is a great example to illustrate the need for such new tools and technologies. To date, almost 20 years after the first gene associated with amyotrophic lateral sclerosis (ALS) was identified, and despite generous funding from the ALS Association and the NIH reaching nearly \$700 million just over the last decade, only one drug is available to patient. This drug is expensive and the benefits to patients are limited to extending their lifespan or time to tracheostomy by an average of three months. One of the main focus of research in ALS has been to recapitulate this human and complex disease in animal models, and obviously, even if we have learned a lot about the mechanisms of the disease the investment in animal models has not been successful and needs to be reevaluate.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Speech is one of the most unique features of human existence and communication. The power of speech cannot be underestimated as it defines who we are, our intentions, hopes, and beliefs. Although the neural mechanisms of speech and language have been a topic of investigations for centuries, we still lack the complete understanding of how the speech sound and our thoughts are transformed into a motor speech output. We understand quite well the mechanistic aspects of voice production at the level of the orofacial, laryngeal and respiratory systems, but at the neural level, several aspects of speech production (and to lesser extent of speech perception) remain unknown. Unfortunately, being a unique human behavior, we face a major challenge in the use of animal models for understanding central control of speech production. Although various animals, like songbirds and mice, may be used for the studies investigating the molecular aspects of speech control, the only species that are able to speak are humans and those only can be used for the studies of complexity of brain organization controlling this behavior. The potential benefits from directing a major trans-institutional effort to this research arena are several, ranging from unraveling the multi-level neural hierarchy of speech control at the large-scale level to unraveling the pathophysiological bases of various neurological and mental problems, which impair speech production and lead to life-long disability and social isolation.

Compatibility of the framework with the broad scope of the NIH mission

Understanding of speech production has not to be limited to the mission of the NIDCD and ideally should be included as a trans-NIH mission. Although it has a direct relevance to the NIDCD's mission, speech-related disability and low quality of life are consequences of several neurological problems, such as Parkinson's disease, dystonia, amyotrophic lateral sclerosis, tremor, stroke, as well as psychiatric problems, such as schizophrenia, stuttering, Tourette's syndrome, multiple personality disorder, to name a few. In the majority of these disorders, the underlying bases of abnormal speech control are poorly explored and understood, due to which these patients do not receive an adequate treatment and, while in some cases their primary symptoms are managed through various treatment options, their speech impairments remain unattended. Furthermore, the paucity of basic knowledge about the control of speech production hinders our ability to develop novel therapeutic options for these patients. It is therefore critical to encourage research through different disciplines, which would potentially involve a

combined use of novel and multi-modal technologies and methodologies towards a common goal of understanding the neural basis of normal and disordered speech production. Inclusion of research on speech production within the framework of the NIH-wide strategic plan would be an ideal opportunity for future groundbreaking discoveries as well as for attraction and retention of new and brilliant scientific minds.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

As noted above, the human disability based on impaired speech production may result from neurological and psychiatric problems in addition to laryngeal dysfunction, and therefore cutting-edge research addressing the unanswered questions should also span across different NIH Institutes and Centers that deal with these types of human disability. On the other hand, a few recent research studies have clearly demonstrated that motocortical control of normal speaking involves not only 'low-order' processing of simple motor output but rather requires the complex orchestration of large-scale neural networks for production of a spoken word. Further multi-scale trans-NIH research is needed to match the efforts of a few individual labs across the country in elucidating the neural mechanisms underlying this uniquely human behavior, understanding of which would lead to defining the pathophysiological basis of a variety of speech-related disorders.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

The major research effort has been directed to the understanding of neural bases of speech perception and processing. Less attention has been given to speech production and its interactions with speech perception and cognitive features of speaking. This may be due, in part, to absence of animals models that can produce a meaningful speech as well as methodological challenges in accessing the motor aspects of speech control such as a more difficult access to the laryngeal muscles, the absence of the laryngeal representation in the primary motor cortex in other species than humans, and limitations in respect to the range of invasive studies that can be performed in humans. It therefore would be extremely important to define this research area within the scope of the comprehensive trans-NIH research themes, in addition to the defined mission of the NIDCD, which potentially will boost the interest in the scientific community and lead to the generations of new ideas and approaches for addressing the outstanding lack of knowledge about the central mechanisms of speech production.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

As delineated above, speech production cuts across different disciplines as its impairments result from various neurological, psychiatric and laryngeal problems. Therefore future areas of opportunities to investigate this complex behavior and understand the pathophysiology of its abnormalities would require a major and coordinated NIH-wide effort. Several new and emerging technologies can be applied for detailed investigations of speech production at the systems level in both healthy individuals and diseased human patients. Identified large-scale mechanisms underlying speech production in humans may lead to the development of new ideas about how to better translate and address the unanswered questions about its molecular, genetic and biochemical underpinnings using available and new animal models that share some of the characteristics of human speech production.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework
(*Submitter left answer blank*)

Compatibility of the framework with the broad scope of the NIH mission
(*Submitter left answer blank*)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan
(*Submitter left answer blank*)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine
(*Submitter left answer blank*)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan
(*Submitter left answer blank*)

Future opportunities or emerging research needs

I am not an American citizen but other countries like mine (Canada) will follow the example set by the US in this area. Advance Treatment/Cures--breakdown of traditional disease boundaries: 1. ME/CFS/SEID has no home within your institutes, partly because it is systemic with an as yet undiscovered cause. However, in Norway, 2 oncologists serendipitously discovered that the drug Rituximab, used to treat cancer & RA, also treats 2/3rds of ME/CFS/SEID patients (some have been in remission for 5 years after their last infusion). This aspect of your strategic plan would make this drug a perfect candidate to cross the boundaries of cancer & RA to treat ME/CFS/SEID patients who currently have ZERO approved treatments. 2. Why hasn't the successful NIH SOK for ME/CFS in 2011 produced an RFA? 3. Why has Dr. Lipkin's & Dr Ron Davis' applications been denied? Lipkin is studying a key area that applies across diseases-- the microbiome -- & Davis is studying molecular research -- one of your plan's objectives -- opportunities based on molecular knowledge.] Unifying Principles--Setting Priorities- incorporate disease burden - important but not only factor 1. ME/CFS /SEID is a relatively high prevalence disease with 50% of its sufferers (more than any other chronic disease) with such severe symptoms, they are rendered disabled & unable to work, often for LIFE, costing the economy billions. As time wears on, the comorbidities an individual acquires mount. Coroners have declared ME as a cause of death. Why is it not funded commensurately with both its high prevalence and high disease burden? 2. fostering scientific opportunity -- see info above re: Dr. Lipkin & Dr. Davis' rejected NIH applications. 3. consider value in eradicating pandemic -- ME/CFS is a relatively common disease, causing endless suffering & economic loss. Thank you for presenting your NIH Strategic Plan to the public -- your transparency is applauded.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework
(*Submitter left answer blank*)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

One priority (and hence opportunity) should be to re-evaluate our research training methodology to ensure that we maximize the potential of emerging talent to advance biomedicine in today's (and tomorrow's) world. (There is a similar need to re-evaluate our approaches to research; updating our approaches to training is an essential step in advancing research approaches.) Our current system of training is essentially an apprenticeship system, whereby the bulk of graduate and post-graduate training is undertaken under the supervision of a senior research scientist, with projects being defined by (and generally constrained by) the ongoing research program. From there the trainee tends to continue down this research road in the same or similar lab or departmental environment. It is rare for a trainee to have the opportunity to have the flexibility to rigorously investigate what opportunities might provide the most impact, to explore truly new ideas, and to strategically define and execute a research plan. Yet this is the type of thinking and execution that will enable innovative and insightful solutions to our most pressing problems. Current resources available from NIH for training programs are generally significantly smaller than those for research programs. Moreover they are generally integrated with, and therefore constrained by, the traditional training and research structure. Support mechanisms are needed which provide significant resources for innovative programs in training, including stipend, research, and administrative support to enable total flexibility and therefore innovation in the training approach itself. New concepts in training will lead to new concepts in the approach to research, which, if done right, will accelerate and expand our ability to provide the research advances that will effect improvements in patient outcomes.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Myalgic encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is long past due becoming an disease adequately funded and prioritized to the level of devastation it causes millions of Americans.

Compatibility of the framework with the broad scope of the NIH mission

The Institute of Medicine's report this year validated ME/CFS as a critical health issue of Americans, recommending increased research activity and funding.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Myalgic encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

A planetary system of ethics is a goal that has long been anticipated on the world scene today. Although organized religion has long been celebrated as the standard bearer for the promotion of a virtuous life style, the various conflicts afflicting many of the major world religions clearly expose the inherent weakness to such a simplistic interpretation. Ideally, a scientific foundation for such a global moral perspective should prove exceedingly beneficial. Here, a formal behavioral tie-in with ethical principles proves particularly effective for removing such cultural stumbling blocks. In particular, a foundation within behavioral psychology proves to be particularly effective: invoking instinctual principles shared in common as a human species (as well as the rest of animal kingdom) as general unifying themes. When expanded to include the more abstract human-cultural levels; namely, group and universal authority, the affiliated traditional groupings of virtues/values rightfully enters the picture. A radically new model of motivational behavior is currently called for, one that melds modern behavioral psychology with the long-standing traditions associated with value ethics: a trend encompassing the group, universal, humanitarian, and transcendental realms of inquiry. This comprehensive fusion linking instinctual conditioning with ethical philosophy permits the first such grand-scale synthesis of motivated behavior. The currently proposed motivation solution endeavors to provide the first clear dynamical understanding for the public, providing a grand-scale synthesis of the virtues/values in correlation with behavioral principles.

Compatibility of the framework with the broad scope of the NIH mission

The specific details for such an ethical achievement invoke the entire span of human culture as a ten-level hierarchy of personal, group, universal, humanitarian, and transcendental domains (comprising both authority and follower roles). Furthermore, this ascending hierarchy formally appeals to the schematic principles underlying Set Theory. Here, the elementary concepts of the one, the many, and the absolute are specified in terms of the personal, group, and universal authority realms, respectively. Each of these distinctive conceptual levels is further associated with its own unique complement of ethical/motivational terms. This master ten-level hierarchy of authority/follower roles is uniquely correlated with over two-hundred individual virtuous terms. The traditional ethical listings defined within this system all appear linked on an intuitive level, suggesting a clear sense of overall cohesiveness, the complete breakdown of which now will be described. The key conceptual innovation arises as a direct outcome of the fledgling science of Communication Theory, borrowing the crucial concept of the metaperspective. It is defined as a higher-order perspective on the viewpoint held by another: schematically defined as "this is how I see you-seeing me." The higher-order groupings of

virtues/values are ordered as subsets within this hierarchy of metaperspectives, each more abstract grouping building upon that which it supersedes. Take, for example, the cardinal virtues (prudence, justice, temperance, and fortitude), the theological virtues (faith-hope-charity-decency), and the classical Greek values (beauty-truth-goodness-wisdom). Each of these traditional groupings is further subdivided into four subordinate terms permitting precise point-for-point stacking within the hierarchy of metaperspectives. Additional listings of ethical terms can further be added into the mix: namely, the civil liberties (providence-liberty-civility-austerity), the humanistic values (peace-love-tranquility-equality), the mystical values (ecstasy-bliss-joy-harmony), etc. When taken in concert, the complete ten-level hierarchy of virtuous terms emerges in full detail. ---please see attachment for specific details---

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

This cohesive hierarchy of virtues, values, and ideals proves exceedingly comprehensive in scope, accounting for virtually every major theme celebrated in the Western ethical tradition. It is particularly easy to gain a sense of the increasing degree of abstraction when scanning the individual columns from top to bottom. The traditional sequences of terms line up seamlessly within this hierarchy of metaperspectives. Indeed, it proves exceedingly unlikely that this cohesive style of system could have arisen solely by chance. Furthermore, this ethical hierarchy mirrors the specialization of personal, group, spiritual, humanitarian, and transcendental realms within human society as a whole: which (when further specialized into authority/follower roles) accounts for the full ten-level span of ethical terms. The major groupings of virtues and values serve as the elementary foundation for the master motivational matrix. This grand-scale unification of ethical principles necessarily argues for a radical reinterpretation of the organizational principles currently under consideration. The key salient insight resides in viewing the individual as the rightful product of a diverse range of social and institutional influences. In addition to the most basic one-to-one style of personal interactions, the individual is further incorporated into a broad range of group contexts (namely, work, family, country, etc.), as well as an all-encompassing universal context. These distinctive contexts collectively summate into a unified authority hierarchy consistent with the theoretical principles governing the field of Set Theory. Set Theory remains in full agreement with the three-level model of the power hierarchy: with the unit set, the group set, and the universal set equating with the personal, group, and spiritual levels, respectively. ---please see attachment for specific details---

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

The two-stage interplay inherent to conditioning theory shares many of the attributes of a recursive style of process. Recursion is the process of repeating items in a self-similar way. It represents a procedure by which one (or more) steps of a process work to invoke a repetition of the procedure in the form of mental recapitulation. Recursion in linguistics involves embedding sequences within sequences (of a self-similar type) in a hierarchical structure through the process of reiteration. This process of embedding ideas within ideas is a skill that humans seem to acquire in an effortless fashion, perhaps the one true dividing line between the animal kingdom and human-kind. Such recursive ability enables humans to freely engage in mental time travel, recalling past memory episodes within present consciousness, and then employing this mental-map for imagining future potentialities as mental projections. Such advanced mental abilities appear to arise primarily through progressive increases in short-term memory and the capacity for hierarchical organization chiefly made feasible through incremental increases in brain development. This enters into broad number of cogent speculations concerning global applications for the master motivational system. Perhaps the most dramatic potential applications are an ethical simulation of artificial intelligence, the basis for two granted US patents

6587846 and 7236963 (now expired and in public domain). This novel innovation employs the systematic virtuous system of schematic definitions as a platform for programming of complex sets of ethical parameters. This innovation represents the first affective language analyzer incorporating ethical and motivational terms, serving in the role of interactive computer interface: enabling a computer to reason and speak in an ethical fashion and serving in roles specifying sound human judgment (such as public relations or security functions).

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

N/A -- all applicable

Future opportunities or emerging research needs

The higher-order paradigm of the alter ego state is further reminiscent of a similar concept pioneered in the emerging field of Communication Theory; most notably, the metaperspective format advanced by R. D. Laing and P. I. Watzlawick. In *Interpersonal Perception* (1966) Laing (et al) researched the dynamics of interpersonal communication, characterized as “the spiral of reciprocal perspectives.” In his *Pragmatics of Human Communication* (1967) Watzlawick (and associates) alternately focused upon the informational aspects of communication, defined as “the hierarchy of metaperspectives.” Both such formulations share a common theme; namely, communication between individuals is generally compounded by abstract “meta” messages defining how the relationship is to be conducted. The metaperspective, from the Greek meta- (above), is defined as a higher-order perspective on a viewpoint held by another: schematically defined as “this is how I see you seeing me.” Spontaneous forms of communication are objectified as formal objects of discourse, adding both content and context to a given verbal interaction. In addition to this preliminary class of meta-perspective, even more abstract perspectives are theoretically feasible, leading to what Communication Theorists term the meta-metaperspective. This more advanced perspective is one meta-level further removed from the more basic meta-perspective format, schematically defined as: “this is how I see you - seeing me - seeing you.” Indeed, there does not appear to be any barrier limiting the degree to which reflection can serve as a basis for itself, resulting in a multi-level hierarchy of meta-communication in general. This metaperspective format provides a schematic interpretation of the unified motivational hierarchy of authority and follower roles, an enduring format culminating in an un-precedented 10th-order level of meta-abstraction.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

. . . presents one broad comment as follows: While the specific feedback requested focuses on science topics/scientific themes, “Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine”, there is little to no mention of building stronger alliances or collaborating with other U.S. government agencies (FDA, CDC, etc.) or international research agencies. These could enhance NIH’s ability to identify “Future opportunities or emerging research needs”.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Agreement from the NCI to include a pediatric cancer expert on any study section reviewing a pediatric cancer grant application
Creation of a new Deputy Director for Pediatric Oncology at NCI
Annual report on childhood cancer research from NCI
Release of an advocate friendly explanation of the 4% level of support for pediatric cancer research
Convene a state of the science conference on childhood cancer or individual malignancies
Accounting from NIH regarding support for pediatric outside of the NCI
Improve dissemination of/creation of program announcements or RFAs to address unmet needs in pediatric oncology treatment/research

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

The . . . understands the critical importance of a vibrant NIH for the benefit of our health and our economy. We also support FDA, and especially the FDA's National Center for Toxicological Research (NCTR). NCTR has equipment, staff (150 PhDs) and facilities unlike any of our academic institutions. Moreover, it has 42 years of experience developing and qualifying biomarkers and working in the translational science realm. It is a resource that should be utilized more broadly. In our efforts to increase biomedical research collaboration across all campuses in Arkansas, we repeatedly find instances in which those researchers involved in translational research frustratingly tell us they could do much more if they had better access to the intellectual, equipment, and animal resources at NCTR. NCTR is most eager to collaborate, but program, staff and time constraints strongly limit the availability of their resources. In this situation, taxpayer-supported scientific capability is not being utilized to its fullest potential. As academic researchers apply for federal grants and also seek NCTR collaboration to optimize available resources, the collaboration is not possible due to the inability to obtain post-doctoral and other support. We understand fully that NCTR, as an HHS facility, cannot receive funds through NIH grants. However, in the spirit of the Congressional interest in finding ways to better utilize our national resources through collaboration and partnerships, we believe there is an opportunity for improvement. One possibility, although surely there are others, is an interagency agreement between NCATS and NCTR. Such an agreement could take many forms, one of which is a fund that would be available to NCTR if academic collaborators receive a grant relevant to the NCATS mission, and if approved by NCATS, NCTR would be able to utilize those funds for its expenses in supporting that grant.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity

that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

My son . . . diagnosed with medullblastoma 8/14 at age 14 underwent over a year of treatment that left him with severe side effects. He has hearing aides, doublevision, still has loss of balance/coordination and requires a cane to walk. There must be new treatments available to children to limit these side effects. These drugs are given until the child develops a problem. My son's treatment protocol was over 25 years old. We still do not know what the future will hold. . . is 16 now but I still worry everyday. It is extremely important to provide more than 4% to children. They deserve a future.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

We write in response to NOT-OD-15-118 to comment on the NIH's proposed emphasis on fundamental science, particularly regarding the growing importance of data science in biomedical research. Nearly every corner of biomedical research is being transformed by computational analysis of massive datasets generated through laboratory automation. The promise of data-driven biology, though, cannot be realized if we follow old paradigms that treat computation as a post-hoc service provided to experimentalists after hypotheses have been formed and data generated. The models and algorithms need to be considered from the earliest stages of every data driven study. Further, most of the machine learning methods used currently focus on supervised learning (i.e. classification), whereas in biology we are often interested in processes and networks that require unsupervised methods and integration of diverse datatypes. Bringing the NIH into the era of data-driven science requires a clear recognition that computational biology is no longer an obscure specialty but rather a core part of every aspect of NIH's mission. The recently launched BD2K initiative is an excellent start, but we think it is important to emphasize that truly innovative computation, instead of routine high-performance data processing and management, should be integral to data-driven research that NIH supports. We therefore encourage NIH to fund both small and large grants specifically focused on truly novel computational biology research that enables the creation of new knowledge. Our field now has decades of experience with computationally-driven biomedical research and trained a generation of scientists at the intersection of computation and biology. We also recommend that NIH implement evaluation efforts towards ensuring that project leadership has necessary computational biology expertise and that the outcome of computational analyses are recognized as results themselves and not simply as the basis for experimentalists to hypothesize and perform anecdotal validation.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity

that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

The analysis of electronic health records is an area of opportunity that has not been realized to its full potential.

Future opportunities or emerging research needs

Funding is needed to support research on common diseases that are transmitted in high-risk families. These disorders do not meet the definition of a rare Mendelian disorder or a common complex disorder. However, the study of these families could inform both fields of research. Currently, there are no funding opportunities available to support this kind of research.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

• The . . . community strongly supports acknowledgement of the importance of fundamental science and the inexact nature of predicting which avenues of investigation have potential to provide conceptual leaps. A clear example from our field (the chemical senses) is the discovery of chemoreceptors in the gut and airways, discoveries which have implications for understanding digestive problems, obesity and diseases such as asthma. These discoveries were totally unexpected and arose from understanding the basic molecular nature of taste receptors. • The . . . community also champions efforts to enhance stewardship, particularly in recruiting and retaining an outstanding workforce and encouraging innovation and new partnerships. We emphasize that it is vital to maintain a continuous

stream of new investigators by facilitating the efforts of junior investigators in obtaining initial funding. It is also critical to continue to reduce administrative roadblocks and burden. • A broad pool in the grant reviewer population facilitates support of diverse ideas as does the support of grants funded by the RO1 mechanism

Compatibility of the framework with the broad scope of the NIH mission

- The . . . community considers the framework compatible with the scope of the NIH mission.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

- Take advantage of the changing landscape in scientific communication, including social media, to provide new opportunities for interaction
- Take advantage of advances in measuring behavioral, psychophysical and physiological function to stimulate scientific progress.
- It would be advantageous to generate new, discrete funding and review procedures for initiatives that cross the silos created by traditional institute boundaries. This has great potential to generate novel ideas to address complex biological problems, including preventing and curing disease. These should not compete with the efforts of individual institutes but rather complement interactions between them.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

- Approaching problems at multiple levels-- clinical and molecular, psychophysical and neural is vital for facilitating integrated progress. In the chemical senses, there is a clear need for integration between psychophysical and neural approaches to advance the field.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

- The . . . community did not note any Areas of Opportunity that were not applicable

Future opportunities or emerging research needs

- A concerted approach to understanding where eating, over- and under-eating, addiction, sensory responses, and food marketing coalesce could bring new concepts to the global problems of obesity and inadequate nutrition.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

My responses relate to the NIH's principles of Enhancing Stewardship (ES). One aspect of (ES) is actually researching processes and policies related to the Biomedical Workforce. The NIH needs to engage the research community through funding research on the Biomedical Workforce and its diversity as well as understanding how NIH actions affect the Biomedical Research ecosystem.

Compatibility of the framework with the broad scope of the NIH mission

The framework seems sound. However, I feel the NIH needs to make a commitment to funding research about the biomedical workforce.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

The NIH needs to study whether its policies actually: 1) promote the recruitment and retention of an

"outstanding biomedical workforce"; 2) enhances workforce diversity; and 3) whether peer review actually results in funding the best science. The Enhancing Stewardship principles can only be realized by providing access to NIH administrative data to researchers and funding research projects related to these important goals.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

The NIH needs to study whether its policies actually: 1) promote the recruitment and retention of an "outstanding biomedical workforce"; 2) enhances workforce diversity; and 3) whether peer review actually results in funding the best science. The Enhancing Stewardship principles can only be realized by providing access to NIH administrative data to researchers and funding research projects related to these important goals.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

As recommended previously, the NIH needs to fund research about the biomedical workforce and how NIH policies and procedures affect the biomedical workforce.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The . . . appreciates the opportunity to comment on the NIH Strategic Plan. We are . . . through research, education and prevention, and we represent a multidisciplinary group of scientists including basic and applied researchers, clinicians, epidemiologists and public health professionals. For many years, we have shown the importance of translational research in prevention of Our . . . is also a member of the Federation of American Societies for Experimental Biology (FASEB) and fully support their comments. We agree that investigator-initiated research has been the major driver of progress in biomedical sciences for many years, and we hope that funds will not be diverted from basic research which provides the foundation for biomedical sciences. We believe supporting fundamental science is important and are pleased to see this emphasis in the new strategic plan. Likewise, because discoveries are occurring rapidly, there is a need to be nimble and adaptable in setting priorities. NIH needs some flexibility in being able to respond and we are pleased to see this captured in the strategic plan.

Compatibility of the framework with the broad scope of the NIH mission

We believe the framework is compatible with the broad scope of the NIH mission.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Because many adult diseases have been linked to exposures during development, we hope that the strategic plan will emphasize research into the developmental origins of adult disease along with the importance of understanding how to prevent birth defects and developmental disorders thus improving life-long health.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

No additional comments.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

No additional comments.

Future opportunities or emerging research needs

Developmental origins of adult disease. Thank you for the opportunity to provide feedback on the NIH Strategic Plan.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Although the current framework provides a clear path for fostering biomedical research, we fear this is not the case for the broad trans-disciplinary field of public health. While biomedical research targeted at improving the early diagnosis and effective treatment of diseases are important, we would like the framework to incorporate the critical role of population-based, interventional research as well. In-so-doing, we hope that the NIH's strategic-plan would support more projects in public health, global health, occupational health, and the impact of climate change in health.

Compatibility of the framework with the broad scope of the NIH mission

To address the broad scope of NIH's mission and meet its benchmark of "extending healthy life and reducing illness and disability" we believe the framework should be all inclusive. For instance, in order for NIH to "enhance stewardship of the research enterprise", NIH is encouraged to stimulate and support trans-disciplinary collaboration between the biomedical research workforce and public health researchers.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Health care providers are expected to have a broader knowledge of newly emerging problems. The recent Ebola crisis and H1N1 pandemic clearly demonstrated that this expectation is far from reality. With climate changes, population dynamics, poverty, and increasing global disparity levels, these variables make borders and conventional separation between developed and developing countries less effective. The medical and public health community must continue to integrate their efforts in a global scale to address the health challenges in low- and middle-income countries as well as the developed world. This integration is one of the largest task for academic public health institutions, governmental and non-governmental organizations during the 21st Century. We believe NIH, through its mission, to play a

more visible role in the emerging field of global health. We believe it can help to shape the global health landscape (where research opportunities currently abound) by supporting high-quality, innovative public health research globally – in addition to its current support for biomedical research.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

... like that the proposed framework does not compete with the Institutes and Centers (IC) specific strategic plans. We also like that the current design emphasizes cross-cutting areas of research and challenges. Further, we believe it is appropriate to update the plan every five years. We are concerned that the current design does not more explicitly address trans-NIH support for behavioral and social science research (BSR). In the next iteration of the framework, we encourage NIH to emphasize opportunities and current support for BSR in all relevant sections, particularly in the overview and areas of opportunity sections.

Compatibility of the framework with the broad scope of the NIH mission

The current framework is flexible, enabling the Institutes and Centers to develop their own plans without conflicting with broader, trans-NIH principles and priorities.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

NIH IC support for behavioral and social science research is cross-cutting and should be more explicitly stated throughout the plan.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Numerous NIH ICs are supporting research regarding the early precursors of adult disease and disability. However, more research is necessary to fully understand how pre, peri and post natal development affects long-term health and well-being. We encourage NIH to consider addressing this research theme in the next iteration of the framework and plan.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

. . . is thankful that the NIH consistently recognizes the significant role that environment plays on health. NIH support has significantly increased the scientific understanding of this complex issue. Science that examines the intersection of bioscience and environment is a critical piece to a fully developed understanding of health and addiction issues. Examining these environmental links offers explanatory power for all levels of health including individual level explanations for the extension of human life, reducing illness, and reducing disability. In addition, research exploring the impact of environment on health helps local community members work with other local stakeholders to effectively design and promote effective interventions that apply to their specific community needs. Research is clear that community problem solving and intervention involvement are critical components for creating fully articulated, multi-level health systems in communities. Therefore, NIH support for research that increases the scientific understanding of the environmental/biomedical nexus is critical for a cross cutting strategic plan that creates and maintains healthy communities. Statements demonstrating the continuing NIH commitment, as listed under “Areas of Opportunity that Apply Across Biomedicine” in the RFP, might include the following additions to the current NIH language (additions noted with “ “): 1. Under the heading Improve Health Promotion and Disease Prevention- Importance of studying healthy individuals "and their environments". 2. Under the heading Improve Health Promotion and Disease Prevention - Evidence-Based interventions to eliminate health disparities "both upstream and downstream to include interventions examining how environment impacts these disparities". . . . truly appreciates the important work of NIH to help communities better understand how environment impacts health. On behalf of . . . looks forward to continue its work with NIH and its partners to create and maintain healthy communities.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

We recommend an additional area for consideration of priority-setting within NIH: addressing the needs of primary care physicians to deliver optimal care. Although the vast majority of health care of patients takes place in the primary care setting, the majority of research funding supports research of one specific disease, organ system, cellular or chemical process, and is not related to issues surrounding the totality of patients’ needs in primary care. The importance of what happens in primary care is crucial to improving care and outcomes, and reducing errors. Research is required on important topics such as how primary care services are best organized, how new technologies impact care, how to maximize and prioritize care, how to introduce and disseminate new discoveries to the practice setting and how patients can best decide how and when to seek care. A change in concept from disease to health-related research is needed to improve the lives of our patients. We recommend more emphasis on addressing the translation of scientific research into the practice of medicine. Understanding how to better organize health care to meet patient and population needs, including the integration of behavioral

healthcare, recognizing the impact of social determinants of health, evaluating innovations to provide the best health care to patients, and engaging patients, their families, communities, and practices to improve health has become critically important, and research in these areas must keep pace. It is not enough to state that it is important to study healthy individuals, advance early detection/diagnosis, and examine evidence-based interventions to eliminate health disparities. More attention is critically needed to transform clinical care in the primary care environment, where “real-life” patients live. This area should be a priority, and is ripe for NIH-wide research – cross-cutting the boundaries of the Institutes, Centers and Offices.

Compatibility of the framework with the broad scope of the NIH mission

The NIH Mission which discusses the application of knowledge about the nature and behavior of living systems to enhance health, lengthen life and reduce illness and disability is one we support wholeheartedly. We would like to see these concepts more clearly visible and more strongly developed in the strategic plan framework. In particular, the concept of enhancing health, rather than just reducing disease, is an important area to be amplified within the framework.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

In keeping with our description of the need for more research related to the transformation of the practice of medicine, we would recommend this framework should embrace a more global perspective of health, rather than simply medical cures. Under the section titled, “Improve Health Promotion and Disease Prevention” there is a need for an additional theme. Between community health and disease-centered biomedical research lies a gap that may be translational, but likely is far more expansive. This gap requires funding and should not only improve our understanding of individual health in the context of the rising epidemic of multi-morbid chronic disease, but also explore the increasing blurriness between pre-morbid disease and normal life experiences that suggest the wear and tear of human existence—which may not need to be medicated, examined by high cost imaging techniques, or placed within a disease model. There is no organizational structure within NIH to address across institutes the complexity of caring for this large segment of our population. Including a fourth concept for research into how to better organize health care to meet patient and population needs would be appropriate.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Training future investigators for primary care research: One piece critical to the successful engagement and development of primary care research is the constraint of not having an adequate cadre of well-trained researchers. We believe there is a need to deliberately promote this training with a concentrated program for the development of such researchers. Although NIH has researcher training mechanisms in place, which we believe are important, we think attention should be paid to revisiting them to retool so they can better prepare investigators for new research priorities, such as primary care research. Patient Quality and Safety in Non-hospital Settings: We are all aware of the research related to the many improvements in patient care in hospital settings, and the continued work in this area. Our

patients tell us that one of the key areas that is problematic for them is in the non-hospital setting. For example, the communication between specialist and patient and primary care provider is an area that needs work to understand how to improve. Improved methods for engaging patients in the management of their health conditions is a key area that needs further study. The voice of patients in the development of clinical practice guidelines remains a promise unfulfilled.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

. . . appreciates the opportunity to comment on the NIH Strategic Plan. . . . agrees with current NIH direction to keep advancing treatments for devastating diseases a priority and specifically that unprecedented opportunities open due to increased molecular knowledge.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Around 95% of drugs found safe in preclinical tests later fail during human clinical trials due to their toxicity or lack of efficacy. This leads to delays in approval and increased drugs costs. Improving clinical trials has been a priority in drug development, which has been achieved in large part due to the new standards of transparency, objectivity and consistency in research and reporting of results, established by Evidence-Based approach. . . . seeks to adopt the use of evidence-based approaches to toxicology and safety sciences , such as systematic reviews, quality scoring and meta-analysis tools, in providing a secretariat to the Evidence-based Toxicology Collaboration in the US and Europe. This extends to work toward Good Cell Culture Practice and in vitro methods reporting standards. Furthermore, in the strong belief that mechanistic approaches in the safety sciences improve human relevance, . . . steers the Human Toxome project, systematically mapping pathways of toxicity. . . . suggests NIH-funded research to advance disease cures should broaden to include a focus on establishing the objective criteria for evaluation of the predictive value of safety tests by expanding evidence-based approaches, good cell culture practices and in vitro reporting standards as well a our knowledge of Human Toxome, that will allow us to develop new human biology-based Integrated Testing Strategies based on in vitro, computational and organ-on-a-chip tests that more accurately predict human outcome and reduce clinical adverse events. Information obtained from this research would be of great value to industry, regulators, clinicians and public. Moreover, it will greatly increase the speed at which new human biology-based in vitro tests will get validated and adopted by all stakeholders, greatly increasing the speed of development and approval of safer and more efficacious drugs for human diseases. . . . urges NIH to include research on Human Toxome in its 5-year plan.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

My specific expertise is in food environments and retail-based interventions, and received my doctorate in city and regional planning, though am currently a postdoc at My dissertation research underscored the importance of NIH's efforts to "Improve Health Promotion and Disease Prevention" through "Evidence-based interventions to eliminate health disparities." Yet, it also revealed important shortcomings in current funding strategies for this research. My feedback outlines three main issues, and encourages a broader approach to collect better evidence on interventions to eliminate health disparities. First, the timing of real-world interventions (especially changes in the built environment) can rarely be coordinated with the precision of large-scale clinical trials. Issues like financing, zoning, legal challenges, or weather can expedite or stall a project for unanticipated reasons. Nonetheless, these issues are not necessarily exogenous to the health disparity or local environment. Research must be allowed to accommodate these changes (either by moving more quickly or extending the project), and, ideally, should also seek to study these changes as they occur, rather than write them off as variables to be controlled. Second, the metrics required by NIH determine study outcomes. When obesity measures are requested for investigations of new supermarkets in food deserts, obesity findings are reported, regardless of whether these metrics are reasonable for the intervention. If researchers had greater latitude in selecting outcome metrics, a better evidence base could be built. Third, built environment interventions are inherently interdisciplinary (beyond biomedicine), and could be funded for study as such. Possible partnerships with other granting agencies, such as NSF, could strengthen the presence of social science research in these investigations. When a supermarket fails to produce obesity reductions, social science helps explain why not, and may improve generalizability of findings. Thank you for your consideration.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework
(*Submitter left answer blank*)

Compatibility of the framework with the broad scope of the NIH mission

We agree with current NIH direction to keep advancing treatments for devastating diseases a priority and specifically that unprecedented opportunities open due to increased molecular knowledge. Around 95% of drugs found safe in preclinical tests later fail during human clinical trials due to their toxicity or lack of efficacy. Yet many millions of NIH funding dollars go into re-use of the same preclinical animal tests that over and over have been demonstrated to be not predictive of human outcomes. Cancer, Alzheimer's Disease, Parkinson's Disease are most vivid example. This leads to waste of NIH funds, inefficiencies in pharmaceutical industry, delayed approvals of new drugs, and devastating human costs of adverse drug reactions (ADRs). We suggests NIH-funded research to advance disease cures should broaden to include a focus on putting significant resources into development of predictive human biology-based in vitro and computational methods, their systematic objective evaluation and validation. These tests will allow us to develop new human biology-based Integrated Testing Strategies based on in vitro, computational and organ-on-a-chip tests that more accurately predict human outcome and reduce clinical adverse events. Information obtained from this research would be of great value to industry, regulators, clinicians and public. Moreover, it will greatly increase the speed at which new human biology-based in vitro tests will get validated and adopted by all stakeholders, greatly increasing the speed of development and approval of safer and more efficacious drugs for human diseases. Hence, we urge NIH to include research on in vitro efficacy and safety tests in its 5-year plan.?

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

In 2014 the US NRC issued recommendations for the use of Systematic Reviews (SR) pioneered by the Cochrane Collaboration (CC), for assessing evidence from toxicology for regulatory policy. This will address some of the most obvious problems in toxicology: an aversion to transparency and “cherry picking” of studies for review. As shown in the work of CC, decision-making has been advanced by SRs that adhere to transparency and clearly defined and validated methods for assembling ALL of the relevant literature, extracting and evaluating data with a priori criteria for identifying sources of systematic error (bias). We believe that evidence-based medicine approach that has been demonstrated to be revolutionary in clinical trials, should be applied to toxicology and NIH should demand that all studies, preclinical efficacy and safety included, adhere to these basic principles of good science.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(*Submitter left answer blank*)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(*Submitter left answer blank*)

Future opportunities or emerging research needs

(*Submitter left answer blank*)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Funding for the NIH-wide Strategic Plan must include a commitment to making childhood cancer research a high priority, with funding increased well above current levels. Pharmaceutical companies defer research and development for the pediatric oncology market for business reasons. The NIH/NCI continues to under-fund pediatric oncology projects in favor of adult cancers, many of which have lower-toxicity treatment regimens and very good outcomes. As a result, there have been no significant treatment advances for the majority of childhood cancers in the past 20 years. Outside of the leukemias, overall pediatric cancer mortality remains at 80%. For children who survive, side- and after-effects cause morbidity, suffering, and financial hardship during and after treatment. This is unacceptable. The pediatric cancer population has a right to expect due consideration of it's needs by the NIH. The NIH has a duty to meet these needs . Pediatric cancer research and development of new and less toxic treatments must be a priority, not word-service. Funding for pediatric cancer research needs to be increased well over the current 3.8% of total.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Funding for the NIH-wide Strategic Plan must include a commitment to making childhood cancer research a high priority, with funding increased well above current levels. Basic and applied research into pediatric cancers has potential implications for understanding adult cancers as well. Pharmaceutical companies defer research and development for the pediatric oncology market for business reasons. The NIH/NCI continues to under-fund pediatric oncology projects in favor of adult cancers, many of which have lower-toxicity treatment regimens and very good outcomes. As a result, there have been no significant treatment advances for the majority of childhood cancers in the past 20 years. Outside of the leukemias, overall pediatric cancer mortality remains at 80%. For children who survive, side- and after-effects cause morbidity, suffering, and financial hardship during and after treatment. This is unacceptable. The pediatric cancer population has a right to expect due consideration of it's needs by the NIH. The NIH has a duty to meet these needs . Pediatric cancer research and development of new and less toxic treatments must be a priority, not word-service. Funding for pediatric cancer research needs to be increased well over the current 3.8% of total.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

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morbidity, suffering, and financial hardship during and after treatment. This is unacceptable. The pediatric cancer population has a right to expect due consideration of its needs by the NIH. The NIH has a duty to meet these needs. Pediatric cancer research and development of new and less toxic treatments must be a priority, not word-service. Funding for pediatric cancer research needs to be increased well over the current 3.8% of total.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

The . . . urges that the National Institutes of Health (NIH) include in its proposed strategic plan framework:

- Increased study on the use of cognitive screening including an evaluation of impact and utilization of cognitive screening as part of Medicare’s annual wellness exam.
- Need to develop more accelerated capacity of Alzheimer’s disease research to take full advantage of proposed congressional funding increases (e.g. proposed 50% to 60% FY 16 increase in dementia research funding) at the National Institute on Aging.
- Continued research on evidence-based interventions and person-centered, team based care delivery models that to protect the physical and mental health of informal caregivers.
- Inclusion of the impact on federal health programs, financial burdens on families, and the number of impacted persons, including the number of caregivers, when determining “disease burden.”
- Increased cooperation with international researchers and private entities to share more data and increase coordination with other countries, academia and private philanthropies.
- Convene a working group of stakeholders, including patient advocacy organizations and nonprofit funders of Alzheimer’s and dementia researchers to develop possible frameworks and strategies for a direct public-private partnership to fund meritorious research proposals that are not supported directly by NIH.
- Enhance and expand innovative public-private partnerships like the Accelerating Medicines Partnership (AMP), as well as creating opportunities for pharmaceutical researchers to share data in a precompetitive space.
- Expand opportunities for clinical trial recruitment, including specialized education and outreach to women and minorities.

. . . appreciates the opportunity to present comments on NIH’s strategic plan. Please contact . . . if you have questions or need further information.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

We strongly support the proposed framework's statement and recognition that disease burden per capita is an "important" but not the "only" factor in determining NIH priorities. We strongly support the robust funding of research into diseases endemic to the United States, but it would be unwise and misguided to allocate research dollars simply on the basis of disease burden in the United States alone. Research investment also must follow and prioritize scientific opportunity that can have the greatest impact and contain and halt the spread of deadly and debilitating infectious diseases. Investment in research into infectious diseases is critical to the public health and security of our nation even if it transcends our borders. We applaud the views in the recent article by Dr. Collins and Dr. Fauci in *Science* entitled NIH research: Think globally. As Dr. Collins notes there "it would be unwise to deemphasize diseases that exact their largest toll elsewhere in the world." The recent Ebola outbreak and the rise of anti-microbial resistant strains of flu, gonorrhea and other pathogens underscore the potential for an infectious disease outbreak anywhere in the globe to present a threat to the United States. We also strongly support and agree with the framework's statement that the NIH prioritization process should consider the value of eradicating an epidemic. NIH research is directly responsible for saving millions of lives through AIDS research, and is on the road to an HIV vaccine and a cure that place us on the path toward ending the devastating scourge of the HIV/AIDS epidemic. The failure to continue and accelerate that work has severe consequences. Ending the HIV/AIDS epidemic would benefit not only Americans, but also tens of millions of people across the globe. It would also serve and strengthen the larger global humanitarian and development interests of

Compatibility of the framework with the broad scope of the NIH mission

We note that the framework highlights the importance of "evidence-based interventions to eliminate health disparities." The engagement and understanding of key populations living with and at risk of acquiring HIV infection is essential to elimination of health disparities in all prevention and treatment. Treatment and prevention require application of a variety of population-specific, evidence-based strategies in combinations that will have maximum impact on the epidemic. Research that generates answers about synergistic use of multiple new treatment and prevention strategies must address their application in those populations most at risk. For example, the recently updated National HIV/AIDS Strategy identifies certain communities as suffering from health disparities and prioritizes those populations for intervention. Additional behavioral research is necessary to develop interventions that are specifically aimed at addressing health disparities to key populations, and that have proven effectiveness in engaging them. Social science-based research is needed for the development and assessment of prevention interventions to address structural factors associated with vulnerability (and, conversely, resilience) to disease.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

The Office of AIDS Research (OAR), located within the NIH Office of the Director, coordinates the scientific, budgetary, legislative, and policy elements of NIH HIV research. The OAR, in its role as a planning and coordinating body, exemplifies the type of cross-cutting trans-NIH planning mechanism that might serve as a model for key NIH research priorities.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

We are concerned that the proposed framework does not directly address NIH involvement in Implementation research. Today, there is an urgent need for smart and accelerated "implementation

science” agendas across disease areas that lay out strategic plans for maximizing the impact of multiple new prevention and treatment interventions. Implementation research should be viewed as an integral component of the NIH’s focus on translational research, fitting well within with the goal of translating recent AIDS research into high-impact interventions through implementation of available biomedical prevention tools and treatment strategies. The framework notes the importance of breaking down traditional disease boundaries. This may be best accomplished by recognizing the cross-cutting nature of research on specific diseases. A recent article about Alzheimer’s research notes that research in that area has implications for other diseases. Similarly, new investments in AIDS research fuel biomedical advances and breakthroughs that will have profound benefits far beyond the AIDS pandemic. Researchers have applied AIDS research methods and findings to studying and treating other serious conditions, such as cancer, and hepatitis B and C virus. AIDS research also pays extensive dividends in many other areas of basic biomedical research, including deepening our understanding of immunology, virology, microbiology, molecular biology, and genetics. AIDS research is helping to unravel the mysteries surrounding so many other diseases because of the pace of discovery and the unique nature of HIV. AIDS research continues to make discoveries relevant to other infectious, malignant, neurologic, autoimmune, and metabolic diseases, as well as to the complex issues of aging and dementia. Drugs developed to prevent and treat AIDS-associated opportunistic infections now benefit patients undergoing cancer chemotherapy and patients receiving anti-transplant rejection therapy. AIDS research also has advanced understanding of the relationship between viruses and cancer.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

As you move forward in identifying priorities, we suggest you consider an emphasis on the following areas of AIDS research: • Gaps in targeted HIV prevention and engagement and retention in HIV care and treatment in children and adults. • Co-morbidities associated with HIV disease progression-- including aging-associated diseases that are increasingly prevalent in people with HIV--that can improve health outcomes in children and adults. • An HIV cure. • Improved HIV testing technologies, making them capable of detecting the earliest infection. • New potential biomedical prevention approaches including vaccines and long-acting ARV-based prevention.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

As detailed in our responses below, the Framework includes many points that will further the NIH mission. Advances in clinical methods and technology will drive progress in fundamental science and molecular knowledge that can be translated into new treatments and cures, while data science will improve the efficiency of this process. However, we are very concerned that the current system of awarding grants perpetuates the outdated reliance on irrelevant animal research which impedes progress, causing unnecessary suffering for both animals and people. We recommend prioritizing the awarding of grants for human-relevant, nonanimal research and training in nonanimal methods. This will support efforts already underway at regulatory agencies, strengthening partnerships that NIH can draw on for relevant expertise.

Compatibility of the framework with the broad scope of the NIH mission

The NIH mission is to support research into fundamental knowledge about living systems in order to

extend healthy life and reduce illness and disability, and the Framework identifies fundamental science as the foundation for progress. At the same time, FDA has noted that 92 percent of drugs that are shown to be safe and effective in animal tests fail in human trials. While animals are indeed living systems, knowledge gained from their study is translated into new treatments and cures for people with only very limited success. Given the currently broken system, NIH should focus its efforts on advancing science with the goal of enabling preclinical tests to be based on human biology, which will better predict results in human volunteers and patients in clinical trials. The Framework also includes the application of molecular knowledge to further the NIH mission. A current trend in toxicology is the elucidation of “adverse outcome pathways”, series of events beginning at the molecular level and proceeding through cellular, organ, individual and population levels, that result in adverse outcomes. This approach can be broadened to include the investigation of illness and disability that are not caused by toxicity.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

The NIH Revitalization Act of 1993 directs NIH to support research into methods of biomedical experiments that do not require the use of animals, reduce the number of animals used, and produce less pain and distress; it also calls for training scientists in the use of these methods. These mandates are conspicuously absent from the Framework, despite their being consistent with the NIH’s stated goals of promoting technology to advance fundamental science, harnessing data science to increase efficiency, ensuring rigor and reproducibility, and enhancing the research workforce. Recently, ICCVAM embarked on a new direction which includes member agencies taking a more active role in activities that include establishing means to measure progress in replacing, reducing, and refining the use of animals (3Rs) and creating a 3Rs roadmap for the US. As an ICCVAM member agency, NIH should be an active participant in these efforts.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

In its 2007 report, Toxicity Testing in the 21st Century: A Vision and a Strategy, NRC observed that toxicity testing was poised to take advantage of advances in toxicogenomics, bioinformatics, systems biology, epigenetics, and computational toxicology in order to transform toxicity testing from a system based on animal testing to one founded on in vitro methods that evaluate changes in biologic processes using cells, cell lines, or cellular components of human origin. With programs such as ToxCast and EDSP21, regulators are taking the first steps toward realizing NRC’s vision. Such a transformation would equally benefit the search for treatments and cures to extend healthy life and reduce illness and disability. While the Framework acknowledges the importance of technology leaps, data science, and molecular knowledge, NIH perpetuates the outdated reliance on animal research through the awarding of grants, despite the documented failure of these methods to further its mission. NIH must instead prioritize the funding of human-relevant, nonanimal research and award training grants in these methods. Peer review boards should always include investigators with expertise in nonanimal methods, and existing awards should be periodically reviewed. NIH can draw on the expertise which already exists

within regulatory agencies including EPA, FDA, and NIEHS.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Looking for information on how only funds are distributed by NCI and how it justifies only 4% being allocated to research Childhood Cancer. Also, looking for information as to why children with Cancer, upon their death, do not list "CANCER" as the cause of death. Knowing how the use of treatments meant for adults affect their tiny bodies, of course their internal organs are affected (among other issues), but the underlying / root cause is the Cancer. Does the listing on the death certificate affect the metrics used by NCI in their funding?

Compatibility of the framework with the broad scope of the NIH mission

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Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

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Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

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Future opportunities or emerging research needs

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Potential benefits, drawbacks/challenges, and areas of consideration for the current framework
(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission
(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan
(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine
(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan
(Submitter left answer blank)

Future opportunities or emerging research needs

My healthy 12 year old son was diagnosed with Medulloblastoma. His pediatricians missed the opportunity to have an MRI because he had no prior illnesses. After a 10 month battle and an additional year of recovery he is adjusting to life in his new normal. At his 9 month MRI and oncologist followup a blood test came back confirming that he is positive for APC gene mutation which is linked to Medulloblastoma and puts him at a extremely high risk for colon cancer now and for the rest of his life. My comments to you are can we put some time into the 5 year plan to discuss gene mutations so that there could be early testing. Since children have limitations in the drugs being offered to them it puts them in an even higher risk for premature death. Pediatricians need to be informed continually on the early warning signs of these fast growing cancers. Thank you for your efforts toward pediatric cancer. It's devastating and heartbreaking to see them suffer with so few options.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework
Potential benefits are data science and breakdown of disease boundaries. This breakdown of boundaries should also encompass crossing borders of scientific disciplines, in order to gain the win-win situation in developing new knowledge based on combining already existing knowledge from different backgrounds. Systematic Reviews and meta-analyses of already published animal studies are useful to make better choices of animal models and predictions on efficacy and safety of new treatments for humans. In case also individual data of animal studies are stored, just like human clinical trial data, translational meta-

analyses become possible, which can then provide statistical proof whether animal data can really predict the comparable human situation that has been modelled.

Compatibility of the framework with the broad scope of the NIH mission

Seems fine. A matter of concern is the current low quality of reporting of animal studies in scientific journals: in about 80% of the publications of animal studies e.g. randomisation and blinding are not mentioned. Also many experimental details are not reported, which makes a reliable interpretation difficult. NIH should make conditions that projects that are funded must publish all details of the (animal) studies performed, in order to safeguard good use for money.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Synthesis of evidence methodology, Systematic reviews and meta-analyses methodology are methods that lead to new knowledge based on already existing data/knowledge. By its nature, it requires a crossing of boundaries of the different disciplines, leading to scientific crossfertilisation.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Translational systematic reviews and meta-analysis

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

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Future opportunities or emerging research needs

Synthesis of evidence Systematic Reviews and

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Goal 3: Advance the Health, Safety and Well Being of the American People Recommended New Objective: Develop programs to fully utilize the investment in biomedical and Health Disparities Research to create business and employment in all American communities with goals to increase the numbers of woman and minorities owning biomedical businesses and incentives to locate more biomedical businesses in and around predominantly minority communities. The White House Lab to Market Interagency Summit, stated it is “imperative that the US optimize its investment in Federally Funded Research to benefit public health and wellbeing, create jobs and economic value.” The current plan does not have provisions for minority communities to economically benefit for the Federal investment in health disparities biomedical research. Therefore, minorities are basically consumers of new discoveries with very little chance to own the companies or working in the industry that creates solutions for health disparities... Goal 3: Advance the Health Safety and Well Being of the American People Amend Objective E: Reduce the occurrence of infectious diseases by fully utilizing the nation’s minority serving institutions to facilitate local relations with host countries based on the native country the institution represents. Goal 5: Strengthen the Nation’s Health and Human Service Infrastructure and Workforce Amend Objective B: Ensure the nation’s health care workforce can meet increased demands. The nation must fully invest in minority serving institutions to develop strategies that provide different venues to attract and develop health care and biomedical researchers.

Compatibility of the framework with the broad scope of the NIH mission

Inclusion of woman and minorities prepares diversifies the workforce and prepares the nation to compete in 21st Century global economy.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

None.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Biomedical research should economically benefit every American community.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

None

Future opportunities or emerging research needs

Not applicable.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

I would like to see more emphasis put into research for Childhood Cancer. I became a nurse in 1975. My husband got Leukemia 2 years ago. Because of this, we were at MD Anderson Hospital for 8 months while he had treatments. It was there that I saw so many children being treated for various cancers and learned just how disportionately the research money is given for the adults and children. My brother-in-law died from ALL in 1978, as a teenager. I couldn't believe that we have made such strides in the adult cancers and are so far behind in any new drugs for Children's Cancer. I truly believe we must make this a priority. Thank you

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

In the two and a half years we've been a peds onco family, we've said "see you later" to over 30 of my daughters, her fellow fighters. Our pleas are falling on deaf ears. Our children NEED more funding! Please make our children THE priority! Our kids are our future. Hearing your four year old beg you to promise her she's going to heaven shatters your world. Having to tell her that her friends have died...there are no words to describe the heart break. As a parent, advocate, mother, and human-please, I beg, don't let any more children suffer the way so many have. My daughter was that 1 out of 46 diagnosed daily. Wilms Tumor was first diagnosed in 1893. There is no excuse for not having a 100% effective treatment but we have cars that park themselves. March 11, 2013 we were a normal, typical, healthy family. March 12, our worlds crumbled around us. None of us want this for you or your children. We NEED more funding!

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

childhood cancer research needs more attion than it gets. these kids deserver more than any 4% they are dying daily from cancer. using 30 year old chemo for these kids is very unfare. what if it was your child or grandchild you sure wouldnt want them using it on them. its time to give more to the future of the world which is the children. #more than 4%.

Compatibility of the framework with the broad scope of the NIH mission

#more than 4% FOR CHILDHOOD CANCER THEY DESERVER IT

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

#MORE THAN 4% FOR CHILDHOOD CANCER

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

#MORE THAN 4% CHILDHOOD CANCER

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

#MORE THAN 4% FOR CHILDHOOD CANCER

Future opportunities or emerging research needs

#MORE THAN 4% FOR CHILD HOOD CANCER

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The NIH is the largest funder of research for children, adolescents, and teens with cancer. Currently death results in 1 in 5 children diagnosed with cancer, and remains the top killer of children by disease. A vast majority of the 500,000 survivors of childhood cancer predicted by 2020 will suffer substantial physical and psycho-social long-term effects. The average age of diagnosis for children with cancer is age 6. Those who die represent many decades of lost life. Those who survive with long-term health effects have equally many decades to live with the results of their treatments: emotional difficulties, second cancers, reproductive and sexual development problems, growth, learning and memory problems, heart problems, respiratory problems, dental, hearing, and vision problems, and digestive system problems. These many health issues meet the criteria of consideration for inclusion in any trans-NIH strategic plan. Most children with cancer are treated in COG hospitals. Children with cancer are heavily dependent on government-funded research rather than industry sponsored for breakthroughs in treatment and the NIH is our best hope for the future. With that in mind, IT IS IMPERATIVE THAT THE NIH RECOGNIZE CHILDHOOD CANCER AS A NATIONAL PRIORITY. Opportunities to elevate childhood to a nation priority include: Agreement from the NCI to include a pediatric cancer expert on any study section reviewing a pediatric cancer grant application Creation of a new Deputy Director for Pediatric Oncology at NCI Annual report on childhood cancer research from NCI Convene a state of the science conference on childhood cancer or individual malignancies Accounting from NIH regarding support for pediatric outside of the NCI Improve dissemination of/creation of program announcements or RFAs to address unmet needs in pediatric oncology treatment/research.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The 5 year NIH-wide Strategic Plan is of great interest to me personally, as I lost a 16 year old daughter to thyroid cancer in 2010, and subsequently founded and direct a 501(c)3 non-profit dedicated to making a difference for families with a child diagnosed with cancer. My involvement in the Coalition Against Childhood Cancer (www.CAC2.org) is also a direct result of my personal experience and passions.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

It is imperative that NIH not only increase funds for childhood cancer research, but make it a national priority. Too few funds have been devoted to researching childhood cancer treatments and medications. While many childhood cancers are "rare" based on number, their impact is far reaching when the number of years are considered.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Childhood cancers need to be made a national priority. Most of the treatments that exist are over 40 years old and are extremely toxic and damaging to a child's growing body.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity

that Apply Across Biomedicine
(*Submitter left answer blank*)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan
(*Submitter left answer blank*)

Future opportunities or emerging research needs

Childhood Cancers are the number 1 disease killers of children. The NCI needs to allocate more than 4% of its budget to childhood cancers. Some childhood cancers, such as DIPG, have no treatment, and no cure.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework
suggest clarification whether the strategy is for guiding the priority goals for the next 5 years, or whether the strategy applies to a longer-term framework (given that the last 'strategy' was more than 5 years ago) if for the next 5 years, then milestones or attainable goals could help make the case to Congress and the American people

Compatibility of the framework with the broad scope of the NIH mission
(*Submitter left answer blank*)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Re focus area-II: •Improve Health Promotion and Disease Prevention ?Importance of studying healthy individuals NOTE: this will be inaccurate without studying developmental programming of health as well as adult-onset disease ?Advances in early diagnosis/detection NOTE: this is an old concept which could be more successful with better understanding of developmental programming of adult onset diseases - and health Contrary to the view expressed by Discussion leader during webinar on Aug 6, fetal basis or developmental programming of adult onset diseases, (as well as health) is not just a 'granular focus' but should be in the strategy - just like Data Science suggestion: this should be discussed further

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

see above

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan
(*Submitter left answer blank*)

Future opportunities or emerging research needs

Developmental programming of adult onset diseases and health needs to be studied comprehensively - and not just confined to 'fetal stage', but to include pediatric age by the time early diagnosis and detection is attained in adulthood, it may be too late to gain significant prevention

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

The US government seems to find that saving children withN is an unworthy cause and only allocates 4% of a billion dollar tax funded research budget to further pediatric cancer research. The directors of the National Cancer Institute (NCI) and National Institute of Health (NIH) have created a new type of medical research called the “trickle effect.” We only use it on our children and this way of thinking incorporates the idea that if it works for adults with cancer it should work with children who have cancer. Here is just one problem with this cheap way of curing cancer, you will not meet one adult fighting infantile leukemia. This rare form of pediatric cancer only affects children, specifically babies, and this is just one form of pediatric cancer that adults do not get. Please remember that children are not small adults and allocate more than 4% of funding to research saving their lives...as THE CHILDREN are our future...let's give them a better chance at one.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

As part of the strategy to reduce health disparities, there is a need to continue the MHIRT program of the existence of health disparities in other parts of the world. MHIRT participants may help identify effective approaches to reducing health disparities.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

I am a taxpayer and citizen of the United States. But more importantly, I am a parent, a parent that has lost a child to cancer. It is for that reason I am compelled to write this. I am not a scientist, so I can only speak from my knowledge and experience. I can speak of how my daughter died of cancer at the age of 8. It was not until my daughter was diagnosed that I realized how little was being done to find a cure for childhood cancers. In addition, with survival, children often live with life threatening side effects from the treatments used to cure their cancer. Childhood cancer is the #1 killer by disease of our children in this country. I am not a grant writer, but I write as a parent that has experienced firsthand the results of the lack of research, discovery of new medicines and development of improved treatments for childhood cancer. It is for this reason that I ask that there is an increase in the funding and research for childhood cancer. As the leading cause of death by disease in our country, with incidence that is steadily increasing, childhood cancer needs to be made a national priority.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Childhood cancer is the #1 killer by disease of kids in our country. The incidence of childhood cancer is steadily increasing. Although there has been progress in some areas, many types of childhood cancer continue to have a grim prognosis. And for those cancers that have better cure rates, there is little if anything done to improve the cure rate. Our children are dying, being treated with medicines made for adults and even with survivorship, children suffer with horrible side effects from their treatment. Childhood cancer is in dire need of greater funding and research, and as it is the #1 killer by disease of kids in our country it should be made a national priority.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Please increase funding for childhood cancer research. It's a national disgrace that only \$.04 of every research \$1.00 goes to pediatric cancer.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

There is an urgent need to move away from incremental to transformative transdisciplinary research by applying information biology approaches that include modeling, big data analytics and portal science for guiding the design of pre-clinical, mechanistic and clinical efforts. However, modeling complex biological systems requires multiscale modeling frameworks and substantial computational resources, robust calibration databases and validation studies. Informatics technologies are evolving at an unprecedented rate and analytical tools and techniques need to be redesigned and customized at the same pace. To address these challenges, techniques, models and tools have to be developed to be versatile, modular, robust, and scalable. In essence, modeling multi-layered and massively interacting systems that span several orders of spatiotemporal magnitude will only be possible if proper methods and infrastructure is used in the process, and the model predictions are appropriately validated experimentally and clinically. Furthermore, the traditional research and funding mechanisms tend to favor supporting incremental research and therefore fail to provide support for revolutionary paradigm shattering discoveries. Projects that are designed to be high risk/high reward can catalyze an exponential growth in information biology and knowledge generation. Such projects should incorporate computational modeling components to drive non-intuitive hypothesis generation and novel research directions.

Compatibility of the framework with the broad scope of the NIH mission

In an iterative systems biology cycle, in silico experimentation guides wet lab research and leads toward often unpredictable discoveries that can advance the development of safer and more effective treatments while increasing the impact of data science and technological advances. This new framework for biomedical research is effective because it evolves around integrated teams of experts. The hypothesis generation and validation experiments are driven by domain experts, while models and

infrastructure are developed by computationally experienced researchers. Furthermore, it will be important that computational modelers work closely with domain experts to build strong predictive models that can be used for insightful *in silico* studies. At the fundamental level, technology leaps can catalyze advances at the clinical level and the latter stimulate biomedical progress and knowledge discovery. In essence, the focus on fundamental science has to be re-designed in the context of broader scope of the NIH missions and be revolutionary and groundbreaking; the steady increase in basic science knowledge provides only an incremental advancement that is ineffective and incomprehensible with the amount and quality of data than can be generated with today's technological means. Moving away from fundamental research to transdisciplinary research is urgently needed.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

In today's Big Data era biomedical research requires the collaboration of a team of scientists with different backgrounds and expertise including immunologists, cancer experts, physiologists, biochemists, molecular biologists, bioinformaticians, statisticians and mathematicians to solve important problems. In essence, there is a need to develop the new field of research that is at the interface of computer science and engineering as well as biomedical sciences and transcends all the above. Furthermore, for transdisciplinary research to work seamlessly and efficiently there is a need of bio and medical informatics and cyberinfrastructure that supports the collection of experimental data (*in vitro*, *ex vivo*, pre-clinical, and clinical) and metadata, the aggregation, analysis and visualization of this data and presentation of analysis results, the model building, calibration and analysis process, and finally the maintenance of quality assurance. There is also a need of computational resources to provide fast, efficient and secure access to data for analytical analysis, modeling purposes as well as large scale *in silico* experimentation. The cyberinfrastructure required to integrate computational modeling, Big Data analytics, portal science and procedural knowledge to engineer synthetic systems-wide information processing representations of biological systems has to have a number of features and capabilities, including customization, flexibility, and scalability as well as Interoperability. There is an urgent need to develop problem-solving teams of researchers that work in the interface of computational and biomedical sciences in ways that transcend both fields. For instance, the flexible and multi-disciplinary team at VBI—with experience in the creation of a very successful pathogen portal (PATRIC) as well as other user-oriented large data and model solutions through MIEP (www.modelingimmunity.org) —is uniquely positioned for creation of such centers.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Biological systems are highly complex and dynamic, self-organizing, and massively interacting systems that span several orders of spatiotemporal magnitude critical for the maintenance of homeostasis and health. Biomedical and clinical research has generally employed reductionist approaches that evaluate in detail the individual components of the system disregarding that they are an integral part of a greater set of networks. These approaches result in incremental knowledge discovery that fails to uncover complex, systems-wide mechanisms across scales or emerging context- and/or location-dependent behaviors. Computational modeling and informatics revolutionized the study of biological systems as massively interacting information processing units, from molecules, to cells, to tissues, to systems and populations. To efficiently probe emerging and non-intuitive mechanisms of action, information processing representations of systems-wide mechanistic interactions between cells, molecules and microbiota components can be engineered by integrating Big Data, multiscale networks and, importantly, procedural knowledge through mathematical formalisms. Development of disruptive information biology technologies driven by high performance computing (HPC), omic data analytic

capabilities, and large complex system modeling are crucial for guiding and underpinning experimental and clinical research. Systems biology enabled by HPC will drive the next generation of transformative biomedical and clinical research. Furthermore, with the advances in computational power and technological advances, experimental research is part of a larger iterative cycle of computational hypothesis generation to data analytics and accelerated path to cures for widespread and debilitating human diseases. The development of cutting-edge translational informatics platforms requires developing novel information biology methodologies, including data analytics, modeling, and portal science. Such translational platforms should be driven by domain experts and architected and deployed by cyberinfrastructure experts. Virginia Bioinformatics Institute (VBI) has the expertise and proven capabilities to lead a team to develop disruptive computational platforms that promote fundamental biomedical research while advancing treatments and cures.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

The current funding opportunities for revolutionary projects are very limited even though these types of projects can lead to shift in paradigm and be truly transformative. There is therefore an urgent need to redesign how funding is allocated and allow projects that truly solve important problems to be funded. There is also a need to shift basic/fundamental research projects to be in the context of larger picture. Fundamental research has to be able to provide immediate solution to existing questions and be valuable to a larger community. Therefore, there is a need to move from basic and fundamental research to transdisciplinary research.

Future opportunities or emerging research needs

Biological systems are highly complex and dynamic, self-organizing, and massively interacting systems that span several orders of spatiotemporal magnitude critical for the maintenance of homeostasis and health. The reductionist approaches that evaluate in detail the individual components of the system and disregard the fact that these components are an integral part of a greater set of networks. These approaches result in incremental knowledge discovery that fails to uncover complex, systems-wide mechanisms across scales. Computational modeling and informatics revolutionized the study of biological systems as massively interacting information processing units, from molecules, to cells, to tissues, to systems and populations. To efficiently probe emerging and non-intuitive mechanisms of action, information processing representations of systems-wide mechanistic interactions between cells, molecules and microbiota components can be engineered by integrating Big Data, multiscale networks and, importantly, procedural knowledge through mathematical formalisms. A systems approach uses model driven hypothesis to guide experimentation towards the most fruitful direction, which can generate new knowledge. The latter is then added as input to the modeling process, and this cycle continues. The technological advances have allowed generation of high throughput data at an unprecedented rate and efficiency. Such advancement is inconsistent with how projects are designed. There is a need to change how bio/medical projects are designed and implemented. The data is extremely underused if projects are based on a reductionist approach to generate new hypothesis. There is a need to revolutionize the biomedical research enterprise and how resources are allocated to solve important societal problems. Furthermore, there is a need for solid infrastructure to manage and store the data that can be accessible for multiple usages including modeling purposes. Finally, data, tools as well as code has be shared among scientists to ensure reproducibility.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

We need more than 4% for Childhood Cancer! ALL CHILDHOOD CANCER! My child is worth than 4%, is yours?

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

As NIH develops their 5-year-wide Strategic Plan , it is imperative that they, very specifically include childhood cancer. In fact, the NIH needs to recognize that CHILDHOOD CANCER IS A NATIONAL PRIORITY. Our children deserve to be treated with cutting edge treatment, the latest evidence-based interventions, and the most advanced care. One out of every five children diagnosed with cancer in the U.S. die. Those who die represent many decades of lost life. A vast majority of the 500,000 survivors of childhood cancer predicted by 2020 will suffer physical and psycho-social long-term effect. Survivors continue to battle against the side effects of their treatment: heart problems, lung and breathing problems, growth issues, dental, hearing, and vision problems. Then there are the emotional difficulties as well as development and learning issues. These issues all meet the criteria for inclusion in the NIH strategic plan. NIH is the best hope for our children. Our children are heavily dependent on government-funded research for breakthroughs in treatment: they must be included in the research for new and innovative approaches to treatment. NIH must look for opportunities to raise childhood cancer to a national priority. Such opportunities are: Agreement from the NCI to include a pediatric cancer expert on any study section reviewing a pediatric cancer grant application Creation of a new Deputy Director for Pediatric Oncology at NCI Annual report on childhood cancer research from NCI Release of an advocate friendly explanation of the 4% level of support for pediatric cancer research Convene a state of the science conference on childhood cancer or individual malignancies Accounting from NIH regarding support for pediatric outside of the NCI Improve dissemination of/creation of program announcements or RFAs to address unmet needs in pediatric oncology treatment/research

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-

NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

See above

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Urgent need to understand underlying mechanism of acupuncture in degeneration/regeneration process. The healthy and pathological states of the human body depend on adult stem cells that are found in almost every type of tissue. These cells are a key components of regenerative medicine in which the body rebuilds and maintains itself by stimulating natural regenerative mechanisms following tissue injury. Several model of injury have shown that muscle injury can mobilize the differentiation of various types of stem cells to stimulate the process of muscle regeneration, via local muscle tissue as well as distant bone marrow (BM)-derived endothelial progenitor stem cells (EPCs) into blood circulation, which participate in muscle regeneration by forming new vessels. Our recent publication showed that mechanism of acupuncture-induced injury is linked to the activation of adult stem as a result of muscle degeneration/regeneration process. The mobilization of stem cell by acupuncture-induced injury offers great potential in the treatment for a wide range of diseases and conditions. While acupuncture can play a positive role in the recovery of many diseases, it may play a potentially lethal role in stimulating the re-growth of cancer tumors following radiation treatment. Current understanding

of the basic biology underlying cancer progression suggests tumor growth relies on increased EPCs into the blood. Since acupuncture-induced injury may increase the circulation of EPCs, it may enhance tumor regrowth. Recent published data show that cupping, therapy modality similar to acupuncture induced injury, enhanced breast metastasis following cancer radiation treatment. Acupuncture is being used for treatment of cancer-related symptoms, but its clinical effectiveness remains based primarily on ancient theories of meridians and energy flow. Better understanding of acupuncture's role in cancer treatment urgently requires a new research direction focused on the underlying mechanism of acupuncture-induced injury and its link to the degeneration/regeneration process.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

This NIH document is not a "strategic plan" rather it is a justification for maintaining the status quo of "investigator-centered" research which encourages researchers to study topics of interest to them and not necessarily things needed by the seriously ill and disabled in society. Curiously it mentions studying healthy people but not the sick and their diseases of which there are thousands with new ones being discovered all the time. "Patient-centered" research is needed instead; the voice of the patient is noticeably absent from the document. Many statements in the document are vague rendering them nearly meaningless, i.e., "Foster scientific opportunity." A "strategic plan" on the other hand is meant to be clear and concise. It sets goals, mobilizes resources (funding, manpower, etc.) to execute actions, and establishes performance measurements to gauge success. Both within and across Institutes NIH's overall goals should be to increase the number of treatments, preventative measures, and cures for human diseases and decrease the number of diseases for which there are no diagnostic tests or biomarkers. These are measurable goals. The real challenge is to select which diseases to fund at any given time and to make the selection process fair, transparent and agreeable to all stakeholders. The document does not thoroughly address this key point.

Compatibility of the framework with the broad scope of the NIH mission

The disease that disabled me 26 years ago, Myalgic Encephalomyelitis (ME), has no diagnostic test or biomarker, no treatment, no preventative measures and no cure--nothing. And there are other diseases like it none of which are addressed by the document. How will ME benefit from the investment in PMI? Will there be an ME cohort in the 1 million person study representing, equitably, the 836,000 to 2.5 million ME patients in the US? How can ME patients benefit from the cost reductions in Whole Genome Sequencing, electronic health records, molecular breakthroughs, immunotherapies, Big Data to name a few major research advances? ME crosses Institute boundaries--how will discovery research be conducted and managed in the current NIH organizational structure? Finally given its cost constraints and finite resources I strongly suggest NIH scale back its overly ambitious plan to study "all living things" and focus on "human health and diseases" especially those like ME which should be prioritized.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an

NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

More emphasis must be placed on the development and use of human-relevant, non-animal alternatives, and less emphasis directed on experiments involving non-human animals. •The trans-NIH strategic plan should promote lessened reliance on animal models in favor of using more human-relevant, non-animal alternatives; •Resources used on animal experimentation would pay much higher dividends in progressing human health if they were directed to more human-relevant research, as data extrapolated across species is highly unreliable due to differences between humans and animals; •Opportunities to move away from animal models have never been greater, as human cell lines, stem cells and tissues and computational models can provide effective non-animal alternatives; •Researchers would be eager to develop and use more human-focused and humane methodologies if challenged to do so; and •More Americans than ever before oppose the use of animals in scientific research —50% according to the latest Pew survey.

Compatibility of the framework with the broad scope of the NIH mission

More emphasis must be placed on the development and use of human-relevant, non-animal alternatives, and less emphasis directed on experiments involving non-human animals.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

More emphasis must be placed on the development and use of human-relevant, non-animal alternatives, and less emphasis directed on experiments involving non-human animals.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

More emphasis must be placed on the development and use of human-relevant, non-animal alternatives, and less emphasis directed on experiments involving non-human animals.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

More emphasis must be placed on the development and use of human-relevant, non-animal alternatives, and less emphasis directed on experiments involving non-human animals.

Future opportunities or emerging research needs

More emphasis must be placed on the development and use of human-relevant, non-animal alternatives, and less emphasis directed on experiments involving non-human animals.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The current framework is outstanding and appropriately provides emphasis on the key areas of

opportunity and the clear vision of the unifying principles of the NIH strategic plan.

Compatibility of the framework with the broad scope of the NIH mission

The framework is logical, creative and compatible with the broad scope of the NIH mission.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Build and maintain collaborative scientific capacity for cross-cutting research preparedness.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

none

Future opportunities or emerging research needs

Build and maintain collaborative scientific capacity for cross-cutting research preparedness.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The proposed NIH Strategic Plan Framework (<http://www.nih.gov/about/strategic-plan/strategic-plan-2015.pdf>) will highlight major trans-NIH themes and guide efforts to advance the NIH mission. It consists of three “Areas of Opportunity” (Fundamental Science, Health Promotion/Disease Prevention, and Treatments/Cures) and two “Unifying Principles” (Setting Priorities, Enhancing Stewardship). As presented, the framework lacks content reflecting the centrality of the patient perspective and the value of patient engagement in the research process. Therefore, we recommend consideration of specific content and language to emphasize integration of the perspectives, values and experiences of patients into the research process. For example, the absence of data about the patients’ experience is frequently a barrier to optimizing the benefits of technology and big data. Therefore, within the area of Promotion of Fundamental Science, we suggest adding development of new technologies to capture and analyze patient reported outcomes in big data repositories (e.g., SEER) and across EHR platforms for knowledge-generation and decision-support. Under the theme of Health Promotion/ Disease Prevention, we recommend development of new methods to increase patient engagement in all stages of clinical trial design and conduct, because inclusion of patients in research planning and conduct ensures that the trial goals are aligned with the priorities of patients. Under the theme of Treatments/Cures, we recommend that future studies build upon the results of past NIH initiatives (PROMIS, NeuroQOL, PRO-CTCAE) to create and adopt uniform methods and measurements to capture patient outcomes. Continued emphasis on use and refinement of patient-centered, uniform approaches and tools is essential to reap the benefits of past foundational work and promotes scientific rigor and reproducibility. Benefits of uniform or standard patient centered inclusion also promotes greater efficiency in study conduct and increased understanding of barriers/facilitators of healthy lifestyle behaviors and treatment adherence that further all three major NIH areas of opportunity.

Compatibility of the framework with the broad scope of the NIH mission

In the proposed NIH Strategic Plan Framework ([http://www.nih.gov/about/strategic-plan/strategic-plan-](http://www.nih.gov/about/strategic-plan/strategic-plan-2015.pdf)

2015.pdf), it states that the “NIH....mission [is] to support research in pursuit of fundamental knowledge about the nature and behavior of living systems, and the application of that knowledge to extend healthy life and reduce illness and disability.” While the crosscutting areas of research listed are appropriate to the mission, it is the crosscutting area of patient centeredness that is missing that we herein recommend should be addressed. The first half of the mission states that a broad area of focus is the, “fundamental knowledge about the nature and behavior of living systems,” however the framework lacks among all three areas of opportunity a patient-centered focus. Recognition that the ultimate “living system” is the person (not just their genetic makeup or disease target) would require incorporation of the lived experience (behaviors, preferences, adherence to healthy lifestyles and treatment regimes, symptoms, functional status, sleep patterns, neurocognition, quality of life, etc) and context (family, geography, sociodemographics, health literacy, and health care access) into the framework. The second half of the mission states that a broad area of focus is, “the application of that knowledge to extend healthy life and reduce illness and disability,” however the framework misses mention of the opportunity to capture the impact of this research vis-à-vis patient-centered outcomes. Examples of additions to the framework to improve compatibility with the broad scope of the NIH mission include: Promote Fundamental Science Patient reported outcomes advance understanding of adherence to therapies Improve Health Promotion and Disease Prevention Human behaviors and context are critical to health promotion and disease prevention Advance Treatments and Cures Patient-centered approaches that include the patient as partner is untapped

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

A focus on the perspectives and priorities of patients and their families is notably absent in the mission and vision statements of almost every NIH Institute, Center, and Office. This is a noteworthy absence given the current widespread national attention on patient engagement, patient-reported outcomes, and patient-generated data in biomedical research. Nonetheless, there are areas within various ICO missions where the key role of the patient perspective is evident, and can inform trans-institute strategic planning. For example, the NCI mission to “Collect and disseminate information on... detection, diagnosis, treatment, prevention, control, palliative care, and survivorship,” depends heavily on understanding the patient perspective -- through direct patient input both about research design, and as a direct source of data. Mechanisms for achieving this mission include patient participation as investigators and advisors for funded studies; addition of patient-reported outcomes to NIH-supported registries; support of research to advance the science of patient engagement and patient-reported outcomes; and inclusion of patient-reported outcomes in NIH-sponsored research. NHLBI strategic plan emphasizes “Bridging the gap between research and practice through knowledge networks” that include patients and other community members. Mechanisms to achieve this mission include community-based participatory and shared decision-making research. NIDDK vision identifies a focus on comparative effectiveness research, which is closely aligned with the emerging field of patient-centered outcomes research, an area specifically considered to require inclusion of patient research partners and patient-reported data. Cross-cutting themes across numerous NIH ICOs include improvement of health disparities; support for health education; and bringing research into practice more effectively. All of these depend on involving patients in the processes of strategic planning, research prioritization, RFA development, and planning/conduct of studies. They necessitate inclusion of patient-reported outcomes (PROs) and patient-generated health data (PGHD) in clinical studies, and support of research to advance the science of patient engagement and PROs/PGHD.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

In the proposed NIH Strategic Plan Framework (<http://www.nih.gov/about/strategic-plan/strategic-plan-2015.pdf>), there are three “Areas of Opportunity” (Fundamental Science, Health Promotion/Disease Prevention, and Treatments/Cures) and two “Unifying Principles” (Setting Priorities, Enhancing Stewardship). Under “Setting Priorities”, we recommend expansion of the concept of “measures of disease burden” to include “assessment of patient-centered outcomes” to denote those outcomes that are deemed by patients that are important including disease response, survival, toxicity of treatment, functional status, and quality of life impact. Many of these endpoints (toxicity, symptom burden, functional status, quality of life) are assessed through direct input by the patients themselves who are the gold standard for describing their experiences and perspectives. The importance of capturing patient-centered outcomes should also be highlighted especially under the theme of “Treatments and Cures”. The NIH has invested significant funds (in terms of grants and contracts) and direct support (in terms of NIH Program Directors involvement in the science) to develop state-of-the-art measures of key patient-centered outcomes including symptom toxicity, functional status, and psycho-social impact. The projects include the NIH’s Patient-Reported Outcomes Measurement Information System (PROMIS) and Toolbox, and the NCI’s Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE). These tools are immediately ready for incorporation into clinical trials and comparative effectiveness research studies to assess the impact of disease and treatment on patients’ lives. Further, patient reported outcomes help make new discoveries in biomedicine clinically relevant. Lastly, as a unifying principle, we must recognize that disease and treatments have lifetime effects on individuals and caregivers lives. We encourage the emphasis on long term follow-up of patient-centered and caregiver-centered outcomes so we may identify these long term effects (physical and psychological) to identify targets for intervention to improve quality of life.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

No comment

Future opportunities or emerging research needs

An emerging research need that is consistent with NIH’s Strategic Plan concerns the best ways to solicit and incorporate patients’ perspectives into research. This includes patients’ perspectives on the prioritization of research, the identification of important endpoints/clinical targets, research design, patient reported outcomes and dissemination. The ultimate aim is to ensure success of the NIH research mission of extending healthy life and reducing illness and disability through collecting data and addressing healthy lifestyle behaviors, toxicity/symptom management, adherence to therapies and overall quality of life. Thus, opportunities are needed: 1) to refine qualitative and quantitative patient reported methods 2) to identify new approaches for incorporation of these data into clinical research and electronic medical records and big data repositories. As more treatment and prevention strategies are developed for specific conditions, there will be a need for research that informs how best to prioritize care in populations with multiple chronic conditions. Answering this question will require: 3) standard, reliable, and valid approaches for assessing patient reported toxicities and symptoms and functional status across many conditions 4) methods for soliciting individual patients’ preferences for various health states. There are significant opportunities created by combining efficient measurement of self-reported health status with fine-grained capture of momentary experiences and biometric data using increasingly available mobile technology. The richness of data afforded by these technologies is advantageous for all trans-NIH areas of opportunity. To benefit from these opportunities, more research is needed to address several critical questions: 5) How do biometric data (e.g., activity level, sleep patterns, blood pressure) relate to people’s self-reported health and health perceptions? 6) How do biometric data and health perceptions influence health decision-making (e.g., to seek care, comply with

treatment, change behavior)? 7) What are the most appropriate analytic paradigms to use with such high-dimensional, longitudinal data reflecting many health parameters?

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

. . . unifies and mobilizes interdisciplinary professionals combating human trafficking through a healthcare lens and serves as a centralized resource on health for the broader anti-trafficking community. Our members include leaders from clinical practice, public health, global health, academia, and government, working in 28 states and at the national and international levels. Among many other anti-trafficking activities, members of . . . have been active members of the U.S. Department of Health and Human Services (HHS) Administration for Children and Families’ SOAR National Technical Working Group and the Institute of Medicine’s Committee on Commercial Sexual Exploitation and Sex Trafficking of Minors in the United States. Our vision is “A world healed of trafficking.” Human trafficking – including both sex trafficking and labor trafficking – has severe and long-lasting adverse consequences for the health, development, and well being of victims and survivors. Attention to human trafficking globally and in the United States has been increasing in the media and among the general public, NGOs, and governmental agencies at the international, national, state, and local level. Nevertheless, the body of reliable research-based evidence remains insufficient to determine many aspects of human trafficking including prevalence, physical and mental health consequences, and effective responses. For example, a 2013 study by the Institute of Medicine and National Research Council, *Confronting Commercial Sexual Exploitation and Sex Trafficking of Minors in the United States*, included as one of its five overarching recommendations: “Strengthen Research to Advance Understanding and to Support the Development of Prevention and Intervention Strategies.” Similar research is needed with respect to the physical and mental health implications of both sex and labor trafficking for adult and minor victims and survivors. . . . strongly urges NIH to include human trafficking research in its strategic plan.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

More science on emerging topics of illness related to humans, as in Multiple Chemical Sensitivity.(MCS) and Electromagnetic Hypersensitivity (EHS) to reduce disabilities and healthcare costs.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Benefits: The proposed NIH strategic plan has the potential to significantly impact EM research. The framework's inclusion of trans-NIH themes relevant to cross-cutting areas of research, and the explicit mention of "breakdown of traditional disease boundaries," are critical. Promoting team science has the potential to break down silos between disciplines and will help advance trans-NIH themes. Emergency medicine-based research crosses many of the 27 ICOs, and often has difficulty being pigeon-holed into a single institute due to multiple disease entities encountered. We are also happy to see the emphasis on minimizing administrative burden and recruiting/retaining an outstanding workforce, as this is critical in this era of declining physician-scientists. Drawbacks/challenges: Grant application and decision processes, while necessarily rigorous, present some challenges to the success of the proposed framework. For example, the often-extended period of time between submission and funding decisions may minimize innovativeness and physician-scientists' ability to conduct cutting-edge research. Another challenge to the success of the NIH framework is the variability of funding decisions even within similarly scored, high-percentile grants. To retain physician-scientists' research expertise, it is important that the funding decision process is transparent and equitable. Finally, it is critical that funded research address both basic science AND clinical utility. Areas of consideration: Steps should be taken to streamline the process of applying for and receiving NIH funding. More abbreviated timelines between application submissions and decisions would help applicants remain competitive in their respective fields. It may also improve early career investigators' rate of successful transition into independent researchers. Clarifying the process for post-review funding decisions would decrease arbitrariness and improve application quality. Including clinician-scientists on review panels would increase the consideration of clinical feasibility and acceptability in the decision process. Finally, it is critical to preserve adequate funding for physician-scientists, without which clinical departments cannot continue supporting researchers.

Compatibility of the framework with the broad scope of the NIH mission

As an organization, . . . is dedicated to the development of leaders in emergency medical (EM) research and to the creation, translation, and dissemination of research that will improve emergency care for patients. Overall, the proposed framework fits well with the broad scope of the NIH mission to advance knowledge and apply that knowledge to reduce illness and disability. However, additional themes and concepts should be integrated into the framework to ensure that it addresses the current challenges faced by physician-scientists working to advance the NIH mission and improve patient care.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

One concept central to the NIH Office of Emergency Care Research (OECR) but also applicable to this NIH-wide framework is the promotion of multi-disciplinary research and team science. Facilitating multi-disciplinary research is especially important for EM given the wide range of conditions studied by investigators in our field. We also have a history of success in identifying highly vulnerable populations who are otherwise difficult to recruit for research. Fostering collaborations between EM physician-scientists and researchers in fields such as cardiology, neurology, and behavioral health would improve the relevance and applicability of research produced by individual disciplines. The NIH could foster such collaborations by creating more funding opportunities targeted towards multidisciplinary research teams or by increasing dedicated funding for the OECR. We would also suggest the addition of a specific component under the health promotion/disease prevention theme: the creation of evidence-based interventions to reduce harmful behaviors and thus decrease injury and disease. Injury prevention and lifestyle modification are essential to the prevention of morbidity and mortality from conditions seen frequently in EM settings, and should be included as a major strategy to achieving goals in the health promotion/ disease prevention realm. Another concept that should be integrated into the framework is an increased focus on diagnosis in the setting of uncertainty. By always focusing on populations with known diagnoses, we may be missing important opportunities to improve the care and approach to patients with less certain diagnoses. For example, despite years of research on myocardial infarction (defined by occluded arteries on cardiac catheterization), little is known about the appropriate treatment for patients, especially women, who present to the ED with recurrent chest pain but no clear diagnosis. Only recently has it become known that micro-vascular disease may be the culprit for symptoms in a subgroup of this patient population.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

A trans-NIH research theme that is vital to the existing themes (fundamental science, health promotion/disease prevention, and treatments/cures) and should be considered for the Areas of Opportunity section is “research translation”. The translation and implementation of research is a process that requires specific expertise and dedicated resources. It is one of . . . core organizational values. While it is important to conduct proof of concept and efficacy trials (known as T1 and T2 translation), it is equally vital to translate/implement the results of research into improved patient outcomes through effectiveness and dissemination research as well as policy and population level research (T3 and T4 translation). Without considering whether interventions improve patient outcomes and the health of populations, even the best research will be futile. In order to successfully translate research into improved patient outcomes, it is also necessary to routinely include patient-centered outcomes when investigating the effectiveness of new interventions. The concept of patient-centered outcomes should also be integrated into the proposed NIH framework.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

There are no components of the Areas of Opportunity section that do not seem applicable to the NIH-wide strategic plan, but we have described several suggestions for additions and improvements.

Future opportunities or emerging research needs

One major challenge to the implementation of the proposed framework is the recent decrease in funding for clinician-scientists. We suggest adding additional components under the “enhancing stewardship” section that include innovative ways to support physician-researchers in the current funding climate. This is central to . . . objective of increasing the number of members receiving federally funded grants. More resources should be dedicated toward the development of junior investigators into independent researchers as well. This challenge is especially relevant to EM, a relatively young field with promising early-career investigators that could be highly successful with appropriate support. Without addressing the decrease in funding opportunities for clinician-scientists, academic institutions and departments will not be able to support the development of faculty into productive investigators. Furthermore, without clinician-scientists, it will be impossible to create clinically valuable work. In reference to the setting priorities section, we suggest that disease burden should be incorporated as more than just an important factor in setting funding priorities. Focused study on high burden but understudied disease processes should be a high priority. For example, acute trauma is the leading cause of years of potential life lost before age 75, but in 2015, trauma research received less than one-tenth of the funding dedicated to cancer research. Trauma research also received fewer dollars than research on autoimmune disorders, kidney and liver disease, pain research, and nanotechnology. Finally, we are encouraged by NIH’s increasing interest in the use of innovative technology (including the Precision Medicine Initiative and increasing interest in mHealth); rigorous NIH-funded research on these topics is critical for their integration into the healthcare system. We caution, however, that without quick movement on RFAs and funding decisions, research scientists will be continually lagging behind industry investigators. Simplifying the administrative burden and time-to-funding-decisions is essential in this area as well.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

The NIH is the best and most important hope for children, adolescents, and teens with cancer. One out of every five children diagnosed with cancer in the US die. A vast majority of the 500,000 survivors of childhood cancer predicted by 2020 will suffer substantial physical and psycho-social long-term effects. The average age of diagnosis for children with cancer is age 6. Those who die represent many decades of lost life. Those who survive with long-term health effects have equally many decades to live with the results of their treatments: emotional difficulties, second cancers, reproductive and sexual development problems, growth, development, and harmony problems, learning and memory problems, heart problems, lung and breathing problems, dental, hearing, and vision problems, and digestive system problems. These many health issues med the criteria of consideration for inclusion in any trans-NIH strategic plan. Most children with cancer are treated in COG hospitals. Children with cancer are heavily dependent on government-funded research for breakthroughs in treatment and the NIH is our best hope for the future. With that in mind, IT IS IMPERATIVE THAT THE NIH RECOGNIZE CHILDHOOD CANCER AS A NATIONAL PRIORITY. Opportunities to elevate childhood to a nation priority include: Agreement from the NCI to include a pediatric cancer expert on any study section reviewing a pediatric cancer grant application Creation of a new Deputy Director for Pediatric Oncology at NCI Annual report on childhood cancer research from NCI Release of an advocate friendly explanation of the 4% level of support for pediatric cancer research Convene a state of the science conference on childhood cancer or individual malignancies Accounting from NIH regarding support for pediatric outside of the NCI Improve dissemination of/creation of program announcements or RFAs to address unmet needs in pediatric oncology treatment/research Thank you for this opportunity to provide input.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

As the population ages, wounds, especially chronic wounds are becoming more prevalent and in need of care. The current system lacks adequate training in this area, as well as an adequate number of caregivers qualified to do this. Additionally, knowledge of the pathophysiology, as well as molecular biology, of wounds and wound healing is still inadequate. Programs supporting research into the basic science of wounds needs to be supported, as do programs that promote development of new technologies that can improve the speed and character of wound healing.

Compatibility of the framework with the broad scope of the NIH mission

Both of these goals fit well within the NIH mission.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Wound healing, in its broadest aspect, should encompass almost all areas within the NIH framework of Biomedicine.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

There are diseases that fall through the NIH attention crack. They do not qualify as “rare diseases” because their prevalence is large. They are therefore not included in the National Center for Advancing Translational Sciences Institute (NCATS). In addition, they are not housed in one of the other institutes because they have been grossly neglected. An example is the disease, Myalgic Encephalomyelitis (ME) (also known as Chronic Fatigue Syndrome aka CFS). The prevalence according to the CDC is between 850,000 to 2.5 million. The burden of the disease is estimated between \$17 and \$24 billion. The quality of life has been shown on various studies to be lower than all other chronic debilitating diseases. Moreover, unlike other similarly burdened diseases, there are currently NO FDA approved treatments! Yet, NIH has buried this disease in the Office of Women’s Health (OWH), instead of an appropriate Institute such as National Institute of Allergy and Infectious Diseases (NIAID) or National Institute of Neurological Disorders and Stroke (NINDS). Because of the inattention and neglect, these diseases do not get appropriate NIH funding in equal measure with other similarly burdened diseases. NIH funding for this disease has consistently stagnated at \$5 million for decades. This is a mere trivial fraction compared to other similarly burdened diseases. The current framework needs to establish a system which can tabulate and consider ALL diseases equally. Diseases that are lesser known, maybe because they do not have much media coverage or lack a famous entertainer who has put a face on the disease, should not receive second-rate care nor insufficient and unequal funding.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The potential benefits of investing in research for a cure of Childhood Cancer are more tolerable treatments, more effective treatments, and better outcomes for a vital resource, our children.

Discovering treatments and cures for Childhood Cancers can transition into treatments and cures for Adult Cancers, as well. Focusing on Childhood Cancer will promote fundamental science, improve disease prevention, advance treatments, and provide cures for our entire population.

Compatibility of the framework with the broad scope of the NIH mission

Increasing Childhood Cancer research fits very well in the mission to support research in pursuit of fundamental knowledge about the nature and behavior of living systems, and the application of that knowledge to extend healthy life and reduce illness and disability. Currently, we continue to lose and maim children with antiquated treatments due to the lack of research. We lose 27,000 children each decade to childhood cancer, tens of thousands more suffer life-altering impacts of treatment. Gaining knowledge about Childhood Cancer will create the opportunity to extend life and reduce disabilities caused by today's current treatments. In addition, research in Childhood Cancer will continue to provide leaps in technology and major scientific advances.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Make childhood cancer research a priority in any NIH budget. Childhood cancer is the #1 disease related killer of children in this country. We continue to lose and maim children with antiquated treatments due to the lack of research. 1 in 285 children will get Cancer. We lose 27,000 children each decade to childhood cancer, tens of thousands more suffer life-altering impacts of treatment. Current treatments are antiquated. More money, time, and resources need to be focused on Childhood cancer to provide cutting edge treatments, cures, and prevention. I understand there is a loss of innovative research proposals because of lack of funds. These are lost opportunities in a neglected field. Childhood Cancer is an emerging research need.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The . . . urges NIH to consider including specific reference to “rehabilitation science” in its strategic plan. The Blue Ribbon Panel on Medical Rehabilitation Research identified several areas of opportunity to better coordinate and enhance rehabilitation research at NIH and across federal agencies. Rehabilitation research is not specific to one institute and should be appropriately reflected in the NIH global strategic plan.

Compatibility of the framework with the broad scope of the NIH mission

Inclusion of a reference to rehabilitation science is compatible with the broad scope of the NIH mission which includes enhancing health, lengthening life, and reducing illness and disability. Rehabilitation

science focuses on this goal and is consistent with the overall NIH mission. The National Center for Medicare Rehabilitation Research (NCMRR) has been designated by Congress to be the lead agency within NIH on rehabilitation science and the Blue Ribbon Panel found that \$300 million is annually spent by NCMRR and a number of other Institutes and Centers. Therefore, rehabilitation research should be appropriately reflected in the NIH strategic plan. It is critical that the strategic plan's framework include rehabilitation science in order to enhance its stature and visibility at the world's premier medical research agency. Better coordination between NIH institutes and centers and among the federal agencies conducting and supporting rehabilitation science is critical.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Rehabilitation science itself is a prime example of cross-cutting research at NIH and should be specifically included in the trans-NIH strategic plan. Rehabilitation research is a broad area and its value is reflected in the improvement, maintenance and prevention of deterioration of function of individuals in their daily lives. Multiple NIH institutes and centers engage in rehabilitation science and coordination of efforts to match research priorities will maximize the return on the federal investment.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Current rehabilitation research activities and priorities have not been adequately identified in trans-NIH themes in the draft NIH Strategic Plan. Better coordination will lead to identification of potentially synergistic research so that rehabilitation researchers can enhance and build upon each other's work. Coordination in this field of rehabilitation research is essential because: • Rehabilitation research is not organ or disease specific; • Rehabilitation research is cross-cutting and virtually every NIH institute and center should be involved in the conduct and support of rehabilitation research; • Rehabilitation needs affect people across the lifespan from infancy to old age; and • Societal, environmental, behavioral and biomedical interventions are required to prevent and treat persons with disabilities and chronic conditions.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

... has no comments for this section.

Future opportunities or emerging research needs

... has no comments for this section.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Please provide additional research funding specifically for Childhood cancers. Pediatric cancers have unique properties not limited to Adult cancers. There is also a greater need for new chemotherapies and clinical trials tailored to Childhood cancer.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Please provide additional research funding specifically for Childhood cancers. Pediatric cancers have unique properties not limited to Adult cancers. There is also a greater need for new chemotherapies and clinical trials tailored to Childhood cancer. Thank you

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The amount of money allotted to child care research must be increased by 100%. It is morally reprehensible that we fund the research for child cancer at less than 4%. Child cancers need cures now. Children are the future of this nation and I demand that the nation put them first and foremost. The suffering they endure is absolutely gut wrenching. 4% is not enough. The time frame for input is also ridiculous. Releasing this 3 days before the deadline is also ridiculous and doesn't show a willingness and reception to input.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

. . . applauds NIH for moving forward to develop a comprehensive NIH-wide strategic plan. Given the challenges and opportunities associated with pediatrics – such as the reality that most pediatric diseases

and disorders are rare diseases, difficulties recruiting pediatric patients for research projects and the growing body of knowledge regarding developmental origins of health and disease that indicates many adult-onset conditions are rooted in the pediatric years or in utero – . . . urges that appropriate attention and considerations be given to the needs of the pediatric population. While most children are, fortunately, relatively healthy, we know that about 50 percent of all patients impacted by rare diseases are children and that 30 percent of such children will die before their 5th birthday. Given these challenges and the related opportunities possible through a greater focus on pediatric research, . . . requests that the plan include a dedicated focus on pediatric priorities to ensure the needs of our children are given appropriate attention across institutes and centers. Furthermore, we urge that NIH not simply define priorities based on the sheer number of patients impacted by a disease or by annual aggregate costs as both criteria would place children and children's health at a sizable disadvantage compared to adult-onset conditions. Finally, we urge NIH to recognize the developmental origins of health and disease put forward originally by Dr. David Barker that recognizes environmental factors (such as nutrition) interact with the genome during prenatal and postnatal life and profoundly affect not only childhood disorders but also adult health. As such, a focus on this topic would stand to benefit all persons from children to adults.

Compatibility of the framework with the broad scope of the NIH mission

. . . believes an overarching NIH strategic plan should be very compatible with the broader scope and mission of the NIH and its component Institutes and Center. The overarching strategic plan should not conflict with the vision of more detailed and institute-specific blueprints. For example, we know many months and a lot of effort went into the creation of the NHLBI strategic plan. The overarching NIH strategic plan should not be in conflict with nor negate the principles of that plan but rather be complementary to the NHLBI work. The NIH strategic plan should establish general rather than specific priorities. Overarching priorities could include targets for multi-institute collaboratives, joint IRB's and activities that would be spelled out in greater specificity by the Institute and Center plans.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

. . . encourages an emphasis on the developmental origins of health and disease and believes this exemplifies the potential through a cross-cutting approach to research. Although the link between low birth weight and coronary heart disease, diabetes, hypertension and stroke in adulthood is well established, the full extent of epigenetic adaptation during prenatal and early postnatal life is yet to be explored. Advances in food production/distribution, new air/water pollutants, migration of parasites from threatened species to humans, and other unforeseen risks, will all affect adult health by altering the epigenome early in life. This places perinatologists, pediatricians and developmental biologists in a position to have a unique impact on both child health and adult medicine. If our strategy to combat these threats is to be determined by polling the community, the results will reflect current makeup and will define the common denominator of our imagination. The NIH has tried its best to use its funds efficaciously but in doing so, efforts missing mission relevance and topic areas mandated by Congress or the "community vote" have often dominated the research agenda. Because we (scientists, administrators, politicians) cannot predict future need, nor can we predict which idea will get us to any desired therapy, the importance of continued investment in testing avant garde hypotheses cannot be overstated. To ensure that the innovation pipeline continues, we must improve the balance between "community selected topics" and investigator initiated ideas as long as RO1s adhere to strict "best science" criteria (innovative, hypothesis driven, and evidence-based investigation into the mechanisms of development and disease; all broadly defined, whether or not included in a topic area blessed by institute directors). We should leave open a window for the unexpected as we all know that serendipity

is the mother of invention.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

. . . strongly agrees with the RFI that basic science is the foundation for progress. We also appreciate the recognition in the RFI that leaps in scientific technology often catalyze research breakthroughs as well as the growing importance of data science in research. We would encourage NIH to recognize this reality by making support for research infrastructure, particularly core research infrastructure shared by multiple institutions, a higher priority. Unfortunately, NIH support for such vital infrastructure has declined, thereby placing a greater onus on research institutions. . . . alone commits about \$5 million annually to multiple cores. NIH support to supplement this investment would be most helpful particularly given the tremendous advances in technology – and the corresponding increase in costs that result from such gains. On the topic of infrastructure, . . . also urges that NIH note within the plan the need to provide support for training and development of early career researchers, particularly clinician-scientists. This support is necessary to develop the future generation of researchers and deserves to be reflected in the plan.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

The ongoing study of human systems consistently reveals increased complexity, which continually demands evermore capability from the biomedical research community. As we tackle larger and more intricate disease challenges, our best success will likely come from investigations that most effectively consider the widest range of relevant data, including molecular, cellular, environmental, behavioral, and temporal factors. The advent of precision medicine will require vast quantities of data in order to have sufficient power to make evidence-based predictions at a subject level. The NIH can empower personalized medicine by encouraging fundamental principles required for success. These include access to patient-derived data at high volume, veracity, and variety across the lifespan; access to a strong expertise base for disease investigations; transparency and self-awareness of capability; operational efficiency; ability to seamlessly translate research findings into clinical success; power to disseminate findings across research networks; and both programmatic and institutional commitment to incentivize team-based science within and across disciplines. Research organizations that are best equipped to consolidate data, materials, expertise, and processes across traditional disease and investigator-specific boundaries will be attractive and productive research partners for NIH-led initiatives. Coordination across NIH institutes to promote a culture of nimble and innovative science, and to quickly identify and replicate successful investigative models that can serve as standards, can foster a culture of continual positive evolution.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Please know that the disease burden of DIPG tumors in our children is fatal to the child and crippling to the family, relatives, friends, and community. The disease burden is greater than financial, as well. The result of one child's death to DIPG is decreased productivity and increased psychological disturbance to scores of other children and adults who love the diagnosed child and watch the horrific treatment and death that follow.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

It is a fact that Childhood Cancer is the number cause of death in children due to disease. Given this fact, it deserves high priority in the Strategic plan. Funding must be increased to address this and find more current treatment protocols.

Compatibility of the framework with the broad scope of the NIH mission

This fits into the natural framework of the purpose of the NIH and their mission.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

The long term effects of the current treatments need to be evaluated and considered closely. The current treatments are limited in many types of cancers presenting themselves in children. Environmental causes need to have closer evaluation and appreciative correlation between the environmental factors and the different types of cancers need more attention.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

More emphasis must be placed on the development and use of human-relevant, non-animal alternatives, and less emphasis directed on experiments involving non-human animals. The trans-NIH strategic plan should promote lessened reliance on animal models in favor of using more human-relevant, non-animal alternatives; resources used on animal experimentation would pay much higher dividends in progressing human health if they were directed to more human-relevant research, as data extrapolated across species is highly unreliable due to differences between humans and animals; opportunities to move away from animal models have never been greater, as human cell lines, stem cells and tissues and computational models can provide effective non-animal alternatives; researchers could be eager to develop and use more human-focused and humane methodologies if challenged to do so; and more Americans than ever before oppose the use of animals in scientific research —50% according to the latest Pew survey.

Compatibility of the framework with the broad scope of the NIH mission

The NIH needs to plan for a future focused on human-relevant models to best increase our chances of improving human health and well-being. At this point in time, I hope that you will take advantage of this important opportunity to end the cruel the use of animals in biomedical research. What kind of monster prefers cruelty to more reliable research models?

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

One of the most difficult things is that there are so many ME/CFS patients who have not been properly tested, diagnosed, or given medical care for their disease. The physicians around the country need to be trained in the same way they were trained about HIV. Proper care at ER and urgent care facilities as well would make a huge difference to patients. The current suggestions of exercise and CBT are NOT adequate and actually cause harm to patients by making their symptoms worse. Immune dysfunction leads to reactivation of viruses such as HHV6, EBV, coxsackie, varicella, and herpes simplex. Lab testing for NK cells, cytokines, T and B cell function, IgG, orthostatic intolerance, low blood flow in the brain, and spinal taps to look for cytokines in the spinal fluid are all imperative to be able to properly diagnose a patient and give medicine as treatment.

Compatibility of the framework with the broad scope of the NIH mission

Currently the large amount of money that is spent is not actually accomplishing any improvement in the quality of life for patients in order to get back to work and live a healthy normal lifestyle. Also, the amount of suffering by the patients is extraordinarily high. Many are living housebound and even bedbound. Many patients are taking their own lives and families are being divided due to extreme amount of care necessary to care for their loved ones that are ill.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Centers of excellence around the country, physician training in medical schools and through JAMA for those already practicing medicine.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The NIH strategic plan must ensure that diseases without an institute home do not slip through the cracks. The NIH strategic plan must fully address multi-system diseases such as ME/cfs which crosses institute boundaries, has no dedicated funding from an institute home, and in fact has no institute home, and is therefore not covered by the strategic plan of any institute.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Stakeholders can and must play an integral role in biomedical research and its process. This has been noted in several reports such as the NIH P2P report on ME/cfs, the IOM report (Beyond Myalgic Encephalomyelitis) both of which were commissioned in whole or in part by NIH. Heed their advice. Stakeholder involvement in everything from generation of hypotheses to consideration of treatment targets, to selecting meaningful (to stakeholders) outcome measures, and much more will bolster the value and applicability of NIH research.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an

NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

While burden of disease should not be the sole rationale for designating priorities, burden of disease must be an important consideration. In developing the NIH draft strategic plan, only 69 categories from the GBD study were assessed. Those 69 categories do not cover many diseases that have significant direct and indirect costs (and therefore significant impact on the US economy). Neglecting the impact of diseases for which no DALY has been calculated leaves gaping holes in NIH's ability to accurately assign priorities. In the 13 August webinar by Dr Tabak and Dr. Lipkin, there was talk of the value of insights derived from research that is applicable to many other areas. Multi-system diseases such as ME/cfs present exciting opportunities for research that would have wide-ranging impact across many NIH institutes. The NIH strategic plan must maximize these opportunities.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

1. Current funding mechanism is that each NIH institute will focus on specific organs and type of diseases. However, our body is a unified organization. The organs interact each other and affect each other during diseases. For example, hypertension and diabetic nephropathy accelerate diabetic retinopathy. Meanwhile, the progression of diabetic retinopathy may be used to predict the progression of diabetic nephropathy and diabetic macrovascular complications. NIH may consider to issue some RFAs or joined funding mechanisms to enhance the collaboration of investigators from different fields to study diseases and physiology in a more interacted and integrated strategy. 2. The New and Early Stage Investigator Policies of NIH greatly enhance the opportunities of young investigator to start their independent research. However, these investigators, esp. early stage investigators, have difficulty to compete for their renewal R01 because they only run their labs for 4-5 years and are much less experienced when writing proposals compared with senior investigators. Many of them have to choose other careers because of this. It would be helpful to give them additional consideration during their renewal so that they can be successful.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

Integrated research, for examples, eye and other organs (e.g brain, cardiovascular system, kidney, infectious diseases), heart and other organs (e.g. brain, kidney), etc.

Future opportunities or emerging research needs

Integrated biomedical science through the collaboration among NIH institutes.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The . . . endorses the proposed framework, which nicely integrates basic and applied research aimed at developing fundamental knowledge of the human and applying that knowledge to enhance and extend healthy life while reducing illness and disability. Biomechanics as a discipline supports such an effort by providing quantitative tools to measure forces, movement and their effects on body tissues. Our membership, . . . , recommends including objective measurement in any research framework. Such an approach will include emphasis on integrative and holistic approaches to medicine. We propose that the interactions between biomechanical and physiological processes are essential to understanding the fundamental basis of health and disease. The outcomes of many medical treatments can be enhanced by adding physical activity, which is essentially a biomechanical pathway to overall health care. This pathway can directly treat obesity and metabolic disease, and can enable healthy aging, all current major health problems. Mechanistically, human physical activity enhances physiological profiles, such as cardiovascular, neuromuscular, musculoskeletal health, as well as psychological health and directly improves responses to medical treatments including pharmaceutical treatments. The . . . also suggests that the focus of NIH funding tends to be short term, since most grants have a 4-5 year cycle. We suggest that NIH consider both new funding mechanisms and enhancing traditional mechanisms for long-term studies of chronic disease that go beyond the traditional grant cycles. As a reference point, the Canadian Institutes of Health Research has now implemented a new program, called Foundation Scheme grants, which incorporates some of these concepts.

Compatibility of the framework with the broad scope of the NIH mission

The proposed framework of the strategic plan fits in the mission of the NIH; however, the focus is primarily on disease. The plan ignores health benefits of prevention and wellness that can be attained through biomechanical pathways such as physical activity and exercise. 79 percent of all health care costs are due to chronic health conditions that are preventable and 11% of aggregate U.S. health care expenditures are associated with inadequate physical activity (i.e., inactive and insufficiently active levels). Thus, increasing physical activity across the lifespan with clearly defined biomechanical standards takes a preventative approach that will reduce U.S. health care expenditures and directly improve quality of life. The NIH should focus on breaking the cycle associated with chronic health conditions. A bold move would be to emphasize physical activity and exercise across disease and disability. Physical activity and exercise directly improve nervous, muscular, organ, and skeletal systems which subsequently improves overall health levels. In fact, as is commonly performed by . . . members, modern engineering tools to study, motion, forces and their effects, dramatically improves our understanding of disease phenomena, provides rigorous functional testing of cell, tissue and body therapies, and leads to understanding of the underlying mechanisms of action. Such biomechanical measurements are strongly recommended to be incorporated into the broad NIH mission.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

The ICO strategic plan should target prevention research, particularly in young and mid-life adults. There are currently no programs that focus on these populations yet these individuals are bearing the burden of society. They are the wage earners, parents, and care providers. They are typically healthy, but lag behind in preventative care because they are too busy and lack the education of best approaches to prevention. Yet, if they do not care for their health, the result will be future increased burden on

medical care costs to society. The goal should be to prevent, stop, or reverse disease progression so that these individuals experience healthy and independent aging and do not require as much medical care. Enhancing healthy behaviors in this population will directly influence children who readily learn behaviors from their parents. Further, these target populations are the hardest hit in terms of health disparities. We can address all these issues through programs introducing adults to safe and healthy behaviors including increased physical activity and improved nutrition. Further, to enhance long term health, health-based physical activity programs should be developed for the pediatric population.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

The framework fails to provide quantitative parameters that would indicate if an optimal functional outcome has been achieved. Current technologies (accelerometers within cell phones, smart watches, etc.) can provide such quantitative data in real-time. Advancing treatments and cures is laudable but understanding general aspects of health and mobility are required to reduce the impact of disability. Emphasis needs to be placed not only on the ability to perform routine activities of daily life but also the richly diverse aspects of well-being believed to constitute quality of life. These ideas are captured within the realms of neuromuscular and skeletal health and physical activity and are beneficial for, but not limited to, people with diabetes, osteoarthritis, stroke, obesity, mental illness, and cardiovascular diseases, primary health threats in the U.S. and world-wide. We recommend a more comprehensive integration of biomechanical, neuromuscular, and physiological aspects within medical research.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

NIH's mission focuses on science in pursuit of fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to extend healthy life and reduce the burdens of human illness and disability. Recently, NIH has participated in initiatives across multiple funding agencies, where the research combines expertise in multiple areas. An example is the National Robotics Initiative. It is highly desirable that trans-agency initiatives continue to be explored where there is biomedical relevance.

Future opportunities or emerging research needs

Mobile platforms and measurement systems are gaining popularity. Conceptually, direct feedback to the patient or practitioner will enable personalized medical care to be received. These concepts will aid in self-management of health and disease. It will also enable real-time analysis in rural areas where access to health care is limited. Integration of real-time analysis into the home and community environments is emerging and will be beneficial towards compliance of home based therapies and fall prevention, for example. Injury prevention and increased mobility will reduce health care costs and are necessary to achieve increased participation in physically active lifestyles.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The strategic plan must recognize the current and likely future funding challenges impacting the NIH and the larger biomedical research community. While we are hopeful that Congress will allocate additional resources for the base NIH budget as well as for a focused innovation fund, even such an infusion will be inadequate to address the sizeable demand that is resulting in meritorious scientific applications going unfunded. At its core, a strategic plan must strive to “do more with less” and to establish – and subsequently direct resources toward – NIH-wide scientific priorities. To do this, NIH must develop a

transparent and agency-wide approach to setting and funding priorities, including a willingness to make “tough decisions” that may upset some stakeholders. In setting priorities, NIH needs to embrace clear and transparent criteria that include disease burden, scientific opportunity and unmet need among other factors. One of the seeming challenges today is the many levels of advisory panels – Advisory Councils to the Director and each institute, the Scientific Management Review Board, the Council of Public Representatives. We would recommend that NIH streamline this to have one agency-wide process to establish trans-NIH research priorities. While we recognize that NIH must be the driver of basic science and that the outcomes of such research are typically highly unpredictable, we urge NIH to follow some of the direction from Congress included in the 21st Century Cures legislation and allocate a percentage of the annual budget toward goal-oriented, high-risk/high-reward and specified research projects at the basic or translational levels. We would further encourage that rather than seek to replicate the DARPA model, NIH instead leverage the half-century-plus of DARPA expertise through a direct partnership with that agency.

Compatibility of the framework with the broad scope of the NIH mission

We recognize that NIH has a broad scope and a critical mission as the world’s largest funder of biomedical research. However, we see a clear strategic plan as being essential to ensure maximum impact of this vital mission. Rather than view the plan as potentially conflicting with the mission, it must be seen as the overarching guide to drive the agency forward and to unite the narrower and targeted plans of individual Institutes and Centers. We see no reason why a clear NIH plan would prohibit or negatively impact individual Institute and Center planning efforts. Rather, the NIH vision should set the framework under which all others should be developed. Such a framework would model how diverse non-governmental operations with multiple business units or divisions address their own planning. We also encourage NIH and other stakeholders to not view establishing priorities as signaling in any way that topics or themes not identified as such are not important. Furthermore, we believe NIH can prevent or allay such concerns by making clear that priorities are expected to be fluid and to change over time based on changes in disease burden, unmet need, scientific opportunity and other factors. As such, a theme or topic not identified as NIH-wide priority today may be one in the future given the continual evolution of science.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

NIH has moved forward, particularly since enactment of the NIH Reform Act, to drive greater levels of cross-cutting activity and multi institute or center collaborations. At the NIH-wide planning level, it seems that the focus should be on setting ICO targets or levels for annual cross-cutting activities rather than being overly prescriptive. This would enable ICOs to have necessary input in establishing their priorities for such activities. Building upon our earlier points and related to provisions included in 21st Century Cures, we would encourage that such cross-cutting activities focus at least in part on high-risk/high-reward research ventures that require the expertise and resources from multiple ICOs to be successful. Like the Common Fund, we would recommend that such initiatives be goal-oriented, time-bound and clearly defined.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

We recognize the necessity of basic science and that NIH plays a vital role in supporting this component of the discovery pipeline. We also recognize that discoveries are often unpredictable as well as the roles technology and “big data” hold in accelerating advancement and making research more efficiency. As part of this use of transformative technology, NIH needs to drive forward a culture and a climate that

strives to make NIH-funded scientific results available as quickly as possible. Too often, results are delayed because PIs are pursuing publishing opportunities. Scientific communication is important to furthering learnings but cannot be allowed to deter a more expedited release of findings. As a consequence of the current system, experts believe a significant amount of research in the Alzheimer's space is duplicating failed projects simply because results are not published in a timely manner. We strongly agree with the point made within the RFI that advances in diagnosis and detection are critically important. We are seeing the importance of this issue right now in the Alzheimer's field with a growing recognition that early diagnosis and early treatment will be necessary to achieve disease modification. Supporting research into detection and diagnosis must, therefore, be a priority. We also applaud NIH for recognizing the need to eliminate health disparities and urge that this be seen as applying across the board including to disparities in minority enrollment in clinical trials. Academics, industry and political leaders are recognizing the multiple challenges this underrepresentation causes, and we would urge the strategic plan to speak to this explicitly. We are pleased that NIH notes the need for partnerships and urge that a finer point be placed on this topic. Specifically, we urge that NIH view industry, particularly in initiatives focused on later-stage activities, as equal partners in setting priorities.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Alzheimer's disease and related dementias pose a significant current and future threat to our nation's health. NIH has recognized this through some unilateral shifts of research funding in recent years. While much appreciated, these shifts are insufficient to provide the resources experts have said is need to maximize our chances of achieving the national goal of preventing and treating Alzheimer's by 2025. Alzheimer's disease and dementia can serve as the poster child for a disease or condition for which public levels of research investment are disproportionately low compared to the burden of the disease, unmet medical need and scientific opportunity before us today. As NIH considers strategic focus areas to be identified in the plan, we urge you to include Alzheimer's disease and dementia within this initial set. Beyond an appropriate focus on Alzheimer's and dementia, we encourage the NIH to include as a strategic priority collaborative projects involving international entities such as the European Union's Innovative Medicines Initiative (IMI). Such multi-national collaborations will be necessary to advance science and the accelerate pursuit of therapies and cures, particularly given the borderless nature of how clinical trials are conducted today. In focusing on such, NIH must also speak to the needs to address any barriers or limitations today that hinder or impede the ability of the NIH and of the United States more broadly to fully engage with international peers. For example, limits on industry participation and receipt and use of non-governmental funds can slow and limit such collaborations. We would urge that NIH focus on addressing such impediments to accelerate and leverage such multi-national opportunities.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Advances in fundamental science are providing opportunities to further our understanding of the links between our genetics and factors in our environment and our diet. While a small fraction of the total burden of chronic disease can be attributed to a single gene, or a single environmental agent, or a single nutritional deficiency, the vast majority of human disease is attributable to a complicated interplay of all three. As we elucidate the molecular events that underlie common disease states (like cancer, birth defects, metabolic, cardiovascular, respiratory and neurological disorders), we are beginning to

understand how a change in function of a particular gene or set of genes can be influenced not only by an individual's inborn genetic sequence, but also by environmental or dietary factors to which we are frequently exposed (such as chemicals, non-chemical stressors, pathogens, individual microbiomes, and excesses and deficiencies of nutritional components). As we uncover this information through the work of synthetic, interdisciplinary fields like toxicology that combine information from a variety of sources, it is becoming increasingly possible to understand the factors that increase or decrease the risk of developing chronic disease, and therefore to prevent these diseases, or to ameliorate their effects in people who already have them. Fundamental research in toxicology provides a basis for addressing human disease that has a significant environmental component. This includes an understanding of basic mechanisms of toxicity, the basis for individual susceptibility at critical life stages (e.g., prenatal), and the identification of vulnerable and resistant populations. Specific areas of research include studies on gene-environment interactions, hypothesis-driven epidemiology, exposure studies, and methodologies to study effects of large numbers of individual chemicals and chemical mixtures in human-relevant model systems. This research will also suggest novel prevention and treatment strategies that are based on understanding of how these diseases start.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

NIH should continue to support integrated, systems biology approaches such as in the Toxicology Testing in the 21st Century paradigm, including high throughput cell-based assays, 'omics methods and bioinformatics/computational modeling tools. These approaches represent a technology leap that will link molecular pathway events to human diseases and lead to advances in predicting toxicological pathologies and disease, improved assessments of health risks from the totality of exposures (the Exposome, e.g., environmental chemicals, non-chemical stressors, pathogens, individual microbiomes, and excesses and deficiencies of nutritional components) at the individual and population levels, and provide improved interventions for disease prevention and cures.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

o Workforce development and training Understanding the causes of chronic diseases that are a product of genetic, dietary and environmental interactions requires individuals with interdisciplinary and integrative science skills. In this regard it is essential that NIH (NIEHS) continues to support interdisciplinary training programs in toxicology and environmental health to ensure that the next generation of scientists possesses the requisite interdisciplinary skills to tackle the complex health challenges that lay ahead. NIH must continue to lead in addressing issues of workforce supply and demand in biomedical fields to help trainees transition to the appropriate professional career path. For example, postdoctoral fellows and graduate students are increasingly discovering that the traditional path to tenure track assistant professor or principal investigator at a pharmaceutical or biotechnology

company may no longer represent a viable option. This changing employment environment will require new or enhanced training program options that will prepare a workforce for diverse career paths in biomedicine that not only include these traditional options, but other critical areas in biomedicine such as science policy, laboratory management, communications, technical writing, patent law, and business development. Promoting scientific and toxicology/environmental health science literacy in primary and secondary school curricula is critical to maintaining a steady pipeline of scientists ready to contribute to the challenges in health promotion and disease prevention. Improving environmental health science literacy broadly across the population will result in better health decision-making. NIH must also continue to lead in building opportunities recruit and retain underrepresented minority group participation in biomedical disciplines.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Making the research opportunities presented by rare diseases a priority is a move in the right direction. There are over 7,000 rare diseases affecting more than 30 million Americans, and 95% of these diseases lack an FDA approved treatment. While industry has made significant progress in the fight against rare diseases, we believe the government can and should play a central and more prominent role in supporting rare disease research. While we applaud the efforts of this framework to make rare disease treatments a reality, we encourage this planning committee to include specific rare disease references in more of the Areas of Opportunity. Specifically, under the Health Promotion/Disease Prevention subheading, we feel that advances in early diagnosis/detection should explicitly reference the desperate need for improvements in this area for rare disease patients. Currently, many rare disease patients are forced to take part in the so-called “patient’s odyssey”, a years-long struggle to find a concrete diagnosis that takes a steep toll on each patient’s finances and health, as undiagnosed diseases typically remain unchecked and continue to progress during this period. Rare disease patients deserve better than this, and the NIH can galvanize their support by adding specific reference to rare disease patients in the “Advances in early diagnosis/detection” language. Research into rare diseases often provides insight into other diseases and contributes to a more comprehensive understanding of the human body overall. This allows for increased speed and nimbleness when attending to all manner of medical needs, and continues to build the groundwork for advancing precision medicine. The 7,000 rare diseases are central to the NIH’s historic mission: breaking down barriers and advancing science to find fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability.

Compatibility of the framework with the broad scope of the NIH mission

As with the NIH’s effort to map out the human genome, the NIH’s focus moving forward should be in developing a robust, comprehensive understanding of the human body and the diseases affecting it. Discoveries in areas of rare disease research are often beneficial to other areas of research, and contribute to a greater overall understanding of the human body. We can never be certain where the most profound discoveries in medical sciences will come from, and research into the largely unknown and untouched fields within the rare disease space can provide innumerable insights into how the human body works.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Nowhere in this strategic plan is the importance of translational research mentioned, and we feel that this is a missed opportunity. The NIH’s own National Center for Advancing Translational Sciences is

working to create methods for effectively incorporating much of the research done by the NIH into broader medical fields, and it is critical that the NIH works to make its discoveries as accessible as possible to all stakeholders. Not only will this ensure that Americans are receiving the safest, most advanced medical care in the world, but it also ensures that the incredible work that the NIH is supporting ultimately has an impact on improving health outcomes for patients.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

The goal of resolving unmet medical needs is critical for improving the living conditions of rare disease patients who currently lack solutions to even the most basic problems a debilitating illness can cause. The NIH has the unique opportunity to step into this uncharted territory and develop meaningful insights that can spur future solutions. We encourage the NIH to incorporate meeting unmet medical needs across its ICOs, allowing for collaborative research that can result in unconventional solutions to patient problems.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

As discussed above, the private sector has made significant progress in the fight against rare disease. However, more could be done leveraging public support to effectively de-risk various areas of scientific research that pertain to rare diseases. NIH funding, for example, could play an integral role in elucidating some of the basic pathophysiology of rare diseases and in doing so, lay the needed groundwork for the development of targeted therapies. This research would go a long way in de-risking and accelerating the rare disease drug development process, which is a top priority for patients in the rare disease community.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

One important area of Fundamental work in science that is not getting attention is the effect of overarching environmental phenomena like ambient temperature and atmospheric carbon dioxide levels on living organisms, i.e. human physiology. A question on the last webinar about "environmental" issues and NIH supported research did not come close to providing the context for this concern. Natural scientists are telling us that the carbon dioxide level is now higher than it has been since before humans appeared on the Earth. This means that all of human development up until this point has been in a milieu with a lower level of a key gaseous element of our atmosphere and at temperature levels that are lower than where human society is headed. Basic biology research should begin to look at what this means: greater genetic mutations? greater or lesser susceptibility to disease? impact on longevity? differing sensitivity of organ systems? There are many very important questions.

Compatibility of the framework with the broad scope of the NIH mission

This falls squarely in the area of the opportunity to promote fundamental science in an era in which some of the foundation that undergirds fundamental science is in flux. If Basic Science is the foundation for progress, which I believe it is, then this important area of basic science should not be ignored. I know that NOAA has tried to make data available to the NIH to facilitate this kind of work, but I do not believe that there are researchers using this data. A more active program may be necessary to introduce the

data and some of the ideas about how to use it to the intra, and extra-mural scientists. There may need to be some specific requests for proposals to get this started since the existing activity announcements and their reviewers would not be likely to validate such avenues of investigation.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

This area does make for a new cross-cutting area of activity.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

I believe this is addressed above.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Specific concerns about rising heat (due to climate change) and air quality and pulmonary disease is an emerging research need. Unclear whether there is sufficient focus on that. Also stronger and longer allergic reactions attributable to longer pollen seasons and, in some cases, more virulent pollen (Bielory 2012), are prompting more people to progress from hay fever type allergic reactions to asthma to more severe asthma--at least according to the anecdotes of allergists from around the country. What is the physiologic mechanism of this observable development and how can it be addressed?

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Potential Benefits: Under Health Promotion and Disease Prevention, we see great benefits in calling out the importance of studying healthy individuals, continuing to support early diagnosis and detection research. Under Setting Priorities, we are not sure one could permanently eradicate a pandemic (an inspirational goal for sure); but rather continue to consider ways to limit the occurrence of a pandemic might be more realistic; for example, vaccine development research, vaccine adherence (distribution, uptake), ways to limit the spreading of various pandemics (behaviors, policies, vaccines). Consider as a priority the burden of chronic illnesses and chronic illness care. Under Treatments and Cures, consider adding partnerships with other funding agencies, e.g., NSF, CDC, Dept of Agriculture. At these intersections innovations and knowledge might be shared and discovered that advances more than one mission.

Compatibility of the framework with the broad scope of the NIH mission

The frame work is compatible with the mission.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

No comment.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

We don't see Chronic Illness Conditions or Care called out. For example, diabetes has many systemic

affects, not all of which are manifested in an individual. It would seem this particular chronic condition would or could be studied across many areas of opportunity and biomedicine.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

No comment.

Future opportunities or emerging research needs

A comment about limiting research administrative burden would be a good goal to be emphasized.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

As with any framework, there often is a lack of having a granular focus on how those priorities/focus areas can address the smaller components under that overarching framework. My intent is to ask that the proposed framework better support biomedical research for improved treatments and mortality rates as they pertain to childhood cancer. Thus, perhaps each section within this finalized 5 year plan will be clearly outlined within each ICO's strategic plan. As per my intent, I will ask that childhood cancer either be a single key initiative for NCI, in addition to the current ones (Precision Medicine, RAS, NCTN, NCORP, GDC, PQ) or that childhood cancer become a separate focus area altogether due to having slow success rates for a disease that remains the #1 killer of children (ages 1-19) in the United States.

Compatibility of the framework with the broad scope of the NIH mission

Develop goals that are forward-looking and inspirational: Per my intent of reinforcing a need to eradicate cancer, in general, but with a more concentrated effort towards realizing a higher success rate in treating childhood cancers and seeing a world with less incident rates of those childhood cancers - how can it not be more inspirational to have a world with 1) more long term survivors of childhood cancer and 2) long term survivors thriving vs. battling late term effects from antiquated protocols? The goals here should focus on non-discretionary funding and legislation (e.g., STAR Act) and more genetic testing. Furthermore, survivors should be valued and continually used towards creating these goals and fostering new ones.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

The plan is not meant to describe all of the research priorities of the individual ICO's: Understood; and I realize I'm getting into a specific ICO as well as proposing suggestions in a smaller piece (NCI) of a much larger pie (NIH). But given that nature of an RFI being one to gather information at-large, as a staunch advocate as well as long-term survivor, I speak with purpose and objective passion (if such a thing can exist).

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

- Importance of studying healthy individuals This clearly goes into more specific research goals of NCI as it relates to childhood cancer, genetic testing and surveillance of its survivors more than general testing

of "healthy" individuals. - Advances in early diagnosis/detection Based on the very slow successes of detection and prevention, although very slim, for the childhood population the only way to realize advances is with increased funding in research specifically targeted at childhood cancers. - Opportunities based on molecular knowledge Clearly it would help if there were increased funding in this area - specific to DCEG within NCI. - Breakthroughs need partnerships, often come from unexpected directions Given that there are >500 independent organizations/non-profits whose sole purpose is childhood cancer, partnerships have been the primary measure of our successes and the voice for children

Future opportunities or emerging research needs

Today, childhood cancer remains the #1 killer by disease for children in our country, the incidence of childhood cancer is steadily increasing. Although there are very few types of childhood cancer which have seen a lower mortality rate there, for many childhood cancers, continues to be a much less satisfying prognosis. The fact that so little, when compared to other adult cancers, has occurred to "save" this future is a perverse decision made by our society and it needs to change.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

. . . is encouraged by the draft framework for the NIH Strategic Plan and appreciates the opportunity to comment. The framework sets the pillars of opportunity that the NIH Institutes, Centers, and Offices may address more specifically and clearly lays out the unifying principles across the NIH. While the areas of opportunity that apply across biomedicine are quite comprehensive, we recommend that further specifics in regards to emerging science and new technologies be acknowledged in the framework. For example, under the area to "promote fundamental science," there may be an opportunity to capture or further clarify two bullets and add an additional bullet. We suggest the following revisions. • "Leaps in Technology Platforms - often catalyze major sciences advances" (this is supported by advances in device technologies like next generation sequencing). • "Information technologies, including data collected from platforms such as MHealth, HER, and wearables, will catalyze transformational changes in clinical research." • "Data science, including sharing basic and clinical data, increase the impact and efficiency of research." Under the area to "advance treatment and cures," there may also be an opportunity to specifically call out emerging areas in science such as precision medicine, gene therapy and immuno-oncology. Precision medicine is poised to play a leading role in the advancement of drug development, with estimates of a 69% increase in the number of therapies developed by the year 2020 (Tufts Center for the Study of Drug Development, "Impact Report," Volume 17, No.3, May/June 2015).

Compatibility of the framework with the broad scope of the NIH mission

. . . has no comment on this topic.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

. . . agrees with the overarching concepts presented in the "Unifying Principles." However, in "Setting NIH Priorities" we encourage the NIH to use additional examples that are more inclusive of the major burdens of disease. We suggest editing the sentence to read "....supporting opportunities presented by decreasing the burden of non-communicable diseases, rare disease research, considering the preferences and experiences of the patient community, and the value of permanently eradicating infectious diseases and contributors to antimicrobial resistance. " NIH plays a critical role in enhancing stewardship, and . . . agrees with the principles laid out in this section. However, another critical component of increasing the efficiency and effectiveness of the research enterprise is to establish

mechanisms that enable sharing of primary data from both basic and clinical research. We recommend that “Basic and Clinical Trial Data Sharing” be added to the list.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

An area of opportunity that . . . believes is important across biomedicine is developing mechanisms that support collaborations across and outside the life sciences. More and more fields such as computational sciences, bioengineering, statistics, mathematics, biochemistry, and others are making significant contributions to life sciences research. It is at the interfaces of these disciplines where innovation is spurred, and the NIH needs to ensure that the framework of the strategic plan supports the establishment of more robust mechanisms to support these collaborations, for example including stronger alignment and coordination with the National Science Foundation (NSF) in strategic planning and dual funding opportunities. . . . is supportive of the areas of opportunity that have been identified in the draft framework. However, we also suggest one potential area for consideration. Over the past decade significant advances in science and technology have led us to better understand the biological basis of diseases -- advances in science through projects such as the Human Genome Project (HGP) have enabled new approaches to drug development based on a person’s genetic profile. Sharing of genetic data will help to enable the development of new cures that improve human health; therefore, we feel it is important that data sharing be identified as a new area of opportunity that has the potential to drive the 21st Century research agenda.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

. . . has no comment on this topic.

Future opportunities or emerging research needs

. . . has no comment on this topic.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The proposed framework focuses on promoting fundamental science, improving health promotion and disease prevention, and advancing treatments and cures. All three areas have the potential to move NIH’s mission forward. I believe the framework could be strengthened by expanding the focus on public health and clinical sciences. Epidemiology, biostatistics, and behavioral sciences are critical to the NIH’s commitment to the application of knowledge “to enhance health, lengthen life, and reduce illness and disability.” I would recommend adding the following bullet under Improve Health Promotion and Disease Prevention: “Public health and clinical sciences are the foundation for ensuring that basic science discoveries improve the health of individuals and populations.”

Compatibility of the framework with the broad scope of the NIH mission

NIH’s stated mission is “to seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability.” The proposed framework is in alignment with this; however, the focus on the fundamental knowledge is much stronger than on the application of knowledge. I recommend giving equal weight to the two parts of the mission.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-

NIH strategic plan

I suggest the following addition to the section on Enhancing Stewardship (under Unifying Principles): “advocating for increased research funding and promoting stable funding”.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

I suggest the following addition to the section on Improving Health Promotion and Disease Prevention. - “Importance of replicating findings across settings and populations” - “Importance of observational research” I recommend those related additions for the following reasons: Clinical trials are necessary, but observational studies are critical too. For example, our knowledge about the role of cigarette smoking in lung cancer did not come from clinical trials. Observational studies require replication in different settings not only to ensure their generalizability but also to support their internal validity. Innovation is critical to NIH, but so should replicability of findings to ensure their robustness.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

No.

Future opportunities or emerging research needs

The framework highlights reducing disparities. This is important. I suggest the following addition: “Importance of improving health care delivery”.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

While biomedical research is often thought of as directed toward treating or curing disease, we cannot understate the impact of NIH research on our ability to prevent disease from occurring. One half of cancer deaths are attributable to preventable causes. Past research supported by NIH and the National Cancer Institute (NCI) has helped develop screening tools and evidence-based prevention strategies for some of our most prevalent types of cancer. Successful prevention of cancer can involve very different approaches other than just drug-based curative treatment, often entailing behavioral modifications to improve healthy activities like good diet, screenings and exercise or reducing or eliminating unhealthy activities like smoking. Understanding how to change behavior to encourage healthy living requires research which is every bit as lifesaving as finding the next screening tool or therapeutic cure, yet often does not result in private-sector marketable products. Accordingly, we strongly encourage the NIH-wide Strategic Plan to appropriately prioritize research focused on prevention and social behavior modification. Evidence-based prevention strategies are a low-cost and highly effective means of fighting cancer and other diseases. Additionally, NIH-supported research can play an important role in reducing disparities in our health care system. Programs that support community-based, participatory research aimed at addressing health disparities must also be strategic priorities for the NIH. We would like to see the NIH increase support for clinical research that has a dedicated and meaningful focus on minorities and other underserved populations. Lastly, with the tightening federal fiscal environment it will be important for NIH to remain dedicated to supporting the kind of basic research that is not likely to be performed by anyone else and which can serve as the foundation for translational work by the broader private sector. --See attached for full comments

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

While basic research should remain the focus of NIH research, this should not preclude strategic investments in translational work. Specifically, NIH and the individual institutes are well-positioned to foster innovative and collaborative trial networks and study designs. As a neutral third-party, NIH can create research opportunities where multiple interventions, some developed by competing companies, can be evaluated in consolidated trials. NCI has recently opened several such trials including MATCH and Lung-MAP. These coordinated trials will be especially important when studying rare diseases, as the number of patients available for study may be extremely limited. Similarly, NIH should help facilitate international coordination on critical research issues like pediatric cancers. NIH should further facilitate maximal use of data collected as part of NIH-funded research. In many cases information like tumor genomes, patient treatment and outcomes data collected for one clinical trial can be used to answer multiple unrelated scientific questions. Fostering data sharing among researchers by instituting the appropriate consent and privacy controls will enable more efficient research and faster discovery. --See attached for full comments

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

NIH's mission is to seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability. Important in that statement is the role of behavior. As noted above, behavioral research plays an important role in disease reduction, and it should be expressly acknowledged in the areas of opportunity listed in the Strategic Plan. Furthermore, the goal of enhancing health goes beyond narrowly addressing pathologic conditions. It is important to note that many cancer patients and survivors, and the growing millions of others living with chronic diseases, experience poor quality of life because of the lack of attention to the symptoms like pain, nausea, fatigue and distress that accompany these diseases. Americans want and need the ability to live independently and to have their quality of life restored while they pursue treatment for their underlying disease. Unfortunately there is not a strong research base into how to improve their care through symptom management and coordination, otherwise referred to as palliative care. What research has been conducted, some of it supported by the American Cancer Society, has demonstrated that better coordinated care, and palliative care in particular, leads to reduced emergency room visits, ICU stays and hospital readmissions. We urge NIH to create a more comprehensive national research program into symptom management, palliative, psychosocial, and survivorship care to better understand how to manage care for the growing population of patients with serious and chronic illness with the intent of facilitating quality of life, wellness and independent living. -
-See attached for full comments

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

. . . applauds NIH for moving forward to develop a comprehensive NIH-wide strategic plan. It is our hope that this exercise yields a high-impact and actionable research blueprint that informs the actions of the 27 component Institutes and Centers. As NIH embarks in this effort, we urge leaders to ensure an appropriate and necessary focus on children. Historically, NIH's investment on child health research has been far below children's proportion of the nation's population overall. While most children are, fortunately, relatively healthy, we know that about 50 percent of all patients impacted by rare diseases are children and that 30 percent of such children will die before their 5th birthday. In addition to this sizeable burden, we also know that it is notoriously difficult to recruit children for research projects, particularly clinical trials. Given these challenges and the need, we would urge that the strategic plan include a dedicated focus on pediatric priorities and issues to ensure the needs of children are given appropriate attention. Furthermore, we urge that NIH not simply define priorities based on the sheer number of patients impacted by a disease or by annual aggregate costs as both criteria would place children and children's health at a sizeable disadvantage compared to adult-onset conditions. Finally, we urge NIH to recognize within the plan that many serious adult-onset conditions, accounting for much of adult morbidity, are rooted in childhood biology, behavior, social factors, and environment influences, and even in prenatal development. Given the potential impact of such research to help unlock critical research mysteries and to improve the health and well-being of children and adults, we would urge that NIH strongly consider making this issue a priority within the plan.

Compatibility of the framework with the broad scope of the NIH mission

. . . believes an overarching NIH strategic plan is very compatible with the broader scope and mission of the NIH and its component Institutes and Center. If done and implemented properly, such a plan should inform further the plans of each Institute and Center and help integrate such activities into a cohesive whole. The larger plan should not hinder Institute and Center efforts to develop more granular and focused plans in their respective areas. But hopefully, the plan can help foster multi-institute collaborations and remove walls and silos that have hindered such collaborations in the past. This is particularly necessary in pediatrics because of the reality that pediatric research is supported by most every Institute and Center.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

. . . applauds NIH for recognizing that basic science is the foundation for progress. We also appreciate the recognition of the growing importance of data science and of the science of health promotion and disease prevention and the profound impact advances in research technology have had in driving research progress. We would urge that NIH build upon these items and recognize within the plan that the NIH has a role to support the acquisition of research infrastructure, particularly shared core research technologies that are conducive to being used by multiple institutions and often cost prohibitive for a single entity. In recent years, NIH has steadily moved away from providing such direct support for research infrastructure. Building on the topic of infrastructure, NIH must recognize that future scientific gains will only come about from appropriately trained researchers, including clinician/scientists. As such, we urge NIH to recognize the necessity of providing training and related support for early career investigators. Such support is needed now more than ever given limited public and private research resources. With most institute paylines at historically low levels, early-career investigators are seeing much brighter prospects outside of academia and investigator-initiated research, to our collective detriment. A robust training and development program can address this problem and help us build the scientific workforce we need for the 21st Century.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Emphasis on health promotion and disease prevention is critical, particularly with individual who have mental disorders and co-morbid mental and physical conditions. Partnerships are also critical. More emphasis and funding should be placed on school and workplace health -- it's where people spend the prime time of their lives.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Need to study the positive aspects of stress (i.e., eustress), in terms of value, neurophysiological correlates, and health outcomes. Also need for studying technology enabled self-help treatments for multiple health conditions, but particularly for distress, anxiety, and depression. Thank you!

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The initiation of a development process for an agency-wide strategic plan for the NIH is a welcome undertaking that will serve to harmonize several broad goals across all NIH Institutes, Centers, and Offices (ICOs). By developing a framework for the agency to marshal the support and expertise of the ICOs, the NIH will be better able to set and advance its priorities for improving health and promoting basic science while creating a mechanism for reevaluating and adapting its goals every five years. However, while pediatricians support certain provisions and goals included in the current framework,

such as the importance of studying healthy individuals and recruiting and retaining a strong biomedical research workforce, more of an emphasis should be made on investments in research early in life as well as a strong focus on exposure to social and environmental factors in childhood that shape health and wellbeing across the lifespan.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Overwhelming evidence suggests that gene-environment interactions very early in development have profound effects on the emergence of adult diseases such as diabetes, cardiovascular disease, cancer, and psychiatric illness. Both the individual genetic code that predisposes to these diseases and the epigenetic mechanisms that control gene expression will likely be available to the clinician and family prenatally or in the first months or years of life. Many adult conditions have their antecedents in childhood, and promoting investments in research early in life will improve disease prevention and advance treatments throughout the lifespan. Further, while the current framework correctly emphasizes the development of evidence-based interventions to eliminate health disparities as an area of opportunity, this concept should be expanded to incorporate and initiate research on early environmental exposures and the social determinants of health across the agency. A major concern in the pediatric community is the effect of excessive and/or prolonged adversity due to factors like socioeconomic status, exposure to violence, family health, and others that can have significant adverse effects on a child's mental and physical development. These factors, in addition to exposure to environmental toxins and chemicals, can have vast effects on health across the lifespan and must be studied as early as possible in life to design and improve effective strategies for health promotion and disease prevention across all populations.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

There is a strong need for opportunities to discover and study non-canonical protein 'structure', such as intrinsically disordered proteins (IDP). Significant amounts of published research shows that these proteins are critical in many disease processes. IDP function is often related to its ability to move beyond what traditional crystallography can evaluate. In addition, even though NMR and other modalities can study small IDP, larger IDP, and complexes are opaque to current investigation methods. The normal functions of IDPs/IDRs are altered through diverse mechanisms in association with numerous human diseases, including neurodegenerative diseases (Parkinson's disease, Alzheimer's disease, ALS, and

others), many different cancers, diabetes, cardiovascular diseases, and infectious diseases. The downstream benefits of such research includes novel pharmacologic targets that could improve human health across the spectrum. Even immune-therapy could benefit since many of the nuclear signaling pathways downstream of immune modulation travel through IDP. What is needed are funding opportunities that truly value the multidisciplinary investigation that would allow IDP investigations to succeed. This requires a critical look at the structure of a study section that is evaluating proposals. Often times, IDP work is most successfully carried out by a team that includes biophysicists, 'structural' biologists, and molecule/disease specific scientists. In order to be successful in funding, a grant needs to be highly scored by 2 or 3 reviewers, thus grants whose team members represent a broad interdisciplinary blend often are scored poorly by a single reviewer. Given the scientific challenges in carrying out these cross-cutting, cutting-edge studies, review panels should be highly motivated to evaluate impact and novelty rather than approach. Scores should be skewed to benefit teams with excellence in their individual fields.

Compatibility of the framework with the broad scope of the NIH mission

nc

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

nc

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Disordered states of biomolecules are ubiquitous in the cell and these are particularly present in the nucleoplasm. A vast amount of nucleoplasm is containing proteins that are IDP. Disordered proteins as a class are less well-understood than stably folded proteins because they are not amenable to conventional structural biology approaches-especially as protein size increases and complexes of proteins are investigated. Intrinsic disorder is an essential aspect of the biological function of many proteins. Disorder is critical contributor in a host of important diseases: age-related dementias, diabetes, CVD, Huntington's, cancer, infectious diseases. One of the key challenges in understanding biology is the ability to study the function of multiprotein complexes. These complexes are often integrated by IDPs and are very difficult to isolate intact from cells. Understanding how these proteins interact, particularly in nucleoplasm is critical if science is to contribute to improved human health. Functional and dysfunctional disorder is a fundamentally important gap in our understanding of biomolecular function. Support of multidisciplinary teams to address these challenges is key to creating novel therapeutic targets and drugs that regulate these targets.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

nc

Future opportunities or emerging research needs

- Basic science of disordered states in proteins: biophysics
- Systems biology of disorder: interaction networks in health and disease
- Methods development for investigating intrinsically disordered proteins in their functional states, both in vitro and in their functional settings in cells
- Multiple, disease-centric research efforts on the role of disorder; these should be managed from a trans-NIH perspective that includes cancer
- Completely new paradigms for drug discovery involving disordered protein targets that involve empiric screening and opportunities for validation.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

BENEFITS: Best parts of plan: (1) Recognition of potential (and efficiency) offered by data science. (2) Elimination of health disparities. (3) Promotion of partnerships. (4) Breakdown of traditional disease boundaries. (5) Need for nimbleness. (6) Reduction of administrative burden. **DRAWBACKS:** The plan fails to note crucial mechanisms needed to serve stated objectives. Among the glaring omissions, the need to: (1) establish/promote registries and biobanks; (2) create a new Institute or other institutional structure which will enable the breakdown of traditional disease boundaries; and (3) devise a modality for obtaining valuable input and information from entities and individuals outside the formal structure of the NIH and its traditional partners. **CHALLENGES:** Many illnesses and conditions do not have an assigned Institute home or have a home which cannot accommodate emerging evidence. The problem is particularly acute with respect to multi-symptom, multi-system illnesses; the very diseases which hold the greatest potential to unlock the clues to a vast array of other conditions. Newly discovered conditions, orphan illnesses and environment-linked maladies also fall through the cracks. The dual task of advancing highly specialized, rigorous research and capturing “outside the box” transformative approaches is a tough one, particularly given financial constraints. The solution lies in designing structures which facilitate broad thinking, easy information sharing, and cross-pollination from groups which have been so-far quite exiled from the process. Much of value may be obtained for “free.” For example, modern communication technology can be readily harnessed for web-based, phone-linked formats which enable informal input from policy experts, health care workers, educators, and patients. Important contributions can be made not just by people with information, but by people posing novel questions.

Compatibility of the framework with the broad scope of the NIH mission

The framework is compatible with NIH goals, but missing elements will drastically limit what should be a sky-is-the-limit potential. NIH is quite right that this is a unique moment of opportunity in biomedical research. But unless better mechanisms are set up for acquisition, organization, and easy access of data, frankly, a lot of money and effort is going to be wasted. Two core missing features can save enormous amounts of money, reduce administrative hassles, and promote quality health care throughout the nation. These are: (1) Improvement of survey instruments and (2) Modernization of classification systems and coding. Computer science, of course, enables massive acquisition of information and opens venues for dynamic and flexible forms of inquiry. Multiple algorithms can data mine narratives, organize information, and pick out patterns which human beings (constrained by time, patience and eye strain) cannot. Data can be broken down into tiny bits and stored. Assumptions underlying research investigations can be identified and kept accessible. We no longer need to rely on findings based on destroyed records or mountains of paperwork sitting in a warehouse. We no longer need be perplexed by hypotheses based on premises that should have gone the way of the dinosaur. We’re in a new age but doctors, medical centers, and research groups are still using highly simplistic investigative instruments (like short paper surveys) which fail to capture crucial data. Right now there is not much incentive for them to do otherwise. The NIH needs to push folks into the 21st Century. A point of emphasis here is that many excellent detail-oriented research groups continue to be hampered by poor data acquisition and maintenance on the part of primary care doctors. How can a well characterized cohort be selected from a poorly characterized pool?

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Collaborative efforts are a major theme. However there has been – and continues to be – little institutional guidance from the NIH as to how productive interaction between different groups may be efficiently achieved. In addition, while rigor and reproducibility are laudable goals, creativity and new hypothesis generation also need to be encouraged. Improvement of NIH (and its sundry agency) web pages should be elevated as a priority. Much of the information is over-generalized. It is especially difficult and frustrating for doctors and researchers to get a handle on new developments in fields outside their own sphere of expertise. Finally, in areas where the nomenclature is changing or where the validity and utility of diagnostic criteria and research definitions are in flux, it would be most helpful for the NIH to include links to materials which succinctly state the various definitions. This can be done fairly easily by communication specialists working in concert with medical associations, university groups and patient organizations. Put another way, in areas open to debate, people need to know what they are debating about. The NIH would be well served to introduce clarity.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

There is no place for the voice of patients in the strategic plan. Avenues must be created to enable patients to become collaborators, particularly with respect to delineation of illness presentation, therapeutic preferences, disease management, and outcome measures. Scientists may have considerable scientific expertise, but they often bring biases to the table and lack in-depth knowledge of their subjects. Human beings are not mice. They do not live in a lab. They have personal histories, life experience, priorities and needs often overlooked by investigators. Those differences need to be recognized and better explored. Not only would researchers gain invaluable information about their subjects, but research design and priority settings could be improved to create larger cohorts. For example, patients who are unwilling or unable to travel to major medical center settings could help researchers design methods which collect data via internet applications or which pool data from multiple primary care tests. Another omission – and one which is truly an imperative – is enhancement of the capability to respond to emerging diseases and other health threats. The federal government is way behind the 8th ball in investigating the risks of electronic cigarettes, for instance. E-cig use is exploding among adolescents. Research is needed and fast to avert a potential future epidemic of cancers and respiratory disease. Urgent attention is also needed to develop a national capability to better respond to large scale environmental, terror, and natural disasters which give rise to immediate medical exigencies and long-lasting public health problems. Sep 11, Katrina, Superstorm Sandy and Fukushima all have lessons to teach. It is high time to learn them.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

Different stakeholders may have vastly different interests. Immediate resolution of competitive or conflicting interests may not always be feasible. Nevertheless public transparency would be enhanced by requiring clear explanations of objectives in terms that ordinary laymen would understand. It may also be worth considering some sort of mediation or alternative resolution system process for resolving inter- and intra-mural disputes. (This could be an alternative to the appeals up the bureaucracy food chain approach.) Such a mechanism might enable groups to work out win-win solutions that save taxpayer dollars.

Future opportunities or emerging research needs

Much greater priority should be given to investigation of multisystem, multi-symptom diseases and syndromes. These present special opportunity for elucidation of, not just the specific subject conditions, but other diseases as well as the human ecosystem at large. Multisystem, multi-symptom diseases also

tend to be particularly dynamic and subject to conceptual reformation as the state of the science progresses. There is thus less professional thought entrenchment and hypothesis orthodoxy to be a “drag” on creative thought. A prime candidate for focus is an illness which has been the subject of different constructs and has been identified as Myalgic Encephalomyelitis and Myalgic Encephalomyelitis/Chronic Fatigue Syndrome, an umbrella term which may recognize a spectrum or conflate two entirely separate illnesses. Nobody really knows. The latest concept was presented by the Institute of Medicine in a 2015 report titled “Beyond Myalgic Encephalomyelitis/Chronic Fatigue Syndrome - Redefining an Illness”. The IOM writes: “ME/CFS is a serious, chronic, complex, multisystem disease that frequently and dramatically limits the activities of affected patients. In its most severe form, this disease can consume the lives of those whom it afflicts.” The IOM report suggested proposed “systemic exertion intolerance disease” (SEID) as a new name. Whether SEID is the same illness as ME remains unresolved. But, regardless, the illness is fascinating and uniquely suited for facilitating the breakdown of traditional disease boundaries. The multisystemic and dysfunctional cascade aspects of the disease should encourage a much needed interdisciplinary approach. It should also attract researchers in emerging disciplines such as symptoms biology (complex interactions and network theory); symptomatology (identifying symptom links and aggregates); epigenetics (investigating gene expression caused by mechanisms rather than DNA); psychoneuroimmunology (focusing on mechanisms underlying brain-to-immune crosstalk); and other emerging fields.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The . . . commends NIH for seeking feedback on its framework for its strategic plan and encourages you to ensure that the incorporation of patient perspectives is a guiding principle of the strategic plan. The . . . brings together all segments of the health community to provide a united voice for the more than 133 million people with chronic diseases and disabilities as well as their family caregivers. . . . Other members include professional societies and membership associations, nonprofit organizations with an interest in health, and major pharmaceutical, medical device, biotechnology, and health insurance companies. We are currently in a transformative period where health stakeholders such as NIH, FDA, PCORI, and biomedical industry have made great strides to incorporate the patient voice into their research, development, and regulatory processes. There is a great opportunity for NIH to ensure that patient engagement is a cornerstone of its work. While there are many aspects of the framework where patient engagement would be meaningful, the two unifying principles (priority setting and enhancing stewardship) are two opportunities to fully incorporate it into everything NIH does. There is no better judge of unmet medical need than patients who currently lack effective treatments. We encourage NIH to set priorities and fund research in areas where people with chronic conditions believe treatment regimens are inadequate. The best way to make this determination is by talking to patients to learn their views on the burden of their condition and views on existing treatment options. We thank you for the opportunity to comment on this proposed framework and look forward to working with you as you develop the strategic plan.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Related to the comprehensive trans-NIH research themes not captured, NIH is strongly encouraged to consider: 1. Impaired function or over-activity of the immune system underlies many of the most costly human diseases. Further research into the basic mechanisms of the immune response is still needed, with a focus on translating findings from animal models to the human. 2. A strong need exists to identify biomarkers that are predictive of therapeutic response to the growing number of biologic drugs for many different disease states. 3. From increased use of biologic drugs, greater numbers of reactions will occur. It is essential to develop a better understanding of the mechanisms of these drug hypersensitivity reactions. 4. The clinical community needs protocols to allow for the administration of medications to which patients have previously had reactions.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Regarding "Future opportunities or emerging research needs," NIH is strongly encouraged to consider: 1. A strong need exists to engage non-academic community clinicians, and academic physicians in clinical research. 2. The NIH should examine ways to engage schools and employers in biomedical research and the delivery of healthcare. 3. A strong need exists to develop programs to build and expand the pipeline for clinical, translational, and basic science researchers. 4. Mechanisms must be preserved for research training.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The . . . appreciates this opportunity to submit comments to the National Institutes of Health (NIH) “Request for Information (RFI): Inviting Comments and Suggestions on a Framework for the NIH-wide Strategic Plan.” . . . strongly suggests that NIH address areas where Congress can assist NIH in achieving its mission, including the need for Congressional action to 1) ensure predictable and sustained increases to NIH funding, 2) enable NIH to carry over unused funds from previous years, and 3) lift the travel restrictions limiting the attendance of government scientists at scientific conferences. Without progress on these issues, NIH will continue to struggle to advance in many important areas, including workforce sustainability and stewardship responsibilities.

Compatibility of the framework with the broad scope of the NIH mission

. . . agrees that the framework of this proposed plan supports the NIH mission, and especially appreciates its emphasis on basic research, the critical foundation of prevention, treatment, and cures. In addition to stating that basic research often results in unpredictable discoveries, the plan should include examples of basic research discoveries that led to unexpected improvements in human or animal health. NIH should emphasize that while there is not always a clear connection between basic research and disease, this does not make such research any less useful or urgent; a lack of connection may, however, make it more difficult for scientists to explain the importance of basic research to those who insist that all biomedical research have a direct impact on disease. The plan should also reiterate the core reason that NIH must maintain a robust basic research portfolio: if the federal government doesn’t support such research, the private sector cannot not fill the void.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Vaccines and adjuvants, which are essential to the prevention and treatment of contagious and/or chronic diseases, are a focus of the NIAID strategic plan and are a cross-cutting area of opportunity that should be included in the “Improve Health Promotion and Disease Prevention” and “Advance Treatments and Cures” sections. Traditional vaccines, which prepare the immune system for future encounters with infectious diseases, are being complemented by the discovery and development of immunotherapeutics, which can boost the immune system and facilitate the destruction of cancer cells and are in clinical trials to treat Alzheimer’s disease, diabetes, and Ebola infection.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

“NIH’s mission is to seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability.” (<http://www.nih.gov/about/mission.htm>). Because the immune system plays a critical role in the detection and clearance of disease, and is essential for the healthy functioning of most organ systems, immunological research should be a cross-cutting theme that is highlighted in the trans-NIH strategic plan. For example, researchers continue to demonstrate that inflammation and immune processes are key contributors to a variety of diseases and degenerative conditions, including acute and chronic infections, cancer, metabolic disease, neurological disorders, osteoporosis, and heart disease.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an

NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

NIH must continue to address the need to recruit and retain young scientists, since the current funding situation has deeply discouraged many graduate students and postdoctoral fellows who wish to pursue careers in biomedical research (particularly those interested in pursuing an academic track). While NIH has taken some steps to improve the funding opportunities for early stage investigators, NIH should continue to make the sustainability of the early and mid-career workforce a top priority.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The framework of the strategic plan does not address the relative priorities of the various areas of opportunity and underlying principles. Budget pressures will (and should) force a prioritization of investment options. We support the highest prioritization of “promoting fundamental science,” realizing that advances in that area underlie advances in other areas of opportunity. However, this is a relative prioritization not an absolute prioritization, as “advancing treatments and cures” and “improving health promotion and disease prevention” are also necessary and appropriate efforts of the NIH. Also, among the list of ways to “enhance stewardship,” promoting scientific rigor and reproducibility are absolutely critical, but reducing administrative burden—both within NIH and at awardees’ institutions—should not be underestimated, as this could have a huge impact on encouraging innovation, retaining an outstanding workforce, enhancing partnerships, and more.

Compatibility of the framework with the broad scope of the NIH mission

The emphasis on promoting fundamental science, improving health promotion and disease prevention, and advancing treatments and cures is appropriate and fully compatible with the scope of the NIH mission.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

One way to “enhance stewardship” is to implement mechanisms for sharing best-practices across ICOs, yet this is absent from the “unifying principles.” Rather than suggest specific concepts from ICOs that should be included in the trans-NIH plan, we suggest that the trans-NIH strategic plan propose methods for continuous sharing of concepts and best practices across ICOs.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Any NIH strategic plan should contemplate ways to leverage public-private partnerships and collaborations with other government agencies, one example being the BRAIN Initiative. Without Presidential or Congressional mandate, how can NIH encourage these types of cross-cutting partnerships with the private sector and other agencies?

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

Areas of opportunity listed under “Improve Health Promotion and Disease Prevention” are applicable, but it is important for the strategic plan to address how NIH efforts differ from and will synergize with related efforts by other agencies, e.g., PCORI, CDC, etc. What is unique about NIH-sponsored efforts in

these areas? How will NIH communicate with other agencies to optimize use of funds?

Future opportunities or emerging research needs

The value of patient engagement in clinical research is becoming well recognized, but patient opinions are often difficult to quantify. Methods to help measure patients' or caregivers' valuations of "risk" and "benefit" can impact clinical trial endpoints, identification of biomarkers, studies to define optimal evidence-based interventions, and the stated NIH priority of "incorporating measures of disease burden."

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The current framework is sound, but understandably vague. It is important that behavioral science be supported adequately. The primary reason to support behavioral science is the nearly all diseases and disorders--all public health problems--come to attention due to human behavior, thereby, putting understanding the underlying mechanisms of human behavior at the center of the NIH mission. Behavioral science is not simply the domain of NIMH, NIAAA, or NIDA primarily, but of all divisions. The challenge for NIH is to enable members of congress to understand that the science of behavior is science and the back bone of the science that NIH can fund.

Compatibility of the framework with the broad scope of the NIH mission

The above seems compatible with the NIH mission.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

As noted above, behavioral science is important to all of public health and should be funded adequately across agencies.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Behavioral science and its importance to all biomedical understanding of disease and disorder should be highlighted.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

None that I can think of.

Future opportunities or emerging research needs

Seeing behavioral science as necessary to all biomedical public health science advances.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The broad tripartite framework proposed above is appropriate in scope. Under "Improve Health Promotion and Disease Prevention", the emphasis should be squarely on prevention, which implies deep fundamental understanding of the complex mechanisms linking environmental and behavioral risk factors to ill health, including for example insights from the social sciences, urban planning, exposure assessment, implementation science etc. the three current sub-bullets don't quite cover the subject, and

the bullet on early diagnosis fits better in "Advance Treatments and Cures" than here in prevention. We want to avoid disease if at all possible - i.e., the public health approach.

Compatibility of the framework with the broad scope of the NIH mission

Good overall fit, with modification noted above.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

There is increasing recognition across the public health and medical communities that climate change has the potential to be one of the most important health stressors of the 21st century. While research has begun in a very small way to understand the complex mechanisms linking climate and weather to adverse health outcomes, our knowledge remains in its infancy, largely due to the fact that the relevant questions, mechanisms, and tools fall in an uneasy gap between the typical interests of NIH on the one hand and NSF on the other. EPA, which might be a natural home for this cross-disciplinary science, and which has done most of the ground-breaking work to-date, is woefully underfunded. Without systematic and substantive engagement by NIH, the country is likely to be ill-equipped over the next 20-30 years to anticipate, prevent, and/or mitigate the emergent health burdens, both in the US and abroad.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Global environmental change and its potentially large impact on human health is an area in need of more substantive engagement.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

I would like to see the NIH make a stronger commitment to implementation science, which is not currently explicit in the proposed framework. Part of this commitment is a better understanding of clinical practice. NIH appears to continue to work from a top-down mentality ("basic science is the foundation for progress") that is questionable when it comes to progress that is meaningful for everyday services. This problem has led some prominent NIH-funded scientists to call for a 10-year moratorium on clinical trials and to focus those efforts instead on treatment implementation. I would not go that far, but I think we are naive to pretend that basic science research will automatically make its way into clinics and communities. Part of the problem here, at least in my fields of mental health and substance use disorders, is that NIH has been operating from a strong biological bias, neglecting psychological, social, and cultural aspects. We forget, for example, that just because "addiction is a brain disease" does not mean it is not also a sociocultural and behavioral problem. For addiction, for the past decade we have been handed "promissory notes" about what the next wave of neuroimaging, genetics, or pharmacological research will offer (with very little gains that have practical consequences), while we have a massive treatment-practice gap along with gaping sociocultural aspects that are neglected to our peril (e.g., the effects of the war on drugs, mass incarceration of African Americans, the effects of

colonization on American Indians, the role of declining communities and loneliness, and so forth). My fantasy would be for NIH to head more directly (at least for some problems) into behavioral and social research, as well as have greater accountability for research agendas that do not directly benefit everyday care and vulnerable populations.

Compatibility of the framework with the broad scope of the NIH mission

Nothing to add.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

As mentioned in my comment above, implementation science ought to be included. I also think that the "importance of studying healthy individuals" ought to be expanded to include "healthy families and communities and exemplar treatment service units." We ought to see health as broader than mere individuals.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Again, implementation science. I also would like to see "social justice" in the NIH strategic plan (a much broader concept than "health disparities").

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

Nothing to add.

Future opportunities or emerging research needs

Nothing to add.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The . . . supports the National Institutes of Health's (NIH's) efforts to develop and refine a new 5-year NIH-wide Strategic Plan to advance the agency's mission and appreciates the opportunity to offer brief comments and suggestions as the process moves forward. . . . strongly believes in NIH's mission "to seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability." . . . and the science center and museum field are especially interested in -- and contribute substantially to -- advancing the public's knowledge about and engagement with science, technology, engineering, mathematics (STEM) and health-related subjects. As NIH, its senior leadership and staff, and the Advisory Committee to the NIH Director finalize the agency's 5-year Strategic Plan and framework, . . . encourages all parties to do all they can to ensure that public education, communication, and outreach regarding health-related information are key components and specifically and explicitly reflected therein. Current NIH offerings like the Science Education Partnership Award (SEPA) program, whose goal is "to invest in educational activities that enhance the training of a workforce to meet the nation's biomedical, behavioral and clinical research needs," remain essential and worthy of both attention and support. The SEPA program "encourages the development of innovative educational activities for pre-kindergarten to grade 12, teachers and students from underserved communities with a focus on Courses for Skills Development, Research Experiences, Mentoring Activities, Curriculum or Methods Development or Informal science Education exhibits, and Outreach activities.

Compatibility of the framework with the broad scope of the NIH mission

. . . welcome the opportunity to continue to support important pieces of the NIH framework. In particular, science centers can assist with public outreach, education, and communication related to "Fundamental Science," "Health Promotion/Disease Prevention," "Treatment/Cures," and "Enhancing Stewardship." Again, . . . supports a specific mention of public outreach, education, and communication in the framework, as it should be a key part of the NIH mission.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

While the aforementioned Science Education Partnership Award program resides in the Division of Program Coordination, Planning and Strategic Initiatives Office of Research Infrastructure Programs, . . . believes that its goals are, in fact, universal to NIH and would/should be of interest to other NIH Institutes, Centers, and Offices (ICOs). As a result, . . . encourages NIH to include similar concepts and ideas in the trans-NIH strategic plan, as all ICOs and, most importantly, the general public, would benefit.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The . . . commends NIH for advancing a framework that is "roomy" and, at least so far, not restricted to a few currently high-profile diseases. However it is not apparent from this framework what particular areas or types of research will eventually be named as priorities: the examples NIH chooses to illustrate points in the framework may well be taken as "the" priorities. Thus we take this opportunity to comment on what . . . hopes to see included. In the overview it would be valuable to emphasize how NIH plans for and supports research that cuts across institute silos (via working groups, Common Fund, offices in the OD) to reassure policymakers that the complex NIH organization remains nimble and responsive to new opportunities and that it encourages multiple perspectives. In discussing the intramural program we urge you to emphasize NIH's unique contributions to science through resources that extramural facilities cannot match: for example, the rhesus monkey cohorts in Poolesville and NIA's Baltimore Longitudinal Study. Also, we ask that NIH acknowledge that while it is critically important that institutes and centers develop strategic plans that can be more specific than an overall NIH plan, there are areas of research that may go unsupported as other areas are emphasized. There should be a process for considering how NIH might manage needed research that the "home" institute has de-emphasized.

Compatibility of the framework with the broad scope of the NIH mission

. . . is pleased to see the emphasis on support of research on healthy individuals and, we would add, normal development. The life-course perspective employed at NICHD, NIAAA and NIA is critically important for understanding how the accumulation of both subtle and acute system damage may contribute to the development of disease, and, as well, how the development of strength and resilience over time may contribute to protection against disease. The emphasis on health disparities is very important. That it arises in the framework under “Health Promotion and Disease Prevention” is appropriate, but of course fundamental research may also contribute to the elimination of health disparities. As a way to enhance scientific stewardship, we hope the strategic plan will prioritize NIH’s work to develop a scientific workforce more representative of the population and development of tools to ensure that grant review is fair to all applicants.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Behavior and cognition as highlighted in the NICHD Strategic Vision are important cross-cutting areas: “Behavioral factors can significantly promote positive health outcomes or increase the risk of adverse ones. Similarly, cognition—with its key relationships to neurodevelopment and learning—is part of a lifelong process that underlies overall human functioning. Basic and translational research that combines neuropsychological, behavioral, and social science perspectives, as well as new tools, will advance our understanding of the mechanisms underlying typical and atypical behavior and cognition. In the future, this enhanced understanding of behavior and cognition can ameliorate an array of developmental conditions or help individuals interact with the world in ways that can sustain or improve their health and well-being.” (p. 10) The NIH plan should emphasize research on factors that underlie many diseases and conditions, such as diet and physical inactivity. Behavioral research on these factors is highlighted in several plans including that of NCI: “Over the past few decades, the incidence of obesity has risen markedly in the United States and in many other countries around the world. Although the so-called “obesity epidemic” has been most commonly linked to the rising incidence of diabetes and related conditions, it also has substantial implications for cancer research and cancer control, since obesity is associated with increased risks of developing cancer at many sites. ...[including] the esophagus, endometrium (uterus), colon/rectum, pancreas, breast, and liver. In the liver, nonalcoholic steatohepatitis, which can develop in obese individuals, is associated with an increased risk of developing liver fibrosis and liver cancer. It is important to refine our understanding of the associations between obesity and specific cancers, determine the mechanisms underlying these associations and their potential reversibility for people who lose weight, and support behavioral research to help overcome obesity at the individual and population levels.” (p. 5-6)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Scientific progress is enhanced when basic and translational research occurs at multiple levels of analysis and when multiple perspectives are employed. This is facilitated by research efforts that include the humane and ethical use of animals, including nonhuman primates as models for human health and disease processes that cannot be studied easily, ethically, rigorously, or in sufficient detail in humans alone. . . . urges NIH to emphasize the importance of trans-NIH research with animal models in the strategic plan given that attacks on this research are increasing. Note that many of the ICO strategic plans emphasize research with animals. From the NINDS strategic plan: “Animal models that recapitulate key features of human disease could provide new insights into disease mechanisms and enable better testing of potential new therapeutics.”(p. 8) And from the current NIDA strategic plan: “Animal models have greatly contributed to our understanding of addiction’s underlying substrates, the abuse liability of novel compounds, the role of candidate vulnerability genes and stress in relapse, and

the persistence of drug taking. They allow scientists to rigorously control and analyze biological and environmental factors related to drug abuse and test novel approaches to prevention and treatment. The noteworthy development of buprenorphine as a treatment for opiate addiction began with studies using animal models, as is the case for most medications being tested in human clinical trials.” (p. 24)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

All of the components listed in the Areas of Opportunity framework are applicable to the NIH strategic plan.

Future opportunities or emerging research needs

Many urgent policy questions cannot be answered without NIH research, and that urgency ought to give this research an advantage in the priority-setting process. A few examples: 1) Communities struggle with effective ways to deliver drug abuse treatment in criminal justice populations given changing policy circumstances, e.g. decriminalization of marijuana, retroactive sentence reduction in cases of crack vs. powder cocaine, and emerging epidemics (e.g. heroin overdose) or secondary epidemics (e.g., hepatitis C); 2) Electronic nicotine delivery systems (ENDS) – do they represent a liability (as a possible gateway to tobacco use) or a remarkable treatment advance (as a cessation aid)? 3) How will dramatic increases in uptake of marijuana affect health in the U.S. given changing attitudes and laws related to its use? Another example relates to research on psychotherapy. New models of therapy to help couples in distress are needed to inform practice: now, therapeutic counseling helps only about 50 percent of couples, but that rate could be much improved. Couples’ distress is a common but very costly problem that impacts the health of its sufferers and other family members and the U.S. healthcare system. But because the burdens of this distress and the benefits of its relief go beyond measures of health alone, NIH support for this research has waned. Research that leads to strengthening families and improving their resilience ought to be central to NIH’s mission.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Is there a strong connection to population health? Is there consideration to support work that is not defined as a disease? Area of focus better defined: Children

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Population education, given the growing diversity and polarization of the US population. The tools that worked in the past will not work in the future. If the future of community health is a more proactive and self reliant community to care for itself, then what role does the NIH play to be a catalyst of this information for all to see and use. Does the NIH need to care about the end consumer of all that it is discovering?

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Given the lack of funding growth in the future, is there a new role for partnerships that needs to be more clearly spelled out in the strategic plan? Much like the NFL and GE have partnered for the advancement of sport related mTBI research, should there be a more well defined road map for NIH partners? Does the NIH need to challenge its business model?

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The . . . appreciates the outlined “areas of opportunity” as the science conducted by nurse researchers aligns with all three components the framework describes. Our comments specifically focus on the “advance treatments and cures” section. . . . firmly believes that the best discoveries come from pairing the minds of researchers from diverse disciplines, including those who have a health professions background and other sciences. . . . questions if under the “advance treatments and cures” section, the term “unexpected” is the best adjective for partnership directions. Breakthroughs do result from unexpected directions and there is need to create a platform in which consideration is given to how these partnerships can occur. However, comprehensive inclusion of who and which disciplines comprise the scientific team should be the result of thoughtful consideration at the onset and a standard we strive to achieve rather than unexpectedly. . . . supports the inclusion of Enhancing Stewardship as an essential unifying principle to this framework and believes it is a laudable benefit to future discoveries. Enhancing Stewardship speaks directly to recruiting and retaining an outstanding research workforce that focuses on diversity. Within . . . membership are 5,290 research-focused doctoral students, 25% of which come from ethnic and minority backgrounds. Many of these highly-skilled . . . scholars rely on, or attempt to secure, NIH support either directly or through a faculty member with an NIH grant. Moreover, we believe it is important that emerging scientists with strong research questions have opportunities to build long careers as investigators. Enhancing Stewardship also promotes collaborative partnerships and as indicated above, . . . supports all efforts to maximize this priority. Partnerships allow for the strong intent behind the Enhancing Stewardship unifying principle which includes, encouraging innovation, optimizing approaches to guide how decisions are made, and promoting scientific rigor and reproducibility.

Compatibility of the framework with the broad scope of the NIH mission

The necessity of NIH’s mission to be broad in scope only further underscores the importance of scientific discovery. Fundamental knowledge of living systems and its application to enhance health requires an open-mind to new approaches and does not limit innovative thinking. The framework is compatible with that overall goal.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

For 15 years, . . . has actively supported the investigation, education, and incorporation of research and best practices in providing palliative and end-of-life care through our We were encouraged to hear during the August 12, 2015 webinar NIH hosted on the Strategic Plan that the agency was aware of the need to consider how best to incorporate the application of biomedicine across the entire life-span. Palliative and end-of-life care is a core component of the National Institute of Nursing Research’s

Strategic Plan: Bringing Science to Life and we support the inclusion of investigations across the life-span.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Additionally, . . . agrees, as the overview section stated, the constraints confronting the research community due to a loss of NIH's purchasing power is of grave concern and we look for this to be further emphasized. A June 18, 2015 letter supporting the 21st Century Cures Act, which . . . signed, discusses how NIH has lost nearly one-fourth of its budget after inflation in the past decade. Like other scientists, competition is intense for nurse researchers within our member institutions. A strong investment in scientific discovery is a national priority as it affects health nationally and globally. . . . is a staunch supporter of all NIH ICOs and support efforts to ensure funding for the agency is sustainable to make the innovations necessary for improving health and quality of life. . . . commends the comprehensive approach NIH is undertaking to develop the five-year NIH-wide Strategic Plan. Soliciting insights from the senior leadership and staff at all 27 Institutes, Centers, and Offices (ICO) has allowed the current framework to truly capture the depth and breadth of NIH's research landscape. The framework for the NIH-wide Strategic Plan is thoughtfully constructed and equally expansive. Each section (the overview, areas of opportunity, and unifying principles) adeptly encompasses trans-NIH themes.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The 3-theme outline under "Opportunity.." is a good balance among basic research and translational research. Additional detailed information will make the statements stronger.

Compatibility of the framework with the broad scope of the NIH mission

It fits well with the NIH mission

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Should promote pre-clinical research studies through "Breakdowns of traditional disease boundaries and breakthroughs from unexpected directions", which have only been listed under advanced treatments

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The three main headings of “Promote Fundamental Science,” “Improve Health Promotion and Disease Prevention,” and “Advance Treatment and Cures” are reasonable primary categories for conceptualizing the overall work of the NIH. However, what is missing is an additional primary heading that explicitly supports multidisciplinary science and, by extension, team science, e.g. “Foster Multidisciplinary and Team Science.” Even the most basic, mechanistic health research should be developed with translation in mind, considering preventative and/or therapeutic applications. In addition, as the pace of discovery accelerates and the depth of information available becomes increasingly complex, research teams with diverse expertise will be required to maximize efficiency and opportunities for success. The breadth and depth of “Improve Health Promotion and Disease Prevention” are not equivalent to the other two categories. An additional bullet should be included to emphasize the importance of disease prevention and support of understanding and promoting health and wellness.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

- Openness/Data Sharing: NIH has already taken important steps to encourage open-access sharing of data and results. NIH’s commitment to the value of openness should be included in the strategic plan.
- Tools for Reproducible Research: NIH should consider what type of funding mechanisms could be channeled towards the development of tools and methods for reproducible research.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

- Multidisciplinary funding mechanisms: Develop means to solicit and review multidisciplinary research that extends beyond the traditional boundaries of the Institutes, Centers, and Offices (ICOs) or would fall under the purview of more than one ICO.
- One ICO: The current system of Institute-specific silos is particularly inefficient in the population sciences. For example, prospective cohort studies are of value to almost every Institute, but currently one Institute is usually responsible for core funding. Obtaining funding from other Institutes is cumbersome, and sometimes the impression is given that funding from another Institute is a sign of lack of commitment to (or betrayal of!) the original Institute.
- Innovative research: Establish flexible funding to support high-risk, high-reward science. This type of funding would provide margins for risk in a climate where conservative, incremental science seems to have a higher probability of funding given NIH budgetary constraints.
- Seed funding and infrastructure investments for emerging research fields, e.g., microbiome/microbiome collection, cohort studies representing

diverse populations, mobile technologies, claims data, electronic medical records. While scientific and technological advancements offer incredible potential for public health and life science research, the scientific community cannot fully realize the promise of these advancements without adequate “cross cutting research platforms and infrastructure,” which is difficult to fund through traditional NIH funding mechanisms. Examples include resources to support large-scale biological and microbiome specimen collections, management and analyses of longitudinal cohort studies, and the development of new technological applications that would enable scientists to collect, link, and leverage unprecedented volumes of data and deliver novel interventions.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

- Recommend that NIH includes in their strategic plan a focus on communication with the public to improve the public perception and understanding of the value of research being performed with federal funds.
- Recommend that NIH has better communication between the CSR system and the institutes, i.e., recommend that NIH has better integration of the framework initiatives with the study section scoring criteria. Continue to assess ways to incentivize the best scientists to commit to study section, particularly those that are able to review grants at the interfaces of disciplines.
- Recommend that NIH focus research in global health issues that really matter in terms of human life. The proportion of funding should be directly proportional to the magnitude of the current and possible predicted disease burden in human health.
- During the current economic situation, put limitations in the total amount of funding that a PI should have. This will not only allow for more labs to be funded, but also broaden the perspective about a given area of research, limiting centric views of a well-funded lab.
- Reduce large budget grant proposals such as (U19/U2) in favor of programmatic (P01) and/or individual/multi-PI proposals such as R01, R21 and R03.

Compatibility of the framework with the broad scope of the NIH mission

N/A

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

- Recommend that NIH include in their strategic plan a focus on managing the changing demographics of the population and how these will be supported and addressed (e.g. increasing age, changes in gender, race, ethnicity and co-morbidities).
- Recommend that NIH has specific opportunities for research that cross NIH institutes and divisions.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

- Recommend that NIH puts more emphasis on crosstalk between the fields of microbiology and cancer. There have been few RFAs relating to this, but microbes are associated with the development of cancer, often kill cancer patients, and are being harnessed for targeted cancer cures. Also cancer treatments predispose to certain types of infection.
- Recommend that NIH provides shared funding between institutes, so outstanding grant proposals can be co-funded.
- Recommend that NIH has better funding for those underrepresented in science. Minority supplements for such individuals should be nearly automatic which has not been the case of late.
- Recommend that NIH has continued balance between basic research and “translational research”. Important new findings come from basic research. Basic research should not be minimized.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

- Advance research opportunities presented by rare diseases.

Future opportunities or emerging research needs

- Recommend that NIH puts more emphasis on the human microbiome and its relation to disease.
- Facilitate the study of human specimens abroad. NIH funded researchers should have the opportunity to use CDC and/or NIH international labs to perform their studies. This will facilitate research that is being limited by the difficulty with human specimens export.
- More emphasis on the human tissue environment in microbial infections and diseases.
- Point of care diagnostics in low income settings.
- Initiate programs in educational training in managing diseases in low income settings prone to epidemics.
- In addition to hypothesis driven mechanistic research allow for discovery driven research that can reveal fundamental aspects of diseases. Focusing purely on mechanisms limits new discoveries.
- More emphasis on analyzing/using experimental systems relevant to human diseases.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The . . . appreciates this opportunity to inform the National Institutes of Health (NIH) 5-year Strategic Plan. NIH has a tremendous opportunity to continue in its support of clinical care and public health by focusing resources on disease prevention research. As frontline health care providers, osteopathic physicians promote preventive care and are well aware of the population-wide benefits that result from prevention. These benefits are most profound for patients, who benefit from improved clinical outcomes and report better quality of life. In addition, by supporting wellness and promoting health, health care systems are able to run more efficiently and effectively, saving costs that can be reinvested to further promote best practices. As our nation focuses on population health and managing our resources most effectively, NIH is positioned to take a key role to produce and disseminate research that demonstrates the value of managing wellness over managing disease.

Compatibility of the framework with the broad scope of the NIH mission

The framework of the strategic plan is well aligned with the overall mission of NIH to foster new discoveries that improve human health. This fundamental evidence base is necessary for developing and implementing clinical practices that advance population-based health, while equipping providers with tools and insight to better address the individual needs of their patients. As such, NIH's mission as expressed in this framework advances both macro-level health systems' improvements and micro-level patient-centered care. As patient-centered care is a core tenet of the osteopathic medical philosophy, we note that this effort aligns with . . . mission and we offer our support to disseminate key findings to providers.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

NIH is favorably positioned to leverage its strength in combination with other federal agencies in cross-cutting efforts. One notable opportunity to undertake cross-cutting work includes public education and dissemination of research findings. As NIH's discoveries hold tremendous value for patient care, we suggest increased collaboration with CDC, other agencies, and partners such as the . . . who are positioned to share these findings with key audiences including providers, payers, and patients. Stewardship of this valuable biomedical information to ensure it reaches audiences in the field will facilitate the application of key insights and discoveries. This activity will also form a bench-to-bedside

bridge to enable swifter and smoother transitions of biomedical information from discovery to application. Increased education and public awareness of health and wellness, backed by NIH's research, will amplify public interest and engagement in wellness and preventive health. Patient engagement in their own health will positively impact health outcomes, and will enable providers to maximize their relationships with patients to support these favorable outcomes

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

As NIH considers augmenting its portfolio, we suggest two areas of research that will support best practices in clinical care. First, research in the efficacy of primary prevention of disease results in clinical benefits to patients and also supports cost-effective care. As disease prevention enables avoidance of symptoms, treatments, and potential complications associated with disease, patients reap benefits from wellness. In addition, as the costs associated with treatment of disease are significant, especially when aggregated at a population health level, the health system overall benefits from increased prevention of disease. This allows resources to be better allocated to further prevention and wellness activities, which result in additional savings. Second, research about the value of appropriate care at each stage of life supports clinicians in making decisions that are best suited to their patients. As optimum care for any single condition will vary based on the patient and their circumstance, further research into the factors that differentiate appropriate care are valuable. This research would demonstrate that appropriate care for patients changes at each stage of life. Such a perspective, backed by evidence, would equip physicians to provide more appropriate care for each patient, as well as be better stewards of health care resources.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

n/a

Future opportunities or emerging research needs

The . . . appreciates NIH's goal "to exemplify and promote the highest level of scientific integrity, public accountability, and social responsibility in the conduct of science." This aim ensures that NIH-funded research is completed according to verifiable methodology and professional standards. As NIH's research has wide reaching impacts across the nation and beyond, we encourage NIH to consider further publicly promoting this goal which will set an optimum standard for other researchers and institutions engaged in scientific discovery. In addition, NIH is positioned to leverage its position as a world leader in the field of biomedical research to engage researchers in dialogue that promotes social responsibility and public accountability in the field. These values will strengthen the process by which research is conducted more broadly, ensuring that research can inform health care, address gaps in knowledge, and promote the advancement of medicine.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework
(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission
(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-

NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

. . . appreciate the opportunity to comment on the NIH Strategic Plan Framework. This comment addresses future opportunities and emerging research needs, as suggested by the RFI. . . agree that breakthroughs often come from unexpected directions and suggest research aimed at advancing treatments and cures should remain a priority. Around 95% of drugs found safe and efficacious in preclinical tests later fail during human clinical trials due to their toxicity and/or lack of efficacy. This leads to safety issues, delays in approval and increased costs. Improving clinical trials has been a priority in drug development, while advancing the tools used in preclinical testing has received little attention. . . . suggest that research to advance treatment and cures should broaden to include a focus on the relative predictive values of existing and emerging preclinical test methods. Although the translation discrepancy between current preclinical safety predictions and actual clinical outcomes is now widely appreciated, the actual predictive value of individual methods is, at best, poorly understood. Information obtained from research into clarifying the value of individual methods, both existing and novel, would be of inestimable value to drug developers when deciding which preclinical technologies to use. They would have access to more information on which to select the most predictive test methods available. Indeed, use of those most predictive is essential to the timely development of safer and more efficacious drugs as treatments and cures for human diseases. As stated, . . . urge NIH to include research on the predictive value of preclinical test methods in its 5-year plan.

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Potential benefits, drawbacks/challenges, and areas of consideration for the current framework
(*Submitter left answer blank*)

Compatibility of the framework with the broad scope of the NIH mission
(*Submitter left answer blank*)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan
(*Submitter left answer blank*)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine
(*Submitter left answer blank*)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan
(*Submitter left answer blank*)

Future opportunities or emerging research needs

Personalized Healthspan Care Initiative Thomas Jefferson described in the Declaration of Independence three unalienable rights as "Life, Liberty and the pursuit of Happiness". Healthspan, the length of time in one's life where one is in optimal health, is relevant to two of these rights. America is facing an unprecedented challenge of high incidence of non-communicable diseases, also known as chronic diseases, which account for > 60% of the death and engulf > 75% of health care costs. Our yearly budget of > 400 billion dollars in research has led us understand well the molecular makeup of our body and the processes of disease development. Our lifespan increased by 10 years in the last 50 years, but sadly not the healthspan. The good news is that lifestyle interventions, such regular exercise, have profound health benefits. However, the overall benefits of these interventions are far from being completely understood and sufficiently implemented. It is the time for concerted, multiple scale efforts in service, research and education to address this tremendously important question. NIH could strategically establish and support Healthspan Centers across the country. The goal is to provide scientific information to ultimately have personalized healthspan care for everyone across lifespan. The Centers will promote interdisciplinary research in areas like physical activity, dietary intervention, circadian rhythm, microbiota, mind-body interactions and scholarship to optimize health and well being across the lifespan from preconception to elderly. The Centers also provide education and community service to promote implementation of healthspan interventions. The knowledge gained will promote a nationwide change in every aspect of life to maximize the healthspan in meeting the huge challenge of chronic disease pandemics.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The framework calls for breaking down traditional disease boundaries and the need for partnership to achieve breakthroughs. The . . . believes that these are beneficial to the framework and the key to improved health outcomes for the American people. The . . . fosters cross-disciplinary approaches that emphasize the importance of Institutes crossing boundaries to look at co-occurring disorders, such as

depressions and cardiovascular diseases, depressions and cancer, depressions and diabetes, bipolar illness etc. We refer to these as “C2C” (Center to Center) approaches and encourage the NIH to establish programs that encourage and grow these initiatives.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

The . . . promotes the treatment of depressions, bipolar illnesses and related mood disorder using a coordination of care model (primary care, PCMH’s, etc). The . . . recommends expanding the “Advance Treatments and Cures” opportunity to explicitly call out Coordination of Care as a model for improving health. Research on the impact of care coordination is necessary to identify the most effective approaches and drive adoption across all sectors.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

The . . . urges the NIH to foster approaches that emphasize the impact of depression on physical health broadly speaking, and the need for new science to integrate behavioral health approaches to improving physical health.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The . . . , which is a collaboration of national non-profit organizations focused on addressing policy issues related to . . . commends NIH for beginning its work to develop a strategic plan. As part of this process, the . . . strongly urges NIH to broaden its definition of “disease burden” beyond the number of people impacted to include diseases with very low five-year relative survival rates. As an example, the Recalcitrant Cancer Research Act (Public Law 112-239) defines recalcitrant cancers as those with a five-year survival rate of less than 50%. We believe that a disease’s survivability is an important criteria to consider when deciding how limited resources should be spent and is a critical piece of understanding a disease’s burden to our country.

Compatibility of the framework with the broad scope of the NIH mission

The . . . encourages NIH to take steps to ensure that the NIH strategic plan is complementary to the individual strategic plans and priorities that have been developed by the National Cancer Institute and the other ICs. For example, the . . . was pleased with the scientific frameworks that the NCI released in 2014 for pancreatic cancer adenocarcinoma and small-cell lung cancer as a result of the Recalcitrant Cancer Research Act and strongly believes that similar frameworks should be developed for other recalcitrant cancers. This process could also be used as a model for other diseases.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

The NIH strategic plan should foster interdisciplinary collaborations and partnerships by encouraging a systems strategy to research initiatives.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

The . . . also encourages NIH to consider the incorporation of “big data” approaches that could revolutionize the standard clinical trial format and accelerate progress for the most recalcitrant cancers.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

The strategic plan highlights the importance of Technology Leaps and Data Sciences in the potential impact of healthcare research and healthcare delivery. We believe the Strategic Plan should also make a particular emphasis on constantly connected devices and the Internet of Things as part of future healthcare delivery and research. The vision for the Internet of Things, related data sciences, and constantly connected devices is well beyond what is seen in medical devices today. The inclusion of 5G technologies in the following 5 to 10 years will enable constant connectivity, real-time monitoring and control and data aggregation from and for a multitude of medical and consumer devices that patients may use in the near future. In order to maximize the potential health-related impact of this vast amount of information, healthcare systems will need to be prepared to gather, analyze, aggregate, and take decisions based on this information. As an example, consider the availability of smart appliances (e.g.

smart fridge), Internet-enabled critical systems (e.g. pacemakers, medication delivery devices), and Internet-enabled health indicator measurement systems (e.g. blood pressure monitoring systems). Future communication systems will be capable of providing highly reliable and secure connectivity to all these devices to gather, analyze and potentially optimize the outcome for each individual in real-time. A highly effective healthcare delivery system will make use of a combination of the information gathered by all these devices to deliver preventive care, diagnosis, and disease treatment effectively and efficiently. “Unlocking the potential of the Internet of Things”, by James Manyika, Michael Chui, Peter Bisson, Jonathan Woetzel, Richard Dobbs, Jacques Bughin, and Dan Aharon, McKinsey Global Institute, June 2015, available at: http://www.mckinsey.com/insights/business_technology/the_internet_of_things_the_value_of_digitizing_the_physical_world “8 Must-Have Implants for the Cyborg Patient”, Sarah Lewin, IEEE Spectrum, June 2015, available at: <http://spectrum.ieee.org/biomedical/bionics/8-musthave-implants-for-the-cyborg-patient>

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Areas of consideration for the current framework include adding a specific reference to “rehabilitation science” so that this critical area of research is reflected in the overall NIH strategic plan. Rehabilitation research was defined by the Blue Ribbon Panel on Medical Rehabilitation Research (December 18, 2012) as “the science of mechanisms that prevent, improve, maintain, restore or replace lost, underdeveloped or deteriorating function as a result of an illness, injury, disorder, or other health condition.” The term “function” referenced in the Blue Ribbon Panel Report’s definition is defined at the level of impairment, activity, and participation according to the World Health Organization-International Classification of Functioning, Disability and Health. While much of NIH research focuses on finding cures for disease, rehabilitation research focuses on improving, maintaining or preventing deterioration of function whether or not finding a cure is possible. Furthermore, a focus on function is critical due to the provisions in the IMPACT Act requiring CMS to develop and implement a standardized patient assessment, focused on functional status and changes in function, across Medicare and Medicaid funded post-acute care and long-term care settings. Trans-NIH funded enhancements in our understanding and measurement of function is required to make this standardization process most relevant and appropriate.

Compatibility of the framework with the broad scope of the NIH mission

The framework, as revised (above) to include a reference to rehabilitation science, is compatible with the broad scope of the NIH mission which includes enhancing health, lengthening life, and reducing illness and disability. Rehabilitation science focuses on this goal and is consistent with the overall NIH mission. The National Center for Medicare Rehabilitation Research (NCMRR) has been designated by Congress to be the lead agency within NIH on rehabilitation science and the Blue Ribbon Panel found that \$300 million is annually spend by NCMRR and a number of other Institutes and Centers. Therefore, rehabilitation research should be appropriately reflected in the NIH strategic plan. It is critical that the strategic plan’s framework include rehabilitation science in order to enhance its stature and visibility at the world’s premier medical research agency. Better coordination between NIH institutes and centers and among the federal agencies conducting and supporting rehabilitation science is critical.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Rehabilitation science itself is a prime example of cross-cutting research at NIH and should be

specifically included in the trans-NIH strategic plan. The focus of rehabilitation science includes significantly influencing future treatment for persons with injuries, illnesses, disabilities and chronic conditions. Rehabilitation science is broader than a mere focus on an individual tissue or body system. The value of rehabilitation science is reflected in the improvement, maintenance and prevention of deterioration of functioning for individuals in their daily lives. Rehabilitation science can facilitate natural recovery and augment the therapeutic effects of interventions toward recovery, but also answers the questions once cure is no longer an option. Multiple NIH Institutes and Centers engage in rehabilitation science and coordination of efforts to match research priorities will maximize the return on the federal investment. Furthermore, a focus on function is critical due to the provisions in the IMPACT Act requiring CMS to develop and implement a standardized patient assessment, focused on functional status and changes in function, across Medicare and Medicaid funded post-acute care and long-term care settings. Trans-NIH funded enhancements in our understanding and measurement of function is required to make this standardization process most relevant and appropriate.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Current rehabilitation research activities and priorities have not been adequately identified in a comprehensive and iterative manner across biomedicine as trans-NIH themes in the draft NIH Strategic Plan. Better coordination will lead to identification of potentially synergistic research so that rehabilitation researchers can enhance and build upon each other's work. Coordination in this field of rehabilitation research is essential because: • Rehabilitation research is not organ or disease specific; • Rehabilitation research is cross-cutting and virtually every NIH Institute and Center should be involved in the conduct and support of rehabilitation research; • Rehabilitation needs affect people across the lifespan from infancy to old age; and • Societal, environmental, behavioral and biomedical interventions are required to prevent and treat persons with disabilities and chronic conditions. The study of plasticity of tissues, including nerve regeneration and brain remapping following spinal cord or brain injury, should be added to the areas of opportunity in the strategic plan. In addition, appropriate dosing of medical rehabilitation interventions cuts across research portfolios of the various Institutes and Centers and is a major area of opportunity for individuals with injuries, illnesses, disabilities and chronic conditions. The high need for rehabilitation professionals makes it difficult to recruit them for research careers instead of clinical practice or academia, thus the need for continuing funding for early career scientists.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

We have no comments to this question.

Future opportunities or emerging research needs

We have no comments to this question.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework
(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission
(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

As NIH develops and implements its strategic plan, the Alzheimer's Association encourages NIH to consider the following funding-related suggestions: • Prioritize biomedical research funding rather than proposing budget increases on a proportional basis across institutes and centers. The current static budgeting mechanism does not proportionately address diseases that are affecting increasing numbers of people and that significantly complicate other health conditions. With strategic, targeted funding for these diseases, NIH can more effectively enhance Americans' health, lengthen lives, and reduce illness and disability. • Increase utilization of Program Announcements (PAs) and Requests for Applications (RFAs) for a more targeted approach to areas in which experts have identified specific unanswered questions that underpin new advances. The use of PAs and RFAs can be targeted in their design and can help to accelerate advances in promising, high-impact fields. For example, the National Plan to Address Alzheimer's Disease, which is updated regularly by the research community, includes scientific milestones to prevent and effectively treat Alzheimer's disease by 2025. Significantly faster progress toward these milestones could be achieved if NIH were to dedicate some degree of its Alzheimer's funding to PAs/RFAs, which can be more targeted in their design. This approach can be applied across disease areas and ICOs. • Confine funding decisions to research proposals that directly advance NIH's core mission. NIH funds some research that more closely aligns with the missions of other agencies, such as health economics research. Federal agencies' adherence to their missions and careful coordination among agencies allows for more efficient use of taxpayer dollars and advancement of those missions. Please see the attached letter for further comment.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

I hope that you include behaviors such as inactivity as well as activity within your RFP as these are some of the most important behaviors that can influence health promotion and theoretically can have impacts on the development and progression of several known diseases. The integration of these behavioral factors as well as nutritional considerations are integrated across the lifespan to influence many metabolic and physiologic parameters and needs more and better research studies with different populations.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Including the above behaviors as interventions with not only health outcomes but relating these to genetic processes to influence progressions such as cancer and heart disease are clearly needed.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The . . . applauds NIH for moving to develop a comprehensive NIH-wide strategic plan. We hope this exercise yields a high-impact and actionable research blueprint that informs the actions of the 27 component Institutes and Centers. Given the challenges and opportunities associated with pediatrics – such as the reality that most pediatric diseases and disorders are rare diseases, difficulties recruiting pediatric patients for research projects and the growing body of knowledge regarding developmental origins of health and disease that indicates many adult-onset conditions are rooted in the pediatric years or in utero – the . . . urges that appropriate attention and considerations be given to the needs of the pediatric population. While most children are, fortunately, relatively healthy, we know that about 50 percent of all patients impacted by rare diseases are children and that 30 percent of such children will die before their 5th birthday. Given these challenges and the related opportunities possible through a greater focus on pediatric research, The . . . urges that the strategic plan include a dedicated focus on pediatric priorities and issues to ensure the needs of our children are given appropriate attention. Furthermore, we urge that NIH not simply define priorities based on the sheer number of patients impacted by a disease or by annual aggregate costs as both criteria would place children and children's health at a sizeable disadvantage compared to adult-onset conditions. Finally, we urge NIH to recognize that many serious adult-onset conditions are rooted in early childhood and even in utero development. Given the potential impact of such research to improve the health and and to improve the health and well-being of children and adults, we would urge NIH to make it a priority within the plan.

Compatibility of the framework with the broad scope of the NIH mission

The . . . believes an overarching NIH strategic plan is very compatible with the broader scope and mission of the NIH and its component Institutes and Center. For example, many of our members were actively engaged in helping shape the Eunice Kennedy Shriver National Center of Child Health and Human Development Scientific Vision a few years back. The overarching strategic plan should not conflict with the vision or similar more detailed and institute-specific blueprints. Rather, it should set the overarching agency strategy and focus, and should establish clear priorities, including targets for multi-institute collaboratives and are activities that would be developed in greater detail through individual Institute and Center plans.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

As noted above, the . . . considers developmental origins of health and disease to be one topic that exemplifies the potential through a cross-cutting approach to research that should be considered within the strategic plan. We are also excited about the promise the Personalized Medicine Initiative holds for all persons and would encourage that NIH recognize within the strategic plan the challenges and opportunities associated with pediatrics as part of this larger undertaking. Furthermore, we are encouraged by the implementation of the Gabriella Miller Kids First research program within the NIH Common Fund focused on genome sequencing of children with childhood cancers or structural birth defects. In developing this program further, we would encourage NIH to regularly engage and consult with the pediatric research community to review the program to ensure it is focused on the highest-priority opportunity within the auspices of the Common Fund.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

The . . . applauds NIH for recognizing that basic science is the foundation for progress. We also appreciate the recognition in the RFI that leaps in scientific technology often catalyze research breakthroughs as well as the growing importance of data science in research. But to truly leverage these possibilities, research institutions need the means to obtain the latest research infrastructure, including shared core research infrastructure that is shared by multiple collaborating institutions. Congress has recognized the value of research networks and to supporting research in such a manner by enacting into law the National Pediatric Research Network Act (PL 113-55). We would urge NIH to recognize that the agency has a role to support the acquisition of research infrastructure, particularly shared core research technologies that are conducive to being used by multiple institutions and that are often cost prohibitive for a single entity to acquire. Building on the topic of providing support for research infrastructure, the . . . strongly believes NIH must recognize that future scientific gains will only come about from appropriately trained researchers, including clinician/scientists. As such, we urge NIH to recognize the necessity of providing training and related support for early career investigators. Such developmental support is much-needed to supplement the efforts of our institutions to attract early-career investigators, particularly clinician-researchers, to careers in pediatric research.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

The . . . wishes to reiterate that a body of research over the past 25-plus years continues to demonstrate the developmental origins of health and disease. With developmental origins believed to contribute to many chronic conditions, including many that do not manifest until adulthood, it is vital that the NIH Strategic Plan recognize the need for an aggressive focus on this issue, particularly given the intergenerational impact of disease. This can be achieved by recognizing that the arc of development encompasses pre-conception through in-utero development, post-natal, childhood and adolescence and that genetics and the environment exert influences on such development. The . . . applauds NIH for noting opportunities to support research into rare disease within the RFI's paragraph regarding priorities. As noted earlier, rare disease is of particular importance to the pediatric population. A strategic plan needs to recognize the collective impact and burden of rare disease, estimated to impact nearly one of every 10 Americans, as well as the challenges, opportunities and necessity of focusing adequate resources and energy on this issue, including ways to better support translational and clinical research on such populations. We also encourage NIH to ensure that the strategic plan focuses appropriate attention on genomics research given the importance of this field to future gains in health

and medicine and to recognizing the challenge and opportunities possible through genomics research focused on the pediatric population. And while the plan is focused on NIH, we encourage that appropriate attention and recognition be given to complementary non-NIH initiatives and resources such as the PCORI Patient-Powered Research Network (PPRN) and Clinical Data Research Network (CDRN) program. This undertaking, if fully realized, could offer much-needed resources across all ages and conditions, including pediatrics.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The current NIH framework doesn't emphasize the need for a system's science approach that is integrative and supports translational and transdisciplinary science. With continuing advances in data science and computational analytics, greater emphasis should be given to how publically funded research findings fit into our overall understanding of health, like a piece in a puzzle. To do this will require a data framework and greater uniformity/standardization/definition of measures and meta-data, so that results of individual research projects can have added value (e.g. be used in meta-analysis and or linked to other studies to create a more comprehensive picture, larger sample sizes, and greater power). Without creating any expectation or incentives for investigators to think about how basic, clinical and population/environmental health research are related, and especially with the new focus on precision medicine, research is likely to continue to have narrowly focused impact.

Compatibility of the framework with the broad scope of the NIH mission

The exposome supports a systems approach, translational research and transdisciplinary team science and provides an excellent theoretical model for conceptualizing the links between basic, clinical and environmental/population health research by focusing on completing exposure pathways and identifying biological mechanisms through which environment affects susceptibility for disease and leads to population level disparities. The exposome provides an excellent framework for precision medicine by looking at the totality of factors which affect health and incorporating a lifecourse perspective that recognizes the importance of life stage in the development and progression of disease.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Health disparities are measures of population health that take into consideration the effects of place on health. The lack of distinction between the causes of poor health outcomes and population level disparities has perpetuated research that has failed to distinguish between minority health and health disparities. Research which fails to take into account the effects of environment are unlikely to have much impact on health disparities.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Systems Approach
Exposome
Transdisciplinary research
Transdisciplinary research training

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The current framework is very broad where biology research is a main focus. There is no doubt that basic science is the foundation for progress but the framework needs to emphasize partnerships between basic, translational and clinical science. A major challenge of the NIH strategic plan is to get from “fundamental knowledge” to “applications that extend life and reduce illness” without bankrupting the health care system. Ideally improved scientific knowledge and improved technology would reduce the cost of treatment. How well are aspects like technology development and implementation as well as quality of care and quality of life covered by this initiative? Some forethought should be given to incentives to both create breakthrough treatments and reduce the cost of implementation. In particular community hospitals where the majority of patients are treated need to be encouraged into the overall program of research funding.

Compatibility of the framework with the broad scope of the NIH mission

The framework does not seem to be patient-centric. There is minimal reference to patients whilst specific reference to healthy individuals.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Approximately the best half of NCI-funded grants are determined by study sections, and the next half are determined by NCI. This politicizes the R01 funding mechanism priorities. The experts in the fields (study sections) should be determining which grants get funded. One of the most powerful features of the NIH grant mechanism is the communication between applicant and reviewer. In theory, reviewers are always experts in the field of the application, but with the continuous narrowing of areas of expertise, providing reviewers whose expertise exactly matches the applicant’s expertise is difficult. Also, truly innovative research often includes changes in paradigms which at first may appear to be unnecessary or inappropriate. Meeting both of these challenges is improved by communication (via the summary statements and introductions to application) between applicant and reviewer. The NCI should focus on influencing research through the RFA and RFP mechanisms. One strategy to stimulate innovative and paradigm-changing research would be to reactivate the A2 application. It also makes sense to fund general biomedical imaging projects (through NIBIB). Under Health Promotion/Disease Prevention another consideration would be to study the role of environment and manipulating environment to promote health and healthy behaviors. Just as the tumor microenvironment is a target for cancer research, the natural and man-made environment contribute to health behaviors and health. Also, under this topic another heading could be “strategies to improve access to needed treatment.” For example, many rural US areas do not have access to radiotherapy, impairing curative treatment for breast, lung, head and neck, cervix, and other cancers. Fundamental algorithmic decision support based research on multi-parametric data sources including molecular, genomic, imaging, clinical information also is crosscutting. The NIH needs to consider strategic funding of community-based research and patient care in order to translate research into meaningful improvements in healthcare.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Specifically recognizing the crosscutting opportunity in imaging science in addition to molecular frameworks would serve the strategic plan well. The area is a bridge between clinical medicine, disease processes and physiology (normal and abnormal) and much like molecular information increasingly

creates the data driven interpretations for treatment and prevention. In “Treatments/Cures” the NIH/NCI needs to specifically encourage partnerships between radiation, medical and surgical oncologists and basic scientists to achieve breakthroughs. While “Breakdown of traditional disease boundaries” is logical in this era of molecular diagnosis/prognosis/targeted therapies, there are shining examples of where such an approach has not worked well (B-raf mutations in melanoma vs. colon cancer). Thus, we still need to advocate for continued disease focused RFA’s. We strongly support the area of opportunity “Advances in clinical research methodologies stimulate scientific progress” as funding for therapeutic clinical trials will increasingly have biomarker or molecular imaging endpoints. Support for work on biologic/molecular endpoints of radiation response as well as drug response needs to be supported to succeed in the multimodality treatment of cancer.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

Emphasis on support and funding for both broad themes (as suggested within the framework) but also targeted themes within broad areas, such as predicting radiation response in the “Breakdown of traditional disease boundaries”, where radiation response is not necessarily disease centric.

Future opportunities or emerging research needs

Treatment regimens are based on clinical experience and clinical trials and have not yet been modified or optimized based on each patient’s molecular information. In other words, the promise of individualized therapy has yet to be broadly explored [specifically in radiation therapy]. Nevertheless, there are unprecedented opportunities on the basis of molecular/genetic knowledge that can be brought to the field of radiation oncology to improve outcomes significantly via the personalization of treatment regimens. Such examples are 1) the radiosensitivity index or RSI—a genetic signature derived from cancer cells able to distinguish between radiosensitive vs. radioresistant tumors and 2) radiogenomics—the use of genomics and radiomics (mathematically extracted information from medical images). Given the importance of radiation therapy and the vast number of cancer patients that benefit from it today, NIH should consider funding for the development and clinical applications of molecular advances in the treatment of cancer with radiation in parallel with the more established advances being made in medical oncology.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The . . . represents almost 9,000 basic biomedical researchers in all 50 states and over 60 countries around the world. We believe that it is critical to the success of biomedical research that strong support for basic research remain a critical part of the NIH research portfolio. The research pipeline, in order to be ultimately successful, must begin with fundamental, basic research, which lays the foundation for later, more targeted research that can ultimately be translated into new and effective treatments for disease. Very frequently, advances made in one area of basic research are found to be significant in other areas of investigation, and often in ways that no one could have predicted from the outset (e.g., CRISPR/Cas technology). Supporting and fostering the important role of basic research is essential for the future progress of medical research. At the other end of the research pipeline, efforts need to be made in the areas of early detection and precise diagnosis of disease. While basic research can magnify our understanding of a particular disease, it will be critical to know which patients will benefit the most from any new understanding. More importantly, it will be increasingly beneficial to know which patients will not benefit from specific treatments, with the ultimate goal of ensuring more effective and targeted treatments for all patients.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Since the completion of the doubling of the NIH budget in 2003, the purchasing power of the NIH budget has decreased by almost 25%. One of the results of this decrease in purchasing power is that NIH study sections have become increasingly restrained in the science they select to be funded. All too often, the research that is funded by study sections is work that is considered risk-adverse and thus almost guaranteed to result in advances in our understanding of basic biology and disease, albeit often incremental or limited ones. At a time of limited funds, we should be making the best use of resources, and thus we also recommend finding ways to prioritize the funding and promotion of highly creative and innovative approaches, which if successful, would greatly accelerate our understanding and have the potential to be transformative. Support for research that moves the bar will not only help advance scientific knowledge but it will also highlight the important role of federally funded research. Congress and the American public would certainly be even more in favor of supporting biomedical research if they knew that they were getting a bigger bang for their buck.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The areas of opportunity and unifying principles noted in the framework are useful but not complete. Under “Unifying Principles” there needs to be stronger explicit recognition that: (1) preventing and reducing the incidence and prevalence of disorders and adverse health conditions are of the highest priority; (2) prevention science (broadly construed) provides avenues (evidentiary frameworks and approaches) for pursuing such reductions; and (3) addressing shared risk factors associated with multiple adverse outcomes—including both individual-level characteristics/behaviors/experiences and environmental exposures—is an approach needing greater emphasis.

Compatibility of the framework with the broad scope of the NIH mission

There is general compatibility but there needs to be greater emphasis on the public health aspects of the NIH mission including greater emphasis on the prevention of disorders and adverse health conditions. There is also a need to focus more resources on the study of resilience in terms of both behavioral and physical health outcomes.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-

NIH strategic plan

Two cross-cutting concepts that are not well represented in the plan are (1) the role of behavioral health in relation to understanding, preventing, and treating disorders and diseases of all varieties, and (2) the importance of childhood experiences/exposures and developmental pathways and trajectories in relation to prevention of later adverse outcomes.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Major chronic illnesses as well as adverse health conditions/outcomes often share in common sets of socio-environmental and biological risk factors and influences. A critical area of opportunity applicable across biomedicine is the development, refinement, and testing of prevention strategies aimed at addressing precursor factors shared by multiple disorders.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

None Noted.

Future opportunities or emerging research needs

An emerging research need is the focus on multiple socio-environmental and biological factors (and their interactions) shared across disorders and IOCs to achieve greater success in prevention. An integrative “ecobiodevelopmental” framework that views human behavior as emergent from the multifactorial interaction of a biological organism with its social and physical environment has emerged as central to inquiry regarding disorders and adverse health outcomes. From sociology and behavioral science to neuroscience and genetics, such models are now catalyzing a critical shift in the way we view disease and disorder throughout the life course. These advances point to an emerging model in which childhood experiences and exposures to socio-environmental factors directly affect the developing brain and body, which, in turn, affect overall outcomes. Further research is needed to further explicate—and ultimately reduce exposure to—the many sources of poor outcomes and identify windows of opportunity to normalize health trajectories.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Ensure that within the Plan’s Health Promotion/Disease Prevention area there is a strong focus on information dissemination to the public, promoting adequate health literacy and engagement with all stakeholders (including patients, researchers, healthcare providers). It is critical that as research and clinical treatment information at NIH grows, the information must be easily accessible by researchers, patients, and health care professionals. Research is most valuable when it is accessible and easily understood and can be applied to inform future research and effective health decisions. The research findings and resulting clinical treatments must be clearly and easily accessible to patients and doctors to make informed health decisions, bringing the bench to the bedside. This includes funding and focusing on initiatives to provide health information in multiple reading levels, appropriate formats (including digital), and languages – all which help patients best understand the resulting health information and health professionals communicate to their patients. It also includes a strong focus by NIH in data science thus ensuring NIH both discovers new methods to collect data for science, but NIH also puts a primary focus in the assembly and analysis of complex and disparate data types to yield new information for not only the initial study but later analysis by other researchers. Finally, access to information should be eased through use of open science as well as other technology and dissemination methods that enable

access, interoperability, and use of biomedical research data and findings.

Compatibility of the framework with the broad scope of the NIH mission

While the framework is compatible with the NIH mission, it does not appear to fully leverage the opportunities for open science initiatives to foster a stronger culture of sharing throughout the scientific community. Fostering a stronger collaborative culture is key to enhancing returns on funds committed to scientific discovery. Consider a strong focus and integration of open science as a fundamental approach across the NIH framework to help ease access to research and research based treatment information. As NIH continues to lead the world in biomedical research data initiatives, the amount of data will only grow at an exponential pace – open science will help ensure this data can be accessible for further uses and future findings. Thus, open science will help NIH more fully meet the larger NIH mission of not only discovering knowledge of the nature and behavior of living systems but using open science to better advance the application of that knowledge to enhance health, lengthen life, and reduce illness and disability. Such an open science approach should be applied to both research and dissemination efforts across NIH.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

The following additional concepts should be included: Health promotion, outreach and education efforts – especially with the primary focus of improving health and science literacy for lay audiences (i.e., patients and families of patients). Also, the plans should account for patient and lay audience engagement, including efforts to both translate research and clinical treatment findings to formats (including digital) that are easily accessible and usable by advocacy groups and the general public as the engagement of these key stakeholders directly broadens NIH reach to meet NIH’s primary goal of enhancing health, lengthening life, and reducing illness. Finally, NIH should ensure research initiatives are designed so data is available to more than just the study that created it. Consider hosting research data in central clearinghouses that make it accessible to all researchers (with appropriate use covenants) for further use.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Data science, data sharing, and data mining will continue to become seminal components of advancing research initiatives. It will be equally important to have IT-based systems or products that promote the interoperability and extraction of data and an expansive workforce trained in quantitative sciences. Further, as personal technology advances, it will be important to meet the growing demands for public to participate in research initiatives, thus enabling public users to donate their personal health records to research initiatives and empowering NIH researchers with a broader set of data to drive advances for both broad public health treatments and personalized medical approaches.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The proposed framework provides an effective foundation from which to address the pursuit of knowledge concerning the nature and behavior of living systems. Benefits include a scientific and data-based infrastructure, the inclusion of health promotion, disease prevention and healthy individuals, innovation centered on traditional disease boundaries and an increased emphasis on partnerships.

There is no doubt that forward progress towards attaining an increased knowledge and understanding of the nature and behavior of living systems must be based in scientific inquiry. However, equal attention must be placed on the translation the results into practice and it cannot take 17 years for this to happen if the ultimate goal is to improve the health of this Nation. As the Nation's health care system focuses more on the creation of health and less on the cure of disease, it is imperative that healthy individuals are examined and the biology and processes by which they maintain health are identified. There has been a reluctance to financially invest in prevention. The impact of prevention is harder to measure and takes longer to identify than the impact of disease treatment. Yet, the creation of a healthy Nation depends on the identification of the behaviors of living systems and their environment that are associated with health and well-being and the processes by which they become the norm. The growing focus on common molecular structures underlying multiple types of cancers and away from organ-specific cancers represents an important advancement and an example of treatment progress as a result of the breakdown of traditional disease boundaries that could be applied to all diseases. Finally, partnerships are an important element of developing cures for disease. It is imperative that funding opportunities encourage such partnerships so that like initiatives are not taking place at the same time in different labs.

Compatibility of the framework with the broad scope of the NIH mission

NIH's mission is to seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability. The proposed framework is well-suited to support seeking fundamental knowledge about the nature and the behavior of living systems. However, the framework appears to fall somewhat short of addressing the application of the knowledge that results from scientific inquiry to enhance health, lengthen life, and reduce illness and disability. To ensure a more timely progression of inquiry to discovery to application, it is important that this process is clearly communicated in the framework.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Although the NIH Strategic Plan is not intended to be "all things to all people", it is essential to include the "whole person" concept in the strategic plan. Some concepts that address the "whole person" in health care and that cross ICO strategic plans include: (1) palliative care and end-of-life, (2) quality of life, (3) co-morbidities – their interaction and impact for the person in the "real world", including the reduction of the burden of disease.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Comprehensive themes that are captured but not clearly stated include: • Collaboration among NIH Institutes, Centers and Offices would express the desired outcome of the NIH Strategic Plan. • Data science is relevant and important to all areas of opportunities, not just the "fundamental science" opportunity • "Evidence-based" also applies to all areas of opportunities, not just "elimination of health disparities" • The term "bio-health" rather than "biomedicine" would reflect a broader view of the mission of the NIH and, an even broader, whole person term should be considered, such as "bio-

behavioral health” • Partnerships needs to be defined as among governmental, patient/caregiver advocacy groups, non-profit and for profit groups. It should not be assumed to be between the government and industry as discussed on one of the webinars

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

The priority statement “consider value of permanently eradicating a pandemic” seems grandiose and not realistic. A more feasible/realistic priority might be “NIH will lead a response to a pandemic through early detection and rapid, evidence-based interventions”.

Future opportunities or emerging research needs

Enhancing the dissemination and implementation of scientific discoveries

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

We agree that the greatest opportunities for cross-cutting research are promoting fundamental science, improving health promotion and disease prevention, and advancing treatment and cures. A major objective of the . . . encouraging optimal health behaviors. Fundamental science is key to evaluating risk assessment, risk communication, and other risk management strategies, and is essential for promoting various aspects of overall health, including oral health. Engaging dental health professionals is a means to address two of the treatment and cures objectives, namely breaking down traditional disease boundaries and developing partnerships. The developing evidence base on approaches to eliminate health disparities demonstrates efficacy of involving the complete spectrum of health professionals, which includes dental health professionals. The . . . is encouraged that this is part of the framework NIH has proposed.

Compatibility of the framework with the broad scope of the NIH mission

The proposed framework for the NIH-wide strategic plan appears wholly consistent with its mission to seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability. Enhanced understanding about risk assessment, risk communication, and other risk management strategies will be needed to ensure that the knowledge that is developed is translated into the desired outcomes of enhancing health, reducing illness and disability.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

We recommend additional emphasis be placed on evaluating the safety and effectiveness of new and existing diagnostic, therapeutic methods, instruments, and technologies used in the prevention, management, and treatment of disease in overall health including oral health. Understanding the factors affecting access to and appropriate utilization of health care including dental services will be required for NIH to succeed with its mission. Funding support should be given to expand the use of non-invasive samples, including those available in the oral cavity (e.g. saliva, gingival crevicular fluid) that can be used for screening, diagnosis, and disease monitoring. Another area that should cut across the ICO strategic plans is an emphasis on data science. Developing approaches to improve access to data and people trained in its exploration are critical to its meaningful use.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity

that Apply Across Biomedicine

We suggest emphasizing the investigation, development, and clinical evaluation of therapies and therapeutic materials appropriate for prophylaxis, tissue engineering, healing and/or regeneration of structures and soft tissues, including those in the oral cavity. In addition, we encourage resource allocation to develop, test, and validate methods for assessing integration of evidence-based clinical recommendations into clinical practice, including dentistry. Multidisciplinary efforts examining the interrelation of all systemic conditions and diseases as well as the impact of their treatments will be required to improve the overall health and healthspan of the public.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

We are encouraged by NIH's recognition that 'data science increases the impact and efficiency of research' and contend that it will result in increased support, dissemination and application of evidence-based practice in healthcare including dentistry. Additional efforts should be taken to further develop and implement improved methods and processes coming out of the work of practice-based research networks, to help ensure clinically relevant research questions are addressed, and to promote collaborative investigation of preventive and therapeutic interventions, which can support advancement of health care, including oral health. Most new advances in prevention and treatment do not reach patients in a timely manner. Dentists and other healthcare professionals fail to adopt new approaches even when they are clearly superior to existing approaches, and they often fail to discontinue using therapies when they are shown to provide no benefit. Research is needed to better understand why practitioners do not adopt new and better approaches and how to get them to adopt appropriate approaches. Increased investment in this area (e.g., implementation of evidence based practices) is vital to improve patient outcomes. This includes the need to develop a strong evidence base regarding efficacy of health promotion activities to help address health disparities. Consideration of those interventions effecting change at the individual, population, and policy level will all need to be examined with respect to their efficacy to attain the desired aims of improving health and preventing disease.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The current framework has the potential benefit of educating the members of Congress who requested it on the ways in which NIH is actually structured, how it functions, how decisions are made on funding issues, and how the currently decentralized grant-making system has worked to create the strongest, most efficient biomedical research network in the world. The concern is that the overall plan might be too proscriptive and result in a lessening of that decentralization, thus unintentionally limiting or even stifling creativity.

Compatibility of the framework with the broad scope of the NIH mission

The current framework appears to be a comprehensive, necessarily broad overview of the current role of NIH in the biomedical framework. To the extent it is possible, it should emphasize a strong future-orientation. The challenge is to draft the actual document with a focus on what NIH could be more so than what it is. From a researcher or a patient perspective, the great benefit of the NIH is that it represents hope for earlier diagnosis, better treatments and ultimately cures for diseases and disorders.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

While the framework is quite comprehensive, it might benefit from a specific mention of the impact on behavioral health on the multitude of disease states. Speaking from the perspective of . . . , we see clearly every day the impact of excessive alcohol consumption, the sharing of intravenous needles, unsafe sex practices, intentional or unintentional failure to follow label instructions on prescription and non-prescription medicines, failure to exercise and control one's diet leading to obesity. The list goes on and on. These are all behavioral disabilities that, if addressed, would lessen or prevent the developments of the diseases that we currently working to treat and cure.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

There do not appear to be any such components.

Future opportunities or emerging research needs

In the field of liver research, there are a number of future opportunities and emerging research needs that must be addressed. Some have begun and others are under active discussion. But, just to give a sampling of some of those issues: • Hepatocellular carcinoma – Hepatitis C is the single largest cause of liver cancer. While a variety of drugs newly-approved on the market will effectively cure hepatitis C, not all patients have access to those drugs and not all patients are aware they have the disease. The development of methods of early detection of HCC, whether through biomarkers, imaging or some other means would be a major step forward in reducing the scourge of this disease. • Non-alcoholic Fatty Liver Disease – The obesity epidemic in America is often discussed in terms of diabetes, heart disease, etc. Less publicized is the impact obesity has on the liver. However, the development of excess fat in the liver leads to a variety of life-threatening complications that are worsening. The disorder is now being seen in children – something that virtually never happened twenty years ago. • Rare liver diseases – The framework mentions “supporting opportunities presented by rare disease research” and the liver community strongly supports this provision as there is much to be learned from such research that can benefit the more common disorders. • Other opportunities/issues – Among the other opportunities or issues mentioned in the framework which we would support are (a) maintaining the existing strategic plans of the ICOs, (b) the expansion of the use of public-private partnerships, (c) recruiting and retaining a strong biomedical research task force, and (d) an enhancement of workforce diversity and an extensive effort to address health disparities.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

We have to create a vision of success in the field of childhood cancer research. That vision must include greater funding than what is currently budgeted. As the parent of a child who lost his life to a brain tumor, and as someone who has devoted the last 15 years to helping patients and families, I ask you to keep this in mind when creating your strategic plan. Even if the funding is not immediately available, without creating a goal we will never move in the right direction.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Investigational research in the US is under existential threat as a consequence of many years of underfunding at the level of R-class grants, particularly R01s. Science has become overly regulated by politics, and the NIH budget has stagnated, in part because of the failure to adequately communicate to political leaders the real returns on funding basic research. This crisis has unfolded despite the fact that investigator-driven research has been the mainstay of the NIH since the 1950s. It is the foundation of discoveries that are considered crucial to the translational goals at the heart of the NIH mission (eg restriction enzymes, reverse transcriptase, PCR, CRISPR/Cas9, RNA interference, RNA splicing, etc). The expansion of targeted programs and large center grants has come at the expense of investigator-driven research, affecting particularly young PIs, and the US is losing an entire generation of young scientists who feel that pursuing their own ideas is a hopeless quest. The effect of low paylines has been to restrict funding for projects in virology and related disciplines to only the most conservative of proposals that have been stripped of all risk, stifling the most innovative ideas. To rekindle innovative research: (1) R01 paylines must not be allowed to fall below 20%, even at the expense of larger block grants and targeted translational programs that often exclude independent PIs, (2) primary Investigator-driven research should never fall below 80% of the total NIH budget. Right now, fewer of the brightest and most talented students and postdocs are pursuing potential careers in investigational medical research. Science and technology have driven essentially all of the advances that humanity has made over the past century, but the current situation at NIH is dire. The US has traditionally been the world leader in promoting improved health, but that position is under direct threat.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity

that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Childhood cancer is the #1 killer by disease of kids in our country. The incidence of childhood cancer is steadily increasing. Although there has been progress in the area of the most common type of childhood leukemia, many types of childhood cancer continue to have a grim prognosis, some are even guaranteed death sentences on diagnosis such as DIPG. Childhood cancer is in dire need of greater funding and research, and as it is the #1 killer by disease of kids in our country it should be made a national priority. . . . Father of . . . (Died at age 5 from neuroblastoma on 1/20/2012)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The major drawback of this strategic initiative is a surprising lack of focus on what causes shortfalls in lifespan, and what leads to illness and long-term disability. I can certainly understand the great benefits of basic science, but for taxpayers, the problems they face are more immediate: health behaviors are poor and among some middle-aged men, actually getting worse, while health-related costs are eating up any wage gains. Neither enhanced basic science, nor early diagnosis, will reverse the alarming trends in lifespan that demonstrate the US is falling far behind their European counterparts with regard to lifespan and disability. And even if basic science comes up with several revolutionary cures, we are still

faced with the challenge of how to treat the fortunate survivors who, in the future, will develop new and different chronic illnesses, some of which may be related to falling into poverty as their income is increasingly depleted by new expensive treatments with questionable clinical benefits.

Compatibility of the framework with the broad scope of the NIH mission

This strategic proposal appears inconsistent with NIH mission statement, which reads in part "NIH's mission is to seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life and reduce illness and disability." Again, the focus of this strategic initiative is, except for a few objectives, focused solely on basic research, and not on the application of knowledge to enhance health. For example, an initiative to enhance data science is proposed, not to improve the health of Americans, but solely to enhance basic science research. If the objective really is to enhance health and lengthen life, aren't there far more immediate and practical benefits of using data science to apply the fundamental scientific knowledge, for example by reducing the shocking number of medical errors, overuse, and underuse in the US health care system?

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

There are several themes that are lacking in the proposed strategic goals. 1. If the focus of NIH is on health, it should pay attention to all factors that affect the health of Americans, ranging from the adverse health effects of stress arising from financial or racial inequality, to the reasons for why the US is lagging so badly with regard to disability and health compared to other comparable countries. 2. A fundamental challenge facing the health of US citizens is the poor translation of scientific knowledge into practice. Why is there this enormous gap between what is known, and how medicine is practiced? This relates to the current NIH mission statement on how knowledge is translated into actual improvements in health. Certainly in my research, I've found huge differences in the diffusion of knowledge across regions, physicians, and health systems, and this has obvious implications for disparities in health outcomes.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

I want childhood cancer research to be a priority in the budget process. I want a transparent budget process. The public deserves transparency. We deserve to understand the NIH plan for childhood cancer research. We deserve to understand how priorities are set. We deserve to know how goals are set and what are the anticipated outcomes. We deserve to know what the real investment is. We need transparent reporting afterwards that gauges the value of the investments and the results. Childhood cancer is the number one disease killer of children. NIH should make childhood cancer research a National Priority. Such a priority position should be reflected in the budget of the National Cancer Institute.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The . . . is pleased to submit comments regarding the five-year NIH Strategic Plan Framework. . . ., a national non-profit organization based in Washington, DC, is widely recognized as the thought leader in promoting research on . . . through advocacy, education, and research. . . . believes a potential benefit of the NIH Strategic Plan Framework is that it provides a general structure for the disparate NIH Institutes & Centers and fits within the NIH mission. In addition, . . . applauds NIH for its interest in advancing clinical methodologies to stimulate progress. A focus on improvements in preclinical, clinical, and interdisciplinary research methodologies will only result in further scientific innovations that improve the health of Americans in the years to come. However, an area for consideration includes structuring the framework to show how the “Areas of Opportunity” lead into the “Unifying Principles” (or vice versa) to exemplify how each activity connects together. . . . hopes such plans are detailed in the forthcoming strategic plan.

Compatibility of the framework with the broad scope of the NIH mission

. . . believes this framework is compatible with the NIH mission to seek knowledge regarding the nature and behavior of living systems. However, possibly due to the brief nature of the framework, it appears to have only limited bearing on translating this research to real world health implications for American families, beyond eradication of a pandemic or elimination of health disparities. This is a specific issue for women, as general understanding of symptoms, prevention, and treatment of disease still emphasizes the male model in research. We believe that NIH should use the draft strategic plan to provide additional details for these and other bullet points, providing clarity on its plans to translate research to cures and treatments for all patients. . . . applauds NIH for incorporating disease burden as an important but not sole consideration for priority setting. However, the U.S. prevalence/incidence of disease should not limit the NIH obligation to consider other factors, such as rare disease, diseases that

disproportionately affect women and minorities, and severity of morbidity/mortality when setting such priorities. Often, these factors can be overlooked when developing funding announcements and setting strategic priorities for the agency. Research supporting an equal academic commitment and financial investment in diseases and disorders that disproportionately affect women and minority populations will lead to greater understanding of sex and racial/ethnic differences in the development and prevention of such illnesses.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

The strategic plan for the National Institute of Mental Health includes a focus on researching sex differences in brain structure as one of many concepts within its contribution to the NIH BRAIN Initiative. Similarly, the National Heart, Lung, and Blood Institute (NHLBI) draft strategic priorities, released July 2015, have addressed the importance of studying sex and gender differences in research. As sex differences exist within a wide array of diseases and conditions in which the NIH conducts research, specific discussion of the strategy to incorporate these concepts across NIH should be addressed in the draft and final strategic plan. In addition, the NHLBI priorities connect their research themes into larger goals that translate to its impact on individual and public health. They also address innovative analytical approaches to use “big data” from electronic medical records and research from other sources to further their understanding of diseases/disorders affecting the heart, lung, blood, and sleep patterns of Americans. Additional NIH Institutes and Centers have discussed the importance of interdisciplinary approaches to research questions. . . . believes that this method of examining research questions could improve trans-NIH collaborations and expedite translating discoveries into cures and treatments.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

The NIH framework does not address the recent policy announcement regarding inclusion of both male and female cells and animals in preclinical research; nor the need to improve the participation of women and minorities in dual sex human subject research. Inclusion of this policy within the framework and strategic plan is imperative to ensuring that it is fully implemented and emphasized across all Institutes and Centers. Expanding this policy to include proper recruitment, inclusion, reporting, and analysis of male, female, and minority participants reflective of the U.S. population in medical research is key to advancing precision medicine and expediting the next generation of cures to patients. NIH should also specify how it plans to translate knowledge gained from research to the general public. One option could include the addition of a “Research Dissemination” bullet point under the “Treatment/Cures” or “Enhancing Stewardship” sections. This bullet point could incorporate developing educational materials, use of social media, and other approaches to reach a non-science/research-focused public with NIH innovations. Finally, NIH should incorporate its plans for the Precision Medicine Initiative into both this framework and the strategic plan. Given the Administrative and Congressional focus on and support for this initiative, NIH should address its plans for recruiting the one million American national research cohort and other activities that may occur over the next five years. . . . advises NIH to ensure that this national cohort is as reflective of the American population as possible, with inclusion of a proportionate number of women and minority participants, to ensure research findings are reproducible and rigorous for all populations.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

. . . believes all the Areas of Opportunity sections are applicable and appropriate to the NIH Strategic

Plan. . . . only suggests the inclusion of a “Research Dissemination” section, as previously detailed.

Future opportunities or emerging research needs

. . . recommends several opportunities for NIH research, as highlighted below: 1) NIH should increase opportunities for building the evidence-based knowledge of sex and gender differences. This can be accomplished through requiring additional subgroup reporting and analysis for all intra- and extramurally funded research. 2) NIH should conduct targeted outreach and recruitment of minorities and women into the Precision Medicine Initiative and other NIH research studies. In addition to building on the evidence-based knowledge of sex and gender differences, this will encourage public trust and engagement in scientific research. If NIH finds minority and female recruitment to research studies difficult, further research into appropriate messaging and outreach should be conducted (including focus groups) that will allow NIH to develop effective communication strategies. 3) NIH should develop research priorities that examine the effects of multiple comorbidities and prior exposures on human physiology, especially in women who are more likely to have multiple chronic conditions (National Expenditures Panel Survey, 2006). For example, an . . .-sponsored research network on domestic violence found associations between prolonged exposure to abuse and increased incidence of a variety of chronic diseases, such as heart disease, stroke, and arthritis. 4) NIH should promote innovative research studies examining gene-environment-hormone interactions that improve (or serve as a detriment to) health. Similar to #3, these studies would allow scientists to examine the interactions of multiple processes, in this case genetics and the environment as well as sex, which affect an individual’s health and disease progression.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The greatest and most obvious challenge is the financial deficit that both limits scientific progress and dissuades young researchers from pursuing the field long-term. Thus, while the proposed framework may help the NIH organize its activities over the next five years, it will be critical to find ways to support research projects even while available resources diminish. Furthermore, creativity is being stifled due to the fear of rejection from funding sources like the NIH. Taking on risky projects that may not come to fruition is now uncommon, yet it is those very projects that are often the cornerstone of innovation.

Compatibility of the framework with the broad scope of the NIH mission

The NIH’s broad mission--to turn discovery into health--is supported by the proposed framework. The three-pronged, interconnected opportunities (fundamental science, health promotion/disease prevention, and treatments/cures) align with the overall mission. However, perhaps another theme that should be incorporated is fostering collaboration among researchers, particularly between new PIs and scientific veterans, so the next generation of researchers has extensive preparation and a strong foundation to build on.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Education should also be included as a feature of the strategic plan, specifically improving workforce training, encouraging Americans’ pursuit of science as a career, and creating more opportunities for high school students to be exposed to and participate in ongoing research projects.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

There are a number of crosscutting areas that should be incorporated into the Areas of Opportunity. Some important examples include: genomic medicine in mechanism-based therapies; induced pluripotent stem cells' use in autologous transplantation; gene editing for next-generation non-human primate disease models; and gene editing and therapies in human trials.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

All components of the Areas of Opportunity appear applicable to an NIH-wide strategic plan.

Future opportunities or emerging research needs

Particularly in the study of genetically linked diseases, longitudinal studies at a population scale represent a significant research need. Beginning at birth and chronicling individuals' health developments over their lifetime, such studies have the potential to unearth genetic links to diseases that we may poorly understand or not even be aware of yet. Incorporating data on individuals' shifting lifestyle habits could add another element to this research by revealing the environmental attributes that aggravate genetic glitches. Determining the gene-environment interaction that provokes a predisposition for common diseases would greater enable us to prevent and address those illnesses.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

In regards to "Promoting Fundamental Science", the statement that "Consequences of basic science discoveries are often unpredictable" applies to many aspects of science including the creation of genetically modified animals. As new gene-editing tools such as the CRISPR technology become more widely available, the generation of genetically-modified animals will increase, not only mice, but also other species including rats and pigs. Veterinarians should play a critical role in the phenotyping and proper utilization of these animals to avoid erroneous results and interpretation. Further, veterinarians should be more engaged in 'translational' science to interpret and improve the utility of animal models of disease. More than 50% of NIH funded proposals use animal models. Using the consultative services of veterinarians with knowledge of comparative physiology and disease may help to improve the relevance and reproducibility of these investigations to better inform advances in human medicine. In regards to "Improving Health Promotion and Disease Prevention", the emphasis on early diagnosis and detection applies also to infectious diseases. More than 70% of infectious diseases in human beings, including influenza, HIV, Ebola and MERS, are transmitted from animals. It is critical to increase our understanding of the course of infection and transmission of pathogens in animals and to identify the environmental factors and molecular changes that play a role in transmission from animals to people.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

In regards to "Advancing Treatments and Cures", we urge the NIH to consider funding mechanisms that would allow the validation of spontaneous diseases in companion animals as advanced stage preclinical

models for the evaluation of drug candidates. Drug development suffers from high risk of failure in human clinical trials. For selected diseases, it may be beneficial to test drug candidates in dogs and cats that are genetically diverse and exposed to the same environment as their human owners. Dogs, cats, and horses suffer from similar diseases as people including cancer, obesity, diabetes, loss of cognitive abilities with age, and autoimmune diseases.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

. . . supports the cross-cutting areas of opportunity NIH has identified. Within the "improve health promotion and disease prevention area" we recommend that the focus go beyond studying healthy individuals to studying healthy populations, including the impacts of the social determinants of health. According to McGinnis, et al., "Drawing on the power of the extensive studies of the past generation, we can now speak about our health prospects as being shaped by our experiences in five domains: genetic and gestational endowments, social circumstances, environmental conditions, behavioral choices, and medical care. The health of populations is the product of the intersecting influences from these different domains, influences that are dynamic and that vary in their impact depending upon when in the life course they occur and upon the effects of preceding and subsequent factors."

(<http://content.healthaffairs.org/content/21/2/78.full>) In considering these domains, we suggest that the health promotion area of opportunity is inclusive of research related to social determinants of health. This includes factors such as food hardship, poverty, family structure/resources, aversive and traumatic experiences, school quality, transportation, neighborhood conditions, community violence, etc. Additionally, we recommend that the "advance treatments and cures" area includes pediatric and rare diseases. Since many adult-onset conditions are rooted in the pediatric years or in utero, we urge that appropriate attention be given to the needs of the pediatric population. While most children are, fortunately, relatively healthy, about 50 percent of all patients impacted by rare diseases are children and 30 percent of such children will die before their 5th birthday. Given the potential impact of pediatric research to help unlock research mysteries and to improve the health and well-being of children and adults, we urge that NIH strongly consider making this issue a priority within the plan and a topic for cross-cutting research.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

We believe that there should be a cross-cutting focus on research to identify the major risk factors and key antecedents of adult disease. "Research into the causes, preventions, and treatments of diseases that begin very early in life will have a profound, lifelong impact on disease burden and financial costs." (Hay, et. al. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3857014/>). Identifying the origins of adult

disease and addressing them early in life are critical steps toward changing our current health care system from a “sick-care” to a “well-care” model. Research has shown that sustained exposure to adverse childhood experiences, also called toxic stress, early in life plays a critical role by disrupting brain circuitry and other important regulatory systems in ways that continue to influence physiology, behavior, and health decades later. There is a growing scientific knowledge base that links childhood toxic stress with disruptions of the developing nervous, cardiovascular, immune, and metabolic systems, and evidence that these disruptions can lead to lifelong impairments in learning, behavior, and both physical and mental health. (Garner, A.S. & Shonkoff, J.P. Early Childhood Adversity, Toxic Stress, and the Role of the Pediatrician: Translating Developmental Science Into Lifelong Health. *Pediatrics* 2012;129:e224; originally published online December 26, 2011; DOI: 10.1542/peds.2011-2662). In order to reduce the burden of disease in the adult population and ultimately reduce health care costs, we encourage prioritization of research to identify the major risk factors and key antecedents of adult disease. We are also excited about the promise the Precision Medicine Initiative holds for all persons and would encourage that NIH recognize within the strategic plan the challenges and opportunities associated with pediatrics as part of this larger undertaking.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

We applaud NIH for recognizing that basic science is the foundation for progress. We also recognize that research institutions need the means to obtain the latest research infrastructure, including shared core research infrastructure that is shared by multiple collaborating institutions. Congress has recognized the value of research networks and to supporting research in such a manner by enacting into law the National Pediatric Research Network Act (PL 113-55). We urge NIH to recognize that the agency has a role to support the acquisition of research infrastructure, particularly shared core research technologies that are conducive to being used by multiple institutions and that are often cost prohibitive for a single entity to acquire. Building on the topic of providing support for research infrastructure, we believe that future scientific gains will only come about from appropriately trained researchers, including clinician/scientists. As such, we urge NIH to recognize the necessity of providing training and related support for early career investigators.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

We encourage future research to prioritize pediatric and rare disease, the antecedents to adult disease and the social determinants of health, as described above. We also encourage NIH to ensure that the strategic plan focuses appropriate attention on genomics research given the importance of this field to future gains in health and medicine and to recognizing the challenge and opportunities possible through genomics research focused on the pediatric population.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The current framework proposed for NIH's 5-year strategic plan acknowledges the role of technology in catalyzing major scientific advances as well as the capacity of data science in increasing the impact and efficiency of research. NetApp, as a supplier of data center technology, recognizes its role in enabling researchers to make groundbreaking discoveries and advance their particular scientific fields of interest.

NetApp predicts that the market for big data storage and access will be dominated by hybrid cloud environments over the next ten years. The hybrid approach enhances choice, flexibility, access and security of data. The issue is that NIH-funded researchers must justify these technology expenditures within the context of a singular research project that is being proposed for funding. The unintended consequence of this funding strategy is a chaotic and disorganized approach to data center development and management at research institutions. While we understand that there is the ability to pursue such technology through the S10 instrumentation programs, it is a separate application process and funding cycle. In order to promote the role of technology and further data science, strong consideration should be given to allowing researchers to make these type of equipment requests through the traditional NIH funding mechanisms. This could be done by allowing researchers to make companion S10 equipment submissions at the same time they submit their research proposal for funding. Since S10 projects must support a group of NIH scientists, this approach would encourage principal investigators to seek out other NIH-supported researchers and collaborate with their central IT personnel prior to submission. Rather than making equipment decisions that are narrowly focused on their own singular research objective, the broader research community will potentially benefit from an organized approach to the development of compute and storage resources.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity

that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

. . . Foundation is dedicated to finding cures for all childhood cancers by funding critical research needed to improve antiquated treatments and eliminate the occurrence of life-threatening side effects and secondary cancers. As discussed below, . . . strongly urges that a trans-NIH strategic priority be placed on research into pediatric disease cures and treatment. Within the Strategic Plan's overview of "Setting Priorities," NIH highlights "advanc[ing] research opportunities presented by rare disease research" and "incorporate[ing] disease burden as [an] important . . . factor." As further discussed below, many diseases affecting our nation's pediatric population are, by definition, both rare (albeit all too common) and measure high as a matter of disease burden. To illuminate this point, for example, the incident rate of pediatric cancer per 1,000 children has not decreased, but increased since 1975. Pediatric cancer as a whole is considered a rare disease, but importantly, almost all types of cancer diagnosed in children are biologically different from those found in adults, making each type of pediatric cancer all the more rare. Moreover, in terms of disease burden, the average age of death for a child with cancer is 8, amounting to 69 years of expected life years lost. Compounding the diseases burden is a dearth of pediatric cancer therapies resulting in adult chemotherapies simply being dosed for children, creating horrific side effects so that children who survive often suffer from profound disabilities as a result of their treatment. As such, pediatric cancer imposes an inordinately high disease burden on its young victims. . . . strongly recommends that a trans-NIH strategic priority be placed on research into pediatric disease cures and treatments within the "Setting Priorities" section of the NIH-wide Strategic Plan.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Thank you for the opportunity to comment. 1. Missing is reference to investment in Dissemination and Implementation (D&I) science as an explicit outgrowth of translational science. The growing D & I literature attests to the crucial relevance of intra- and inter-psychological factors for successful translation of basic scientific outcomes, especially as they are rolled out through empirically validated community dissemination protocols to ensure intervention fidelity. 2. Many of the health-related outcomes that the NIH wishes to enhance are either themselves primarily behavioral/psychological (e.g., mental illness, development / remediation of cognitive, emotional, and social skills) or mediated in part by behavior/psychological mechanisms (e.g., behavioral risk factors for stroke, cancer, heart disease, diabetes). As such, it needs to be clear that basic science should include basic behavioral and psychological sciences as well as basic genetic, molecular, and systems neuroscience. Fundamentally we will not be able to enhance many public health outcomes without addressing behavior, psychological mechanisms, and environmental factors (physical, social, economic). Continued overemphasis on genetics and molecular/systems neuroscience will impede progress. 3. The emphasis of the NIH is increasingly on dimensional views of illness that cut across traditional diagnostic boundaries. This orientation is welcome to an organization such as ours that has traditionally taken a dimensional view of psychopathology. However, there is much we need to know about whether our existing treatments affect mild or subthreshold presentations of illness as well as full presentations. We recommend research that (a) examines whether evidence-based treatments previously shown to be effective for

categories of illness are also effective in treating putative dimensions of vulnerability to illness, and (b) if so, what cutpoints of these dimensions are necessary (or what treatment dosages are necessary at each level of the dimension) before a clinically significant response is shown.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Disordered states of biomolecules are ubiquitous in the cell. Intrinsically disordered proteins (IDPs) are a vastly understudied part of protein science. While the NIH is pouring funding into well supported and mature research fields, areas where little is known provide much lower hanging fruit for the pushing the boundary of the unknown. IDPs represent one such area and should receive more emphasis in funding plans.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

We need to step even further toward high-risk science, using small research teams.

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework
(*Submitter left answer blank*)

Compatibility of the framework with the broad scope of the NIH mission
(*Submitter left answer blank*)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Thank you for the opportunity to comment on the NIH wide Strategic Plan. The . . . was founded on the principles of advocacy for genomic health care by health care providers across the world, and its goals reflect the priorities of global community, integration of genetics and genomics discoveries at all levels of professional practice, and leadership in generating and disseminating evidence for high quality nursing practice. . . . fully supports the recognition of the ongoing benefit of the reciprocal relationships among basic science discoveries, health promotion and disease prevention, and the implementation of treatments and cures. However, . . . urges the NIH to consider the importance of anticipating ‘unpredictable’ consequences through research in the behavioral, social science, and ethical/legal/social issues research programs housed across multiple Institutes and programs. These research programs have the capacity and the potential to inform and benefit from the basic science discoveries in order to minimize risk and reach the goals of improved health for all that is at the heart of genomic discovery. In the Setting Priorities section of the Strategic Plan, . . . also urges the NIH to consider that the term, “disease burden” can encompass not only clinical consequences, but also personal physiologic or emotional sequelae, social adversity, financial costs to individuals and society, as examples of multiple burdens that may be avoided or minimized, with a clear recognition and inclusion of disease burden on individual, family, and community health in genomic health research. The leadership of . . . agrees that this is an exciting time within which biomedical, social/behavioral, and ethical/legal/social issues research can partner to accelerate the vision of extending healthy life and reducing illness and disability.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine
(*Submitter left answer blank*)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan
(*Submitter left answer blank*)

Future opportunities or emerging research needs
(*Submitter left answer blank*)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The framework largely continues the status quo in which most aspects of scientific inquiry are important. A focus on wellness, would seem the most significant modification of the framework to pursue. Who is defining “healthy people”? Is it the absence of disease or disability? The focus on healthy people should be across the life span. A focus on cost-effective, people-focused interventions also

should be highlighted. Social, biological, economic and environmental conditions directly affecting health are missing, and we recommend broadening the framework to include these environments. Not only are they important influences on health, they also can alter molecular risk for disease. Collaboration among the social, environmental, and physiologic sciences has higher impact potential. With increased technology and big data, privacy, security, and ethics become increasingly important. There is a need to produce scientists, skilled in informatics, analytics, and technology, to create science that transforms health care, science that engages patients, providers and communities in yet-imagined systems and structures. The overall framework seems devoid of research participant-partnerships and developing linkages among groups to improve health. The proposed components of the framework do not adequately address reduction in disability and living with illness/injury at the highest level possible. They also do not include palliative care/end of life care.

Compatibility of the framework with the broad scope of the NIH mission

Missing is a focus on what the public wants – patient centered approaches to common problems. Eliminating health disparities requires partnerships with communities in which health care settings deliver services, and requires comprehensive policy research approaches. NIH may be constrained by agency-specific priorities and oversight.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Health promotion, wellness, and critical illness is important since a large portion of health care dollars go to critical care and its aftermath. Cross organizational collaboration among federal organizations (CMS, NIH, FDA), external organizations (payers, health care systems, communities), IRBs, and academic centers could be enhanced.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Implementation science is missing –applying what is known in real health care setting with carefully designed clinical trials to demonstrate effectiveness. Injury prevention should also be specifically identified in the Health/Promotion/Disease Prevention theme. This can be considered across the lifespan and in different arenas ie work, play.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

Clearer NIH-direction needed regarding which institutes fund which “diseases” or conditions, research methods and foci. More collaboration among institutes should be addressed.

Future opportunities or emerging research needs

The public’s priorities around health related research need to be assessed. Although this would seem to be a charge for the PCORI, in fact a narrow focus has been taken.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework (*Submitter left answer blank*)

Compatibility of the framework with the broad scope of the NIH mission (*Submitter left answer blank*)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

One of the unifying principals outlined in the NIH Plan reads: Setting NIH Priorities – NIH sets priorities by incorporating measures of disease burden, understanding the need to foster scientific opportunity through nimble and adaptable methods, supporting opportunities presented by rare disease research, and considering the value of permanently eradicating a pandemic. . . . suggests that a missing component in the establishment and renewal of NIH research and funding priorities has been transparency. Celiac disease, for example, has never been a line item in NIH’s long list of diseases in its annual research budget, and we cannot understand why. Is the “disease burden” insufficient to qualify? And, if so, why? How is “disease burden” measured? Is it the number of sufferers? Availability of treatment, a cure, or a vaccine? Longevity of disease? Pain? Emotional toll on patient and caregivers? Economic impact of disease? Or, is the key influence in this process the relative size and power of the disease’s pharmaceutical lobby or the academic research lobby? Is it the number of celebrities or Members of Congress with the disease? Is it the size of the television advertising budget, or the number of ribbons hung on trees? We recognize that resources are limited, and that there are many competing and worthy demands for whatever is available. What we don’t see, however, is how the life-and-death decisions about research priorities are made? In a democracy, that is an unforgivable but entirely correctable error that is certainly cross-cutting and should be explicitly addressed in this trans-NIH strategic plan.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

In the Areas of Opportunity that Apply Across Biomedicine, the second bullet reads: -Improve Health Promotion and Disease Prevention --Advances in early diagnosis/detection A survey done by . . . of our constituents reports that the average number of years an individual suffered between having symptoms of celiac disease and being correctly diagnosed is more than five years. In addition, it is estimated that only one in six individuals with celiac disease have been correctly diagnosed. That leaves 2.5 million individuals with the disease who are left untreated. The long-term implications are unknown, but the immediate misery is well-documented. We heartily endorse each of the sub-bullets under the overall goal of Improve Health Promotion and Disease Prevention. What is missing, however, from these goals is the recognition that possessing the tools realized by “advances in early diagnosis/detection” does not necessarily lead to improved health promotion and disease prevention. Celiac disease sufferers fail to get a timely diagnoses, or even a diagnosis at all, despite the presence of a relatively simple and cheap blood test developed in 1990s. The health disparity our community confronts is the random chance of finding a primary care or GI doctor who has sufficient training and insight to order the test. Many in our community report seeing 5, 10, even 20 doctors before being tested for celiac disease. As celiac disease is not an especially rare disease, we can only imagine how this issue impacts other, rarer diseases that may also have relatively simple diagnostic screens that are not ordered out of ignorance. We maintain, therefore, that advances in early diagnosis and detection cannot exist in a vacuum without giving healthcare providers better tools/information/training to order these screens. Is this a matter for NIH

going forward? And if not NIH, then whom?

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The framework appears to largely continue the status quo in which almost all aspects of scientific inquiry are important but with continued support for the “rare” and unusual as well as perhaps the highly “innovative.” Rare and innovative unfortunately may hold no promise to relieve illness burden. A focus on healthy people would seem the most direct change to pursue and an area that has been grossly underfunded for years. At the same time, a focus on inexpensive (not necessarily high tech), people-focused interventions should be highlighted. The development of field instruments to measure physical activity, sleep, and diet needs to be considered. The meaning of “health should be clearly defined by multiple stakeholders, and should include a focus on preserving wellness; especially functional capacity and quality of life. Healthy People 2020 Leading Health Indicators could be incorporated to improve health of the population. Early detection should include childhood. The NIH basic science framework should be broadened to include basic science of physical, social, economic environments since we know these can alter molecular risk for disease and affect disease progression and healing. Molecular knowledge is certainly important but the interaction among the molecular, physiological, social and environmental sciences has the potential to yield higher impact. While omics is important and innovative, we must retain focus on what we know contributes to health, including social and environmental conditions that affect health outcomes. The importance of privacy, security, and ethics are increasingly important concepts as we consider the use of big data, social networking and technology as research and clinical tools. We need to produce scientists who are skilled in informatics and technology to lead health care transformation, and a need to engage patients, providers, and communities in the design of health care systems and structures yet to be imagined.

Compatibility of the framework with the broad scope of the NIH mission

Missing from the focus is a real focus on what the public wants. Consideration of patient centered approaches to common problems is needed to maintain public interest and support of the advancement of science. Additionally, in order to accomplish big goals, such as eliminating health disparities, will require partnerships with health care settings and perhaps require health services and health policy research approaches, which NIH has been largely unwilling to fund. It is not clear that the proposed components of the framework adequately address the NIH mission to reduce disability. Certainly by curing or preventing a disease one can prevent disability, but NIH should also have a focus on ‘living with’ illness/injury at the highest level possible. In addition, fundamental knowledge about the nature and behavior of living systems is central to the mission, and implies a commitment to science that extends well beyond the biomedical. In the overview, NIH indicates that this is a unique moment of opportunity in biomedical research – but the mission implies although biomedical is an important component it is not the sole component. Clarification of NIH’s intent is needed.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

For NINR, health promotion and wellness are key components of its mission. Additionally, NINR has invested in the patient experience and caregiver management of critical illness; understanding critical illness care and its long-term sequelae is important since a large portion of health care dollars go to critical care and its aftermath. Cross organizational collaboration between federal organizations (CMS, NIH, and FDA), external organizations (payers, health care systems, and communities), IRBs, and Universities is missing from the framework.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Applied (implementation) science is missing – taking what is known and applying it in real health care setting with carefully designed clinical trials to demonstrate effectiveness. Implementation science requires funding in order to speed the use of scientific knowledge in clinical practice. Injury prevention should also be included in the health promotion/disease prevention domain. This should be considered across the life span since injuries can occur at any point. Injuries such as those caused by falls, guns, road traffic, sports, and workplace accidents/injuries are not captured. Injury is a priority global health problem (including in US) with road traffic injury a priority for WHO that affects millions worldwide.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

Applied (implementation) science is missing – taking what is known and applying it in real health care setting with carefully designed clinical trials to demonstrate effectiveness. Implementation science requires funding in order to speed the use of scientific knowledge in clinical practice. Injury prevention should also be included in the health promotion/disease prevention domain. This should be considered across the life span since injuries can occur at any point. Injuries such as those caused by falls, guns, road traffic, sports, and workplace accidents/injuries are not captured. Injury is a priority global health problem (including in US) with road traffic injury a priority for WHO that affects millions worldwide.

Future opportunities or emerging research needs

The overall framework seems to be devoid of people, partnerships with research participants, and developing linkages between and among groups to improve health. Additionally, to meet some of the goals of the strategic plan, cross organizational collaboration between and among federal organizations (CMS, NIH, FDA), external organizations (payers, health care systems, communities), Institutional Review Boards, and Universities is missing. These collaborations are not trivial, with each agency or organization having their own priorities and bottom line. In doing research, some of these barriers to patients and outcomes need to be addressed, including the laws that prohibit us from even talking to one another. Finally, psychosocial health and wellness of the public should be specifically addressed in future NIH research opportunities across all institutes.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Circadian rhythms are increasingly found to be fundamental to biology and medicine. Circadian clocks are found in every cell of the body and regulate the transcription of large numbers of genes. A deeper

knowledge of both normal and pathological circadian function is proving central to understanding body processes in health and disease. If there is any question of the widespread role of circadian rhythms, a glance at a PubMed search for circadian rhythms & humans will bring up scores of recent papers in areas including (but not limited to) cardiology, oncology, urology, neurology, metabolism, psychiatry, immunology, surgery, infectious diseases, endocrinology, pediatrics, and ophthalmology. These time of day considerations span many areas of NIH-sponsored research. We also know that different patients have different chronotypes. Some have body processes cycling earlier in the day, others later. Some are so extreme as to have sleep disorders, and in some cases their rhythms are not entrained to 24 hours. Treatments in many areas could be more effective if applied relative to the patient's individual rhythm. Virtually every area of medicine is affected by circadian processes making this an appropriate trans-NIH theme and an Area of Opportunity that Applies Across Biomedicine. A better understanding of circadian rhythms, cellular rhythms and circadian rhythm disorders has the potential to improve treatments and functioning across all disorders and demographics.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

A Potential Benefit of NIH Research Studies: Making the results of NIH research studies easily understood by the general public in third world countries is important because of many misperceptions about public health diseases in those nations. An Area of Consideration for the Current Framework: Expand the funding of NIH sponsored research to include the involvement of scientists in the developing world.

Compatibility of the framework with the broad scope of the NIH mission

Scope of the NIH Mission: Disseminating the findings of NIH funded biomedical research to the scientists and citizens of the developing world is well within NIH's overall mission.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Additional Concepts in ICO Strategic Plans: If necessary, the budgets of the 27 ICOs should be increased: 1) to expand the dissemination of biomedical research findings of studies conducted in the developing world; and 2) to support the greater involvement of developing world scientists in NIH clinical studies.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

A Trans-NIH Research Theme: It is critical to increase the NIH's role in quickly identifying common and emerging disease epidemics, especially among children in third world countries, (e.g., the WHO's poor performance in the recent emergence of Ebola in West Africa).

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

An Emerging Research Need: With currently deteriorating economic conditions and widespread corruption associated with many governments in developing countries, there are few local funds available for third world research institutions and scientists. NIH should consider increasing funding for well designed cooperative research opportunities in third world nations.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The framework includes a big focus on “basic science.” While we recognize the importance of basic science, it is imperative that the NIH not emphasize basic science at the expense of clinical research, evidence-based healthcare, and prevention. The second “area of opportunity” should be highlighted to promote the shift in focus at NIH to effectiveness of health care and evidence-based assessment of clinical care. Prevention, rather than disease management, should be a top priority.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Health Disparities: Having more information on evidence-based interventions to eliminate health disparities is incredibly important so providers can best help patients achieve health goals. Professional associations, like . . . , can use this information to create best-practice resources for providers to improve care. Health Literacy: Health literacy has been found to underlie many of the disparities in health and healthcare outcomes. This is particularly important as health literacy essentially applies to all centers. Future research into the effects of health literacy on healthcare and the development of tools to help providers recognize health literacy as a significant contributing factor in healthcare provision, as well as development of resources to counter the negative effects that health literacy has on outcomes, will be important in the NIH strategic plan.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Family Planning: NIH should continue to focus their attention to one of the biggest public health issues in the world – family planning. Specific scientific focus on family planning, contraception, and safe abortion practice is needed. Genetics: The field of genetics, including technology and the application to healthcare, is exploding and far outpacing research to define its use in clinical medicine. Considering the existing technology, as well as the continued development and decreasing costs of whole genome sequencing, it is imperative that the NIH strategic plan consider research to establish the applicability and incorporation of genetics-based technology in the provision of healthcare, to include cost-effectiveness analysis.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Preterm Labor: While rates of preterm labor have declined thanks in large part to research done at NIH on the benefits of progesterone to preventing repeat preterm birth, we are still left with unanswered questions and unexplained disparities. As part of its work, NIH should continue to focus on the causes of preterm labor to advance prevention and improved outcomes. Fetal/Neonatal Brain Injury: While considerable advances have been made in the knowledge and understanding of the processes contributing to neonatal encephalopathy and long-term neurodevelopmental outcomes, there continues to be a need for additional research. Additional research should focus on identifying the factors that contribute to adverse events before delivery and in the NICU, interventions designed to decrease harm to these patients, and additional patient safety research. Postpartum and Interconception Care: There is a lack of evidence-based studies on optimal maternal and infant postpartum management, leading to practice recommendations primarily reliant on expert opinion and observational studies. Additional research is needed to determine how to most effectively address the unmet needs of mothers during the transition from childbirth to motherhood, to optimize maternal health during the postpartum and interconception periods.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

No comment provided.

Compatibility of the framework with the broad scope of the NIH mission

No comment provided.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

No comment provided.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

There is a strong need to advance the academic study of the history of the research enterprise in biomedicine; and an equally strong need to study how biomedical research has affected society and culture. With both efforts, one needs to convey this research in ways appropriate to non-specialists. Current efforts at or supported by NIH in historical and cultural studies of medicine are relatively small and continue to diminish. One hopes for more, and more sophisticated accounts of the ways that research is funded, contested, and defended, and how that research plays into and responds to the social forces of American and world societies. This effort ought not to be considered an afterthought or add-on to the current research agenda. Narrative accounts are concise and comprehensive ways of conveying truth; and history provides a mode of understanding that both allows leaders in biomedicine to understand better their enterprise and its effects, and thus enable them better to lead that effort; as well as to provide the American public with a richer account of this national enterprise. When done well, such accounts go beyond narrow policy analysis or public relation campaigns to provide fundamental insight that is crucial to the functioning of the national biomedical enterprise and its efforts for the future. Specific suggestions: Include history in the Overview that begins the Strategic Plan Add an Area of Opportunity: Historical accounts provide insight in to the challenges for success.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

No comment provided.

Future opportunities or emerging research needs

As noted above, the history of medicine is a vital research area, undertaking new and rich types of analysis and enthusiastically embracing digital information as it expands its research modes and capacities. This is a great opportunity for increased support, which will result in a great flowering of results, helpful to the entire biomedical enterprise.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

With obesity a major health problem in USA it is important that . . . members underscore the importance of physical activity research in the work of the NIH. Such research will be helpful, now and in the future.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

One potential benefit of the current framework is the stronger emphasis on clinical research, translational research that applies directly to humans and interdisciplinary research. The proposed structure appears to allow for more trans-NIH initiatives that could advance knowledge specifically about the diagnosis and treatment of complex diseases with profound systemic consequences. Vital research needs to be conducted on time-sensitive, life threatening systemic conditions such as cardiac arrest, shock and sepsis. These conditions involve multiple organ systems which interrelate and impact each other with overall physiologic compromise. Being primarily organ directed (i.e., heart, brain, kidney), the current structure of the NIH is not conducive to supporting the kind of interdisciplinary research that is needed to advance care for these common, life-threatening conditions but the proposed framework may mitigate some of these issues. There also needs to be more emphasis on the translational aspects of getting the results of the research more quickly applied to the care of patients and populations.

Compatibility of the framework with the broad scope of the NIH mission

The proposed framework is generally compatible with the broad NIH missions to support research in pursuit of fundamental knowledge about the nature and behavior of living systems, and the application of that knowledge to extend healthy life and reduce illness and disability. While the pursuit of fundamental knowledge has been traditionally emphasized at NIH, the framework appears to re-emphasize how fundamental knowledge will be directly applied to the human condition, both in health and disease by setting funding priorities and by incorporating measures of disease burden, understanding the need to foster scientific opportunity through nimble and adaptable methods and considering the value of permanently eradicating a pandemic. In particular, there is a compelling national need to better define the impact of NIH supported research on directly improving health promotion, preventing disease, advancing treatments and cures, especially given the financial constraints affecting clinical investigators, academicians and health care providers and systems. This focus on human health and clinical disease will enhance the stewardship of the research enterprise by recruiting and retaining an outstanding biomedical clinically oriented research workforce, enhancing workforce diversity, encouraging applicable innovation, optimizing approaches to guide how decisions are made, enhancing partnerships across the broad healthcare enterprise, promoting scientific rigor and reproducibility, reducing administrative burden, and employing risk management strategies in population management decision-making.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

The complex diseases of cardiac arrest, trauma, and sepsis are highly morbid and highly lethal. Research on early diagnosis and early intervention is lacking. These common conditions represent a large disease burden and threaten the impact of advances made in other disease conditions. Thus, it would be of great benefit to include them as priorities in a cross cutting trans-NIH strategic plan.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

One cross-cutting trans-NIH theme that is not captured in the Areas of Opportunity that Apply Across Biomedicine is the concept, importance and role of time in the treatment of disease processes. That is, the fundamental basis for different diseases and the effectiveness of treatments may differ depending on the time at which interventions are made. Not only does the concept of time traverse multiple NIH institutes, it also traverses the primary Areas of Opportunity listed in the NIH-wide Strategic Plan Framework. While age in years might be considered one measure of time (e.g., for treatments related to the age of onset for cancer or the time of initiating treatment for chronic diseases), other treatments and cures depend on a time scale of minutes to hours. For the fields of acute care medicine, surgery and emergency care research, the time-sensitivity of certain conditions (e.g., cardiac arrest, STEMI, stroke, sepsis, ischemic bowel, ruptured aneurysms, etc.) may determine whether certain treatments are effective. There are likely time-based windows for treatments and cures, that open and close at different points along the time continuum of disease, which may have complex mechanistic explanations and large resulting impact on human health. Placed in the context of acute care, the hypothesis has been stated as “rapid diagnosis and early intervention in acute illness or acutely decompensated chronic illness improves patient outcomes” (Neumar R. The Zerhouni Challenge: Defining the Fundamental Hypothesis of Emergency Care Research. 2007. *Ann Emerg Med.*). Such a hypothesis is not specific to one disease or one organ system, but rather traverses multiple disease states and multiple organ systems. Such a theme can only be tackled through a trans-NIH initiative that allows the partnership of multiple institutes, inter-disciplinary investigators, basic science, clinical research and the collaboration of scientists who understand the interplay of time and

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

The NIH-wide Strategic Plan should not include components of the Areas of Opportunity of basic science as the foundation for progress and the consequences of basic science discoveries are often unpredictable. In the current construct, NIH has disproportionately placed basic science as the foundation for structuring the institutes, intramural programs, standing extramural programs and scientific review committees. While the consequences of basic science discoveries are often unpredictable, there is a compelling need to translate the impact of discoveries to impact. This needs to be emphasized in NIH-wide structures and functions. Thus, the components of the framework to Promote Fundamental Science should emphasize advances in clinical research methodologies, technological applications and data science in addition to components listed under Improve Health Promotion and Disease Prevention and Advance Treatments and Cures.

Future opportunities or emerging research needs

The “promotion of fundamental science” should not only include efforts for the early diagnosis and detection of longitudinal disease states but also “acute care medicine” in which the entire disease process can be defined in an acute incident such as trauma or acute infection. These efforts would have important, extended implications in the response to time-sensitive global health events and their implication on U.S. Health. Opportunities for “evidence-based interventions to eliminate health disparities” include the development and implementation of evidence-based clinical practice guidelines. Furthermore, such guideline incorporation into clinical performance measures would do much to improve the quality of patient care in this country. These efforts could be an extension of regulatory science in seeking to improve assessment of diagnostics and fostering the development and evaluation of tools, methods and standards within applied science. Rewarding collaborations between institutes, medical specialties, and traditional basic science area silos would foster synergistic partnerships to promote translational discoveries and their subsequent valuable implementation in direct patient care. Just as critical to the promotion of fundamental science, clinician scientists are central in the determining the impact of often unpredictable basic science discoveries.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

I would like to remind ourselves of the spectacular success of structural biology, which, however, has completely ignored intrinsically disordered proteins. These proteins play important functional and pathological roles, but they cannot be studied by traditional means of structural biology. The recognition of structural disorder has brought a revolution in structural biology, thus it is imperative they are given a special attention in the grant system.

Compatibility of the framework with the broad scope of the NIH mission

N/A

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

N/A

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Despite their basic importance, disordered proteins cannot be addressed by traditional structural biology and are not covered in PDB.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

N/A

Future opportunities or emerging research needs

I would stress that these proteins are involved in almost all diseases, and thus they represent a novel category of drug target. We cannot afford not to address this problem at the grant system level.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

My suggestion regarding the NIH-wide Strategic Plan Framework focuses on the unifying principle of Enhancing Stewardship. Specifically, to recruit and retain an outstanding and diverse biomedical workforce, the Strategic Plan Framework should explicitly commit to support the advancement of investigators who work less than full-time. These individuals, primarily women, have the training and desire to contribute to NIH's mission—"seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability." A concrete step would be to allow investigators with less than full-time appointments to apply for career development awards; currently, criteria require full-time appointments. In my case, I hold a part-time faculty appointment at a research-1 university. Two years ago, I withdrew my application for a full-time tenure-track position because I was uncomfortable assuming a full-time position with two young children. My situation exemplifies the persistent and widespread challenge of "brain-drain" – the attrition of women from the academic pipeline, often corresponding to family formation (Bilimoria, 2008). Fortunately, progressive leaders in my department solicited applications for the part-time faculty position that I now hold; this has allowed me to successfully balance my work and family commitments. However, although I am at the appropriate stage for a career development award and would be 75%-time when funded, I am ineligible because I lack a full-time appointment. Not only does this disadvantage me in the short-run, but in the long-run, hinders my ability to generate preliminary studies required to successfully compete for R-level awards. Thus, current eligibility criteria work against the large and growing number of talented, mostly women investigators who choose to work part-time. Committing to support investigators who work less than full-time would be a much-needed step towards promoting gender equity among biomedical researchers.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an

NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Improve consistency and validity of outcome measures for wound infection and wound healing outcomes. This will help unify a field that is placing huge economic, social, clinical and patient burdens on our health care system. Once clear operational definitions are in place for these outcomes comparisons of safety and efficacy of interventions will become more meaningful and improve clinical, patient-oriented and economic decision making. This will also position the field of wound management to optimize use of scientific analysis and informatics techniques.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The focus on individual investigator initiated basic research is important and should be emphasized to an even greater extent. Such focus will ensure future discoveries that can be translated towards improvements in human health. Overall the framework seems a bit vague and obvious.

Compatibility of the framework with the broad scope of the NIH mission

The framework is so open ended and vague, it certainly encompasses the scope of the NIH mission.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Practical matters: e.g., increasing the size of modular budgets from 250K to 300K

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

I strongly support . . . statement of the importance of studying intrinsically unfolded proteins and regions thereof. It has become increasingly evident protein disorder is relevant to numerous biological and disease-related processes. For example, many stresses result in the in vivo formation of stress granules depends on intrinsically disordered regions. Further basic research into the role of disorder in biology will pay considerable dividends on many fronts and is highly appropriate to be considered as a trans-NIH research theme that has not been captured in the Areas of Opportunity that Apply Across Biomedicine.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The current framework could be enhanced if it emphasized not only extending healthy life, but ensuring the quality of that extended life. Also, since part of the mission of NIH is to reduce illness and disability, the framework should include habilitation and rehabilitation. To reduce illness and disability, NIH could conduct research that strives to improve functioning in everyday activities and participation in communities, across the lifespan.

Compatibility of the framework with the broad scope of the NIH mission

The . . . supports the Unifying Principles identified in the NIH-wide Strategic Plan Framework. With regard to “Set NIH Priorities”, we urge NIH to consider a broader view of measures of disease burden. When individuals have a disease or chronic condition/injury, the ramifications of the disease extend beyond the family and individual’s social support system. Understanding the intrinsic and extrinsic factors that can be barriers or facilitators to performance of daily activities can illuminate the pathways to improved health and well-being, life satisfaction, and quality of life. . . . views NIH’s role of enhancing stewardship of the research enterprise as vitally important. The training and career development awards (e.g., K12 awards) offered by NIH should be continued so that the scientific workforce is rigorously trained and prepared to address the nation’s health research priorities. The K awards are particularly helpful for the rehabilitation professions since it is challenging to recruit talented rehabilitation professionals for scientific careers, given the more lucrative offers in practice and academia. NIH’s work to increase workforce diversity is lauded and should be expanded so that a greater number of researchers from diverse backgrounds can address the complex social and cultural determinants of health, such as reducing health disparities.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

. . . requests that NIH consider funding more knowledge translation studies and implementation science so that evidence-based interventions can be more rapidly scaled up into routine clinical care.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

. . . supports NIH’s efforts to encourage cross-institute collaboration because many of the answers to research questions are not organ/disease specific, and greater impact on the nation’s health could be achieved if institutes and centers were not only encouraged but rewarded for co-funding research and partnering with associations and foundations.

Future opportunities or emerging research needs

. . . is pleased that certain institutes and centers of NIH are using registries and pragmatic trials to answer research questions. We hope NIH will continue to be open to new research methods and training the research workforce in emerging research methodologies. Some of the newer approaches can help maximize research resources (e.g., registries) and more clearly identify areas for randomized trials. A variety of research methodologies are needed to answer the multitude of questions NIH addresses in a nimble and flexible manner. The . . . appreciates this opportunity to comment on the Framework for the NIH-wide Strategic Plan.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Broad based regional cores and repositories (both material and data) can have a significant impact on a large number of individual programs, and significantly reduce financial waste associated with duplication of effort at individual institutions. Support for these kinds of facilities and the broad impact they can effect seems to be missing from the Trans-NIH strategic plan.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Relatively little investment in infrastructure for Cores and Repositories (data and material) can effect the largest number of researchers per dollars invested, yet very few opportunities exist for these kinds of non-hypothesis driven efforts. The ability of any investigator to make dramatic advances depends, at least in part, on the quality of materials and facilities available to them. To support infrastructure that would make high quality materials, reagents, data, and services available to a large number of researchers reduces overall costs by avoiding duplication of costly processes in multiple laboratories within an institution, state, or region. As funding becomes more limited, it allows all researchers access to the same quality materials for investigation, increasing the overall opportunity for significant advancement in basic sciences. Please consider adding this to the trans-NIH strategic plan.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The . . . notes three areas of potential benefit for the current NIH-Wide Strategic Plan framework. First, the . . . is grateful the current Strategic Plan framework recognizes the importance of basic, fundamental science to scientific discovery and innovation. Basic research provides the foundation for advances that improve the diagnosis, prevention, and treatment of diseases, including diabetes. Second, the . . . is pleased NIH incorporates measures of disease burden as it sets its priorities, and makes this clear in the NIH-wide plan. Research is essential to making progress in care, prevention and an eventual cure for many diseases, including diabetes. The continued need to consider the health and economic burden of diabetes and other diseases in priority setting at NIH should remain in the current framework. Third, the . . . is pleased the current Strategic Plan framework emphasizes the role of NIH in improving disease prevention. Two examples of this work are the Diabetes Prevention Program (DPP) study, which found that lifestyle changes can reduce the risk of type 2 diabetes by 58% percent, and the Diabetes Prevention Program Outcomes Study (DPP-OS), which provides a longitudinal look at the DPP population and has the unique ability to illuminate the long-term effects of prevention on outcomes. Including disease prevention in the current framework is important to ensuring the evidence-base necessary to make informed decisions to prevent diabetes and other diseases.

Compatibility of the framework with the broad scope of the NIH mission

The . . . believes the current Strategic Plan Framework is compatible with the broad scope of the mission of the agency. NIH's mission, which is, "to seek knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability" is reflected in the proposed outline of the Framework Overview, the Areas of Opportunity and the Unifying Principles. Additionally, the current Strategic Plan Framework complements many of the goals of NIH, including the goal of, "fostering creative discoveries, and innovative research strategies and their application as a basis for ultimately protecting and improving health."

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

The . . . urges NIH to include research regarding the genetic basis of type 1 and type 2 diabetes and the complications of diabetes in its NIH-wide plan, as an example of research under each of the Areas of Opportunity. These are cross-cutting examples outlined in the 2011 Strategic Planning Report of the Diabetes Mellitus Interagency Coordinating Committee (DMICC), and may impact research in Institutes and Centers beyond the National Institute of Diabetes, Digestive, and Kidney Diseases. Knowledge of the genetic factors of type 1 and type 2 diabetes, the complications of diabetes, and obesity at the most fundamental level may lead to discoveries producing improved disease prediction, prevention, treatment, and cures not only for diabetes but also for heart disease, blindness, and kidney disease. We view the inclusion of these genetic studies in the current Strategic Plan framework as broadly benefitting NIH, including work at National Heart, Lung and Blood Institute and the National Eye Institute. Additionally, the . . . urges NIH to include prevention of type 2 diabetes in the NIH-wide Plan, as an example of research under the Health Promotion and Disease Prevention Area of Opportunity. The NIDDK has and continues to conduct valuable research on type 2 diabetes prevention through the Diabetes Prevention Program clinical trial, which found a successful, proven method for preventing a type 2 diabetes diagnosis in individuals with prediabetes through lifestyle changes that, if more widely implemented, could help many more of the 86 million individuals with prediabetes to avoid a type 2 diabetes diagnosis, and the deadly complications of the disease. With one in three Americans and one in two Americans of color projected to have diabetes in 2050 according to the CDC, we ask that prevention of type 2 diabetes be included in the Strategic Plan framework.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

The current Strategic Plan framework should address ways NIH can better support investigators at every stage of their careers, but particularly as they transition to independence. For example, it remains difficult for investigators to obtain initial R01 funding, and has become increasingly challenging for many early and mid-career scientists to obtain R01 renewal awards. Since these awards provide career stability and are the most important source of NIH grant funding for researchers, the NIH should include ways to address this issue in its framework to ensure this growing pipeline issue is resolved. Diversifying the base of NIH researchers will help foster the discoveries and breakthroughs that will lead to cures and improved treatments for diabetes and other diseases and conditions.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

In order to compete internationally with top universities, Congress must invest in biomedical science and encourage funding of junior-career or mid-career scientists with the potential to impact their respective fields. Researchers still face serious and growing problems in funding their research programs, especially when competing with senior investigators with multiple R01/R21 grants. Perhaps a limit of 2 R01 application per lab will allow for additional grants opportunities to underfunded investigators.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Wound healing is a multi-billion dollar financial burden in the US and worldwide. Despite this fact, the available funding for wound healing research is scarce, and limited progress has been made to develop novel treatment strategies to reduce the financial and psychosocial burden of non-healing wounds. Information obtained from wound healing studies can directly facilitate new directions in cancer research and regenerative medicine. The area MUST be a focus of the NIH in the new strategic plan. There is not a specialized study section or special emphasis panel designed to assess wound healing grants. This leads to highly qualified and promising research proposals being reviewed by non-experts, who are not well-versed in the field.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

We need more disease-focused study sections.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity

that Apply Across Biomedicine

For the section on "Area of Opportunity that Apply Across Biomedicine" and the bullet on "Evidence-Based interventions to eliminate health disparities" (Pg. 2) This work aligns with HRSA activities, recommend including information on how NIH will support, coordinate and collaborate with other HHS agencies to advance the utility of existing research investments to address persistent or emerging issues.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Recommend incorporating some of the psycho-social-environmental determinants of health as a stated priority along with the strong "bio-medicine" focus, it would be helpful in demonstrating that NIH is aware of the philosophical and policy evolution of how health is viewed, and trying to be improved, throughout the country and globally as well. That is, the science is absolutely important, as are employment, education, housing, etc.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The Coalition for the Life Sciences (CLS) represents over 60,000 biomedical researchers, most of whom rely on NIH grants to fund their research. CLS endorses this Strategic Planning process. In our view the strategic plan must: • Strengthen the commitment of NIH to long term, stable funding of fundamental research, recognizing that our incomplete knowledge of basic life processes is the limiting factor in understanding, treating and preventing human disease, • Strengthen the support of investigator-initiated research, the proven way to explore the novel ideas that lead to the unpredictable fundamental discoveries and are required to understand the causes, treatment and prevention of disease, and • Maintain and strengthen the integrity of the NIH peer review process to ensure that the most meritorious grants are funded without inappropriate external influences. • Develop a system that will train researchers to advance scientific discoveries, create multiple career pathways for young scientists to make meaningful contributions to society, and recognize the value of a diverse scientific workforce to leverage broad perspectives and experiences.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

The researchers represented by CLS recognize that most breakthrough discoveries emerge unpredictably from basic research, so rather than predicting emerging trends in research we recommend that the strategic plan: • Be flexible and dynamic to allow the direction of research to adjust rapidly to ongoing discoveries and opportunities, • Foster the rapid development of new technologies and tools, including those required for precision medicine, and • Commit to understanding the basic biology of complex transmissible diseases, prepare by developing the vaccines and treatments, and be organized to allow for nimble reactions to new infectious threats. We thank you for the opportunity to respond.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

I want to address only one issue regarding NIH reviews of Extramural proposal. Currently the practice to my knowledge is picking General experts in a subfield to review proposals in a variety of specialties in this field. the result is an expert say in Image processing reviews a proposal say on data-mining of EHR, in which such a reviewer is basically an intelligent laymen . the result is a mixed quality reviews. An EHR expert will write a knowledgeable review while a image processing expert will typically write a superficial review assessing by technicalities, rather than by deep knowledge expected from a reviewer of a scientific manuscript. Many times it is obvious the reviewer, did not understand /or even read the whole proposal, making judgment by say the Aim page only. the more complex and specialized the subject of the proposal , the larger is the disparity exposed between the reviewer with professional knowledge in this field, versus those which has such knowledge in other fields. The impact is that funding decisions are made by superficial factors ,rather than by deep professional review. this reality is known to many people who submit proposals to NIH, and could be exposed by conducting an objective scientific study questioning such a population if they are guaranteed anonymity. for perspective consider the review system used by top level scientific journals in Biomedicine, where editors make efforts to identify experts in the subject of each submitted paper. Just imagine the quality of papers in such journals, where NIH funding awardees are typically publishing ,if the journals would have employed a reviewer selection criteria used by NIH extramural. Yes I know, "a broad based panel of experts can supposedly assess the impact of a proposal". My answer is that they can not ,if they do not understand the proposal. Recommendation :use small panels(5) of domain experts.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Under Health Promotion and Disease Prevention there are strong potential benefits secondary to inclusion of physical activity research. In light of the current epidemic of chronic disease, physical activity holds promise as a cost and clinically effective intervention. More research is needed to expand evidence to include minority and disadvantaged populations as well as specific disease states. Most importantly, the minimal effective dose of exercise needs to be identified in order to promote or maximize participation.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

-the discovery of intrinsically disordered proteins (IDPs) has led to a paradigm shift in structural biology. -IDPs often act like chameleons that can adopt different structures when interacting with different partners. -IDPs are often promiscuous and present at the crossroads of signaling pathways integrating information and providing decision making functions. -How specificity in these processes is achieved is not understood. -Understanding cellular decision making and signal integration requires significant improvements in the understanding of the working mechanism of IDPs. -Given the key roles IDPs play in signal integration, it is not surprising that altered expression of IDPs or mutations in them have been associated with multifactorial diseases such as cancer and neurodegeneration. -Significant steps forward in the understanding of the pathogenesis of various cancers and neurodegenerative disorders will not be possible without a better understanding of the biophysical and molecular principles that govern the behaviour of IDPs. - Interestingly, promising new ant-cancer therapeutics exploit interaction sites of IDPs (e.g. the Genentech drug Venetoclax). -Interaction-sites of IDPs and IDPs themselves provide new targets for drug development.

Compatibility of the framework with the broad scope of the NIH mission

Not applicable.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Not applicable.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

-IDPs are involved in nearly all biological processes, and it is believed that cellular complexity and the increased abundance and relevance of IDPs go hand in hand. -Understanding higher organism behaviour requires a better grasp of how adaptive and stimuli-triggered responses can emerge from cellular complexity, which in turn requires a better understanding of the promiscuous players in the complex interaction networks of cells; these are mostly IDPs. -Systems biology and systems medicine are only likely to work if all relevant players of cellular systems are well characterized and their mode of action understood. This is not yet the case for many key players but particularly those that are intrinsically disordered.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

Not applicable.

Future opportunities or emerging research needs

-Systems biology and systems medicine: IDPs as signal integrators and disease hubs. -Structural biology: New methods for new challenges posed by IDPs -Rational drug design

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The NIH-wide framework could be strengthened by including a statement that promotes information or research sharing within the NIH, with NIH's growing partners, and with the public. The framework is appropriately broad, but will require NIH to maintain a close awareness of how it overlaps with the missions of many federal health and science agencies. If this interdependence is embraced and multiple agencies engage together on the bigger picture, this could be an incredibly powerful catalyst for interdisciplinary discovery. The challenge of keeping up with strategic thinking across agencies would be an important example of NIH facing the same challenges nationally that researchers face with keeping up with everything that could possibly impact their domains.

Compatibility of the framework with the broad scope of the NIH mission

To achieve greater compatibility of the strategic plan framework with the broad scope of the NIH mission, the Medical Library Association and Association for Academic Health Sciences Libraries encourage NIH to expand funding opportunities for junior investigators across diverse settings. These are the innovators of today and tomorrow, and accessible funding will attract and keep those focused on research in the biomedical field. Strategies for measuring disease burden by those prioritizing NIH funding should be transparent to assure compatibility of this framework with the broad NIH mission. To ensure successful participation under the broader scope of the NIH mission, NIH should enable widespread access to core training in the responsible conduct of research and community-based participatory research for non-university entities. We encourage NIH to fund projects aimed at using

technology and user-centered design to improve the workflow of the research cycle, reduce administrative burden, and meet regulatory requirements. An evaluation of delays and reasons for no-cost extensions of NIH grants could reveal preventable or addressable issues that speed discovery. To further the broad scope of the NIH mission with less purchasing power, NIH could increase its intramural purchasing power and reduce the carbon footprint of its science program through strategic sourcing initiatives that create a workflow to order protocol supplies through the protocol tracking management system. Extramurally, NIH-funded Clinical and Translational Science Awards Consortium could seek similar economies of scale among members. The framework seems to require that NIH consider the overlapping missions of other federal health and science agencies, and identify synergies or areas of collaboration with a thought to reducing redundancies both within NIH and the federal government. Collaborating with knowledge professionals to enhance research stewardship would facilitate managing information and creating cross-agency resource awareness.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

In order for concepts in ICO strategic plans to be addressed more globally and uniformly, it is imperative to coordinate funding opportunities with other federal funders, as well as private funders. Targeting these funding opportunities to relevant researchers by mining researcher bio-sketches would ensure greater visibility and more compelling responses to funding opportunities. ICO concepts can be made more trans-disciplinary by developing a federal data directory or catalog that unifies all federally deposited data. This would make data more easily found, accessible and would allow data sets to be re-purposed, similar to how research studies are brought together through the systematic review process. To link concepts in ICO strategic plans with those that cut across disciplines, a crosswalk between PubMed Central and other public access data streams, as well as a place to publish and share negative results, is needed. Semantic linking of ICO concepts to those that are trans-NIH through Semantic Medline and other semantic tools can enrich the information ecosystem upon which excellent science is founded. Research that cuts across traditional disciplines will not find a funding home until concepts in ICO strategic plans are linked and leveraged for greater impact. Having a multi-disciplinary approach to traditional research increases the odds of break-through science. All of the strategies addressed above, coordinating and targeting funding opportunities, developing a federal data directory, linking concepts in ICO strategic plans with those that cut across disciplines, developing a crosswalk between PubMed Central and other public access data streams, semantic linking of concepts to enrich the information ecosystem are all the work of information professionals who are experts at knowledge management. Engaging trained knowledge workers as core team members at every level of the NIH strategic plan is critical for future success, and finding new cures in a cost cutting environment.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

As NIH advances fundamental sciences, it must apply advanced knowledge of dissemination research and implementation sciences to ensure findings have influence. Research on biomedical science knowledge sharing and uptake, including open science and electronic lab notebooks, and reproducibility of NIH-funded research should be a trans-NIH theme complementary to other agencies' focus on dissemination of clinical effectiveness research. NIH should be a thought leader in disseminating scientific knowledge and encouraging collaborations, adoption of methods, and re-use of data. Supporting training and conceptualizing career ladders for Masters-level data scientists, information professionals, and research support leadership may speed up the work of labs on this theme. Building on the importance of studying healthy individuals, NIH should support studying healthy groups and populations as entities to address broader health questions. NIH may need to encourage expansion of

group-level methodologies and data collection and analysis structures that increase our understanding of group contributions to health, as well as report these characteristics in NIH-funded data sets. Partnerships to advance treatment that involve industry whether for technological, scientific, or medical purposes must be transparent and cautious. Consumers and health professionals are sensitive to hidden agendas and profit margins. Maintaining public trust in NIH-funded research and in NIH as a source of sound ethical science is crucial to being able to engage individuals and communities in a shared pursuit of knowledge to improve health. Breaking down disease boundaries should address both co-morbidities that impact treatment decisions and outcomes, but also the growing cross-over among researchers studying related areas and populations where several conditions may occur. NIH should encourage matchmaking across extramural applicants, or among intramural and extramural researchers working with similar populations or on related conditions. Better visualization of trans-NIH data on research on certain problems in certain areas could address overburdening study populations and facilitate addressing gaps.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

All components of the Areas of Opportunity that Apply Across Biomedicine seem applicable to an NIH-wide Strategic Plan. However, the progress that can be made successfully over five-years in several of the areas seems dependent on whether those with whom the NIH-wide plan seeks to engage beyond NIH are ready for this strategic collaboration. It would be helpful to have a sense of how the plan will be calibrated for areas where NIH is clearly the leading partner as compared to areas where progress depends on a positive and energetic response by other organizations.

Future opportunities or emerging research needs

NIH has been a leader in promoting public access to research findings and improved data management and sharing. As other funding organizations implement new data and public access requirements, NIH can facilitate funders are communicating with each other and the systems and processes are easy to use and understand. Researchers should be able to focus their time and effort on their research. By supporting projects that develop or improve technologies and systems that assist in study management and discovery, such as improving the usability of ERA Commons, NIH Reporter, My NCBI, ClinicalTrials.gov, etc., NIH can save researcher time. Many opportunities could be leveraged and time and money saved with improvements in communication, transparency, and sharing of information within NIH, with NIH partners, and with the public. We encourage NIH to leverage the findings from the informationist supplements by emphasizing information organization, dissemination, and reproducibility as key research skills that should be present among the research team personnel being proposed for potential funding and considering specifically information management expertise in the environment in which research will be performed. Improved information management can reduce wasted time and money while advancing science more quickly. Furthermore, opportunities for improving information management within NIH should be explored. Finally, we encourage NIH to explore unique and innovative methods for funding, researching, and distributing research. NIH should partner with other federal agencies to fund projects that bring diverse thinkers from other disciplines together to consider new possibilities. New methods for applying and managing funding, which focus on supporting early-career researchers and projects that are risky in terms of definite or immediate outcomes, should be sought.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

With regards to physical activity, there is no greater "need" than to discover the most effective strategies to "reach the unreachable". The biomedical research establishing the benefits of regular physical activity, dose response, safety in special populations, etc. abounds. The "ground forces" are highly motivated and want to improve overall public health by getting the population at large moving. The fitness and recreation industry wants to engage more of the population to broaden its captive market. It is all good - but we continue to fail miserably, and consistently only "activate" 20%, or so, of the "inactives". If the NIH can place some focus on this particular area, and come up with some answers, there will be a groundswell of dedicated, inspiring professionals amongst the public ready to deliver and produce dramatic positive effects on the health and well-being of the U.S. population. Can we look forward to a "30 by 30" campaign (30% actives by 2030)???

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

There is a need for better coordination and collaboration across institutes. To give a small, but telling, example, the common data elements for NINDS family history module asks about over 20 different conditions, many not common, but omits alcohol dependence and substance dependence, which are quite common and have major impacts on most neurological diseases. This is not an isolated example. Substance use disorders have major impacts across nearly all diseases studied by NIH yet with the exception of institutes focused on them appear to be ignored.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity

that Apply Across Biomedicine

The impact of alcohol and other substance use disorders across the spectrum of diseases and treatments.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Since its creation, the National Institutes of Health have supported biomedical research that has led to innumerable successes in battling diseases affecting millions of Americans. At the root of this success are the individual researchers whose groundbreaking work has produced advances in understanding basic principles in molecular and cellular biology. The most important means of NIH support for these investigators comes in the form of investigator-initiated grants, the goal of which is to support a discrete, specified project to be performed by the investigator(s) in an area representing his/her interest and expertise. Recent history has demonstrated the benefits of attacking health-related issues at their core via basic research: Developments in treatments for cancer, diabetes and HIV/AIDS, for example, have been initiated at the bench. The NIH is the largest funder of biomedical research in the United States. Through its support of basic scientific research, the agency has helped decrease the nation's disease burden while expanding basic scientific knowledge, positioning the United States as an unrivaled, global scientific leader. The major emphasis on investigator-initiated research has been the driving force through which this outstanding record has been achieved. Recently, there has been a growth in NIH-mandated research initiatives, and an increase in Requests for Applications (RFAs) with NIH leadership directing scientific effort and resources to specific areas and diseases. In 1998, R01-equivalent grants comprised about 44% of the research portfolio. Today, that number is 35%. While being responsive to the needs of the taxpayer, the targeted research opportunities have come at the expense of curiosity-driven research. The NIH should find a balance between targeted, and non-targeted, investigator-initiated research that reflects the great success of investing in basic science.

Compatibility of the framework with the broad scope of the NIH mission

The framework adequately provides an outline of the broad scope of the NIH mission. However, it does not adequately portray the fundamental role that basic discovery research plays in the research continuum. In fact, a 2014 internal analysis of the National Institute of Neurological Disorders and Stroke performed by then-Director Story Landis found a trend away from basic research in the NINDS research portfolio. Many fear this trend is the norm across the 27 institutes that make up the NIH, as recent policies have increased emphasis on translation of basic research discoveries. The NIH must be proactive to ensure the basic research portfolio remains robustly funded to continue to provide knowledge and understanding of the underlying mechanisms of disease. This will provide the foundation upon which tomorrow's treatments and cures will be based. This is especially important because private industry has largely vacated the basic-research space leaving the NIH as the largest funder of basic biomedical research in the country.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-

NIH strategic plan

The NIH should play a leadership role in training the next generation of scientists. The ASBMB recently published an article in the Proceedings of the National Academy of Sciences, "Toward a sustainable biomedical research enterprise: Finding consensus and implementing recommendations" in which we identified specific steps to be taken to improve training. These recommendations include: • Institutions and federal agencies should increase compensation for postdoctoral scholars; • Institutions and federal agencies should seek to reduce graduate student and postdoc training periods; • Institutions and federal agencies should train students and postdocs for the breadth of careers available to them; • Institutions and federal agencies should shift support of trainees towards fellowships and training grants; and • Institutions and federal agencies should increase the use of staff scientists. We encourage the NIH to consider these recommendations, consult with the scientific community and develop implementable plans to be included in their strategic plan. Finally, the strategic plan should outline ways in which the biomedical workforce can be made more diverse.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

We feel that the themes have been adequately captured and have no additional themes to be added.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

Improvements in health invariably rely upon increased awareness of preventative measures and appropriate treatments, the implementation of which rely on effective communication from experts. Moreover, increased scrutiny of taxpayer-supported scientific research requires that federal agencies demonstrate a focus on, and commitment to, public engagement by researchers who receive government funding. This awareness aligns with a growing movement that has inspired the development of a number of outlets aimed at providing open accessibility of NIH-funded research (RePORTER, availability of journal pubs, etc.). The NIH should therefore support and encourage efforts, both internal and external, that imbue scientific researchers with the skills and ability to transmit their knowledge in a clear, effective manner to those outside of their area of expertise. Such an approach will strengthen and enhance professional development of trainees and senior researchers alike, and will aid recruitment of the next generation of researchers from across the socioeconomic spectrum by empowering scientists to share their passion with their families, friends and local communities. It will also serve as a pathway to increase public awareness of the importance and successes in the NIH mission.

Future opportunities or emerging research needs

Private industry plays a critical role in translating the basic research discoveries found at the NIH to commercially viable products to be used by patients in need across the globe. The pathways to these innovations, and to partnerships with the private sector, are often obscure and difficult for researchers to navigate. Steps should be taken to facilitate public-private partnerships that allow for the leveraging of resources available to publicly funded researchers and privately funded companies. Additionally, the NIH should take whatever steps necessary to decrease the regulatory burden on funded investigators.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

. . . supports the framework of the NIH-wide strategic plan but we would like to provide insight into some potential drawbacks/challenges and areas of consideration for the current framework. Specifically,

we believe that there should be a statement addressing prevention. In the current framework, mention is made of early detection, but there is not a statement explicitly stating or outlining prevention as an area of opportunity being applicable across biomedicine. One of the six established priorities in the National Quality Strategy is: "Promote the most effective prevention and treatment practices for the leading causes of mortality, starting with cardiovascular disease." The goal of rehabilitation nursing is to assist the individual with disability and chronic illness in the restoration and maintenance of maximal health which is accomplished through an individual's return to function and the prevention of complications or chronic illness. We also want to ensure that rehabilitation nursing is represented in research initiatives and that duplication is avoided in terms of the "cross cutting" themes proposed. . . . would also like to highlight that this section is focused on the disease only and often treatments for the disease have long-lasting effects, such as cancer treatment. We would encourage NIH to include a statement about addressing treatment-related effects.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The training mission of the NIH is critical in preparing the future biomedical research workforce. Concerns about the current training system have been raised in two recent reports. The NIH Biomedical Research Workforce Working Group Report included findings and recommendations to achieve a more vibrant workforce and to address concerns about the glut of trainees and the dearth of academic positions. Specific recommendations included capping the number of years that NIH would support graduate students and providing supplements to training grants to help prepare students for alternatives to academic careers, such as master's degrees geared toward an industry career. It also recommended shifting funding sources for graduate students from investigators grants to training grants and fellowships. In *Revisiting the STEM Workforce*, the National Science Board recognized the changing relationship between science education and careers as well as the need for skill retraining and renewal. It specifically mentioned newer business needs-oriented educational efforts like the Professional Science Master's (PSM) program that can provide a bridge between education and skills training. In *Enrollment and Degrees in Professional Science Master's Programs: 2013*, The Council of Graduate Schools reported that the number of underrepresented students earning degrees from PSM

programs between academic years 2009/10 and 2012/2013 increased 104% from 166 to 338. Suggestions: Innovations in science master's training, such as the PSM, should be supported by the NIH through a pilot program that would provide internships for PSM students and the opportunity for employment following degree completion. Such a pilot program would broaden the current focus beyond undergraduate and doctoral levels. It would specifically recognize and support the critical role of master's students in biomedical research as well as grants sponsored and laboratory technical positions. It may also help increase diversity in the U.S. biomedical research workforce.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

No response

Compatibility of the framework with the broad scope of the NIH mission

No response

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

The promotion of Public Health through a "One Health" approach should be included in the 5-year NIH-wide Strategic Plan. This may be included under the Unifying Principles section, or within another section of the framework. Human, animal, plant, and environmental health intersect, as seen with emerging infectious diseases, food production and safety challenges, and zoonotic disease prevention and control. Promotion of health and wellness is also impacted by the human-animal bond. Collaboration by professionals across sectors is essential to effectively address these complex issues and must occur at local, state, federal, and international levels to improve integrated understanding. These observations are echoed in letters recently sent to the White House from the . . . , seven Senators, . . . , and the One Health Commission. Links to these letters are provided in the attached word document. As noted in the Senators' letter the Centers for Disease Control and Prevention states that approximately 75% of all recently emerging infectious diseases are zoonotic in origin, including the ongoing Ebola virus outbreak. Also, environmental and agricultural determinants such as antimicrobial and chemical

exposures affect health. A One Health approach to public health directly aligns with NIH mission to enhance health, lengthen life, and reduce illness and disability, most directly through improved prevention and early detection of health threats. The . . . urges NIH to add this “One Health” principle into the Strategic Plan. Suggested language is provided below. Unifying Principles Supports a One Health Framework—NIH acknowledges the need for a One Health approach to Public Health, and fosters collaboration on the local, state, federal, and international levels in order to collectively address human, animal, plant, and environmental health issues.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

No response

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

No response

Future opportunities or emerging research needs

No response

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Contributions were collected from the membership of the. . . Comments fell into 4 categories: Approach, Quality Control, Funding Issues, and Studies to Focus on Healthy Individuals. (All comments are grouped together in this first response box.) APPROACH Investigate common mechanisms of injury across diseases, e.g. inflammation, to increase efficiency and validity of research. Basic science should include and expand upon human observational studies as a framework for non-human studies. Prevention should be added along with early detection and diagnosis. Implementation of scientific advances is often tricky for NIH, but who else will fund this last step? Will be important to find a way to accelerate translation of scientific advances into realm of public health and clinical practice. QUALITY CONTROL Critical to focus on rigor and reproducibility. The excessive drive to publish in high profile journals, at the expense of rigor and reproducibility, is a major impediment to progress and of great concern to many in the research community. FUNDING ISSUES Increase support for individual scientists throughout their careers, rather than for specific projects (similar to HHMI and the pilot RPA.) Allocate NINDS funding to support/continue to support Program Project Grants, which are studies with high impact. Increase RFAs and/or emphasis on translational grants that include BOTH proof-of-principle animal studies and early human studies (small scale prospective clinical studies or retrospective data/biosample analysis) STUDIES THAT FOCUS ON HEALTHY INDIVIDUAL Focus on health promotion and the study of "healthy" or "typical" individuals. Study not just healthy individuals, but those who are exceptionally resilient and vigorous, e.g. Ultracentenarians (individuals who have made better than expected recovery from brain and spinal cord injury, or exceptionally athletic and intellectually vigorous people)

Compatibility of the framework with the broad scope of the NIH mission

All of the above areas of focus are compatible with the broad scope stated in the RFI.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

There is a large benefit to reconsidering the framework for NIH and to the implementation of a new framework. The current Institute model and disease specific funding no longer fits the capability of scientific teams to move across disciplines. The challenge will be getting people to move outside their comfort zone. That includes people within and outside of NIH.

Compatibility of the framework with the broad scope of the NIH mission

The new framework will have many advantages for the NIH mission: 1) First, a cheer for a return to the support of basic science. Too often scientists must contort their project into something that they can imply has clinical implications. We all know that basic discoveries are paradigm shifting, and scientists studying fundamental and important biologic questions should be allowed to run free. We can blame the NIH "roadmap" for the situation where some study sections pass any application without human subjects. 2) Advance treatment and cures. If I understand this meaning, the concept is to advance research by breaking down disease specific barriers. Another cheer for this! With the current structure, funding exists primarily in Institute "silos" and is not interdisciplinary, despite the verbiage that interdisciplinary research is where it's at. The current NIH funding framework, via disease or organ specific institutes, works against the study of diseases that are trans-disciplinary and does not make sense. For example, if a scientist studies diabetic retinopathy, they may talk to program officers from NEI, NIDDK, and NHLBI, each of which has a very narrow scope; a project that spans the areas of interest of institutes is often in limbo, so the scientist must modify the Aims to "fit" the Institute. NIGMS is an exception that spans disciplines most of the time. But even at NIGMS, although you may be studying a process within their portfolio, if you stray too far into diabetes you need to go to NIDDK. The concept of Institutes is outmoded, and is similar to the outmoded concept of academic departments, which now have similar woes.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Enhanced scientific communication should be considered. NIH should encourage strategies that permit dynamic data sharing and interaction for scientists studying similar processes. Communication of

negative data, for example, needs to be encouraged and considered part of the scientific process. Conferences that result in knowledge synthesis would be valuable.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

The idea of breaking down traditional disease boundaries is critical. Please consider the field of wound healing and chronic wounds. This disease spans many disciplines, and progress is truly thwarted by the NIH structure. Recently I was involved in a center grant application on the topic of chronic wounds. NIAMS was interested, but only if the project did not stray too far into diabetes. NIDDK was interested, but only if the project focused on the disease as a diabetic complication. Heaven forbid you might bring in a vascular expert, because although this is a critical component of the disease, neither NIAMS nor NIDDK could deal with a project in that sphere as it would be out of their portfolio. How can we make progress if we cannot bring together experts studying diverse aspects of this problem? I am sure there are other disease states that suffer from similar issues.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

1. Promote Fundamental Science Comments: this is important research, while it may not be the major mission for the National Institutes of Health. NIH mission should be different from the mission of National Science Foundation. It should emphasize that NIH supports the basic science research, which is ONLY directly related to human health. It would be better to state what percentage of the NIH budget used for each of the 3 categories: e.g. ~10% of NIH budget goes to fundamental science, 90% of NIH budget supports "improve health promotion and disease prevention" and "advance treatments and cures."

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

1. Promote Fundamental Science Comments: this is important research, while it may not be the major mission for the National Institutes of Health. NIH mission should be different from the mission of National Science Foundation. It should emphasize that NIH supports the basic science research, which is ONLY directly related to human health. It would be better to state what percentage of the NIH budget used for each of the 3 categories: e.g. ~10% of NIH budget goes to fundamental science, 90% of NIH budget supports "improve health promotion and disease prevention" and "advance treatments and

cures.” 2. Advance Treatments and Cures Suggestions: It should state the role of pathological features in developing treatment and cures for human diseases or disorders. Developing the pathology-dependent treatment but not disease/disorder-dependent treatment. It would be better to add “Advances in understanding the pathological progression of given diseases/disorders”. It is very important for understanding the special features of each phase of the progression of the disease/disorder. This understanding provides the base/guideline for developing therapeutic strategies. It will offer a new direction for NIH to explore the new notion that same disease may be treated differently or have different therapies---in a phase pathology-dependent manner, and that different diseases may be treated with the same therapy or have the same treatment--as many diseases may share the same pathological features.

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

My vision for a democratic science is one in which public institutions of science – which are responsible for distributing limited, much-needed resources – identify, cultivate, and sustain historically marginalized, less powerful citizens in science. With the exception of Asians, racial minorities are underrepresented among those receiving advanced degrees in Science and Engineering (NCSES 2015), including Biomedicine (Ginther, Schaffer et al. 2009). And, Black and Asian grant applicants are less likely to receive NIH funding than their White peers, even after controlling for productivity, citations, education, and previous grants (Ginther et al. 2011). In light of this research, I propose that NIH: • Create (if it does not exist already) a mechanism for data collection and storage for the purposes of studying and understanding sources of racial discrepancies in NIH funding. Such a mechanism must have technological support as well as resources/permission/authority for finessing inevitable tensions that arise between the forthright study of peer review bias versus concerns about applicant and reviewer privacy (Chubin and Hackett 1990). • Because NIH “applications with good scores were more likely to be funded, regardless of race/ethnicity” (Ginther et al. 2011), we must work to understand disparities in funding outcomes by understanding disparities in scores. As such, it is critical for the aforementioned mechanism to record not only demographic data, but applicant scores, including scored review criteria, preliminary overall impact scores, and overall impact scores. • Get a start on such research by conducting studies proposed by prize-winning submissions to NIH’s Peer Review Challenge on New Methods to Detect Bias in Peer Review (NIH 2014). . . . • Publish the results of such research in a continued effort to increase the transparency of peer review at NIH (NIH 2009).

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

While we enthusiastically support the inclusion of a “Health Promotion/Disease Prevention” opportunity area in the Strategic Plan, the illustrative bullets cause us concern. The Strategic Plan should support a life course approach to prevention and the creation of long-term health. In addition, as recommended by the NRC and IOM in their Shorter Lives, Poorer Health report, we believe NIH “should commit to a coordinated portfolio of investigator-initiated and invited research devoted to understanding the factors responsible for the U.S. health disadvantage and potential solutions, including lessons that can be learned from other countries.” The plan must forthrightly address how the investment in NIH will ameliorate health disparities in the U.S. Such approaches do not fit well into any one NIH institute, which make their inclusion in an NIH-wide and trans-institute strategic plan most appropriate. Mechanisms to promote and fund such research need to be developed. The draft framework suggests that NIH will not provide sufficient emphasis to advancing translational research, which involves the clinical, prevention, implementation, and organization/systems sciences. Substantial research investments are required to advance the sophisticated research required to empirically evaluate the probability of success, costs, and value to society of translation at multiple levels of the health sciences continuum. NIH also should address its role in providing research findings to help policy makers determine how to best invest in health.

Compatibility of the framework with the broad scope of the NIH mission

The strategic plan must explain to the taxpayers --with some specificity-- how the NIH will advance the nation’s collective health and not solely advance scientific knowledge.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

NIH should place a strong emphasis on research regarding the broad range of social and environmental influences on population health, as well as on research to quantify and document how improvements in population health can lead to enhanced economic productivity and prosperity, while reducing demand on the health care system. We believe it is essential for NIH to address how it will support research on the health effects of environmental change as well as the impact of the environment on health more generally.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Potential benefits is that it would permit inclusion of such cross cutting public health relevant themes as climate change and global environmental change.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

NIEHS current strategic plan includes "Goal 5: Identify and respond to emerging environmental threats to human health, on both a local and global scale." This goal is cross cutting, particularly as relates to the need for research on global climate and global environmental change and health and should be included in this trans-NIH strategic plan.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Emerging research need includes global climate and global environmental change and health.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

The . . . is a global interprofessional health society dedicated to increasing awareness and research regarding the impacts of violence and abuse upon health across the lifespan. . . . seeks to improve the health and safety for all by assuring that prevention, identification and treatment for the health impacts of violence and abuse are incorporated into healthcare. Violence and abuse are major drivers of illness,

disability and premature death. The estimated total cost/burden of disease associated with violence and abuse is on par or greater than other major health problems like heart disease and cancer yet the research needed to help prevent, identify and treat the harms associated with violence and abuse is funded at pennies to the dollar compared to these other major health problems. This should be corrected. Despite the existing lack of funding, research findings have demonstrated what is asserted above. Please increase funding for research addressing all areas regarding the health impacts of violence and abuse. The IOM has published reports addressing some of these areas e.g. child maltreatment. Attached are three brief sections from the joint effort between the . . . and the National Health Collaborative on Violence and Abuse entitled “ACEs: Informing Best Practice.” The entire document can be found at: http://www. . . .health.org/aces_best_practices/aces-best-practices.html.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

The . . . is a global interprofessional health society dedicated to Violence and abuse are major drivers of illness, disability and premature death. The estimated total cost/burden of disease associated with violence and abuse is on par or greater than other major health problems like heart disease and cancer yet the research needed to help prevent, identify and treat the harms associated with violence and abuse is funded at pennies to the dollar compared to these other major health problems. This should be corrected. Despite the existing lack of funding, research findings have demonstrated what is asserted above. Please increase funding for research addressing all areas regarding the health impacts of violence and abuse. The IOM has published reports addressing some of these areas e.g. child maltreatment. Attached are three brief sections from the joint effort between the . . . and the National Health Collaborative on Violence and Abuse entitled “ACEs: Informing Best Practice.” The entire document can be found at: http://www. . . .health.org/aces_best_practices/aces-best-practices.html.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

In 2009 NIH Director Francis Collins initiated the Basic Behavioral and Social Science Opportunity Network (OppNet), expanding NIH’s funding of basic behavioral and social sciences research (b-BSSR). OppNet included all NIH Institutes and Centers for a five year Trans-NIH research program focused on understanding the fundamental processes underlying connections between health and behavior to improve health outcomes. By all accounts, including an NIH evaluation, OppNet was a great success. NIH officials thought the trans-NIH approach of OppNet to be an appropriate, strategic response, primarily because basic behavioral research is so relevant to understanding, preventing and treating a wide range of diseases and health conditions. OppNet became voluntary after five years. That resulted in a significant decrease in trans-institute behavioral research funding of the type that earlier led to so much excitement. Basic research funding in areas such as cognition, emotion, social behavior, perception,

behavioral genetics, behavioral and cognitive neuroscience, psychobiology, even methodology is now reduced. This means less understanding of the mechanisms and processes within and among individuals and groups that influence health. Results from earlier b-BSSR informed new approaches to ensure adherence, increase adoption of healthier practices, and reduce risky behaviors. Based on conclusions from multiple Surgeons General reports, the IOM and of course from NIH itself most major public health problems facing this nation have significant behavioral components – everything from heart disease, diabetes and cancer to addiction, teen pregnancy and violence involve significant behavioral elements in their etiology, treatment and prevention. Therefore, one trans-NIH research theme . . . feels is missing from the NIH Strategic Plan framework is basic behavioral research. APS encourages NIH to revitalize support of a robust trans-NIH program in order to maximize the contributions of basic behavioral science to human health.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

its trans-NIH strategic plan should promote lessened reliance on animal models in favor of using more human-relevant, non-animal alternatives; resources used on animal experimentation would pay much higher dividends in progressing human health if they were directed to more human-relevant research, as data extrapolated across species is highly unreliable due to differences between humans and animals; opportunities to move away from animal models have never been greater, as human cell lines, stem cells and tissues and computational models can provide effective non-animal alternatives; researchers would be eager to develop and use more human-focused and humane methodologies if challenged to do so; and more Americans than ever before oppose the use of animals in scientific research —50% according to the latest Pew survey.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an

NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The . . . commends the NIH for its focus on supporting advances in early diagnosis/detection of diseases, and urges you to consider allocating resources specifically to research on advances in early diagnosis for vestibular (inner ear balance) disorders. As our population ages we face a “silver tsunami.” Many programs focus on fall prevention but ignore possible vestibular causes which, if identified, can reduce or eliminate fall risk. Many vestibular patients remain undiagnosed for months or years, which results in lost productivity, loss of family income, increased medical expenses, and increased risk of falls, not to mention the emotional burden on patients and their families. We need to develop measures of disease burden, such as those mentioned above, and foster research into diagnostic tools that will help primary care providers identify and treat vestibular patients quickly and effectively.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

While Offices, such as the Office of Research on Women’s Health (ORWH), are nominally included in the NIH-wide strategic plan, it is highly likely that the Plan will be primarily based on input provided by the 27 Institutes. As such, strategic planning for diseases NOT within an Institute will be short-changed. Example is ME/CFS (Myalgic Encephalomyelitis/Chronic Fatigue Syndrome) which is currently housed within the ORWH even though 25% of patients are men. Although a Trans-NIH Working Group is appointed to consider this disease, membership has often fluctuated, preventing the development of expertise, and it is apparent that some members of the Working Group are not well-informed about the disease. Grant applications from respected researchers have been rejected with the comment that

ME/CFS is psychogenic in origin, even though research has been clearly showing for years that the disease is biological, not psychological. ME/CFS imposes a significant disease burden on more than one million Americans as documented by the recently released reports from NIH (Pathways to Prevention, <https://prevention.nih.gov/programs-events/pathways-to-prevention/workshops/me-cfs>) and the Institute of Medicine (<http://iom.nationalacademies.org/Reports/2015/ME-CFS.aspx>). This chart (based on CDC and research literature data) shows the disparity in research funding for ME/CFS compared with other diseases that affect similar number of patients and have a similar economic impact.

# patients	Economic impact	Research spending/yr	Research per patient
ME/CFS	836,000 - 2.5 million	\$17-24 billion	\$5 million
Multiple Sclerosis	250,000 - 350,000	\$15.2 billion	\$103 million
HIV/AIDS	1.2 million	\$345 million	\$36.4 billion (2002)
		\$3 billion	\$2,500

We ask that special care be taken to incorporate ME/CFS, in particular, fully into NIH's strategic planning. We further ask that ME/CFS be assigned to an Institute (NINDS) so that it can get the priority and funding it needs for the future.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Pemphigus and pemphigoid are two families of rare and potentially fatal autoimmune blistering diseases currently without FDA-approved therapies. The mission of . . . is to provide support to patients and doctors who contend with these diseases. Our patients voice frustration that very few professionals specialize in pemphigus or pemphigoid. Without physicians and scientists to promote discovery of disease mechanisms and treatments, our patients will continue to suffer. The . . . urges the NIH to continue support of pemphigus and pemphigoid research. In this harsh funding climate, very few physicians and/or scientists can maintain a research program dedicated to these diseases. Due to the small size of our research community, if we do not maintain a pipeline of senior, mid-career, and new investigators, the critical intellectual resources and research infrastructure will be lost. Although rare disease research is mentioned in the current NIH framework, several challenges persist. Proposals in pemphigus and pemphigoid suffer due to the rarity of disease and the lower number of patients that can be enrolled for therapeutic, mechanistic, or translational studies. Only a few weaknesses can make the difference between a funded and non-funded proposal. Additionally, flat-rate budget cuts at institutions disproportionately affect researchers with 1-2 grants versus those with more, as there are

fixed costs to running a laboratory. Graduated cuts based on total amount of federal funding would address this, as well as critical review of large lab operations with greater than three R01 equivalents or \$750,000 in direct costs. The preservation of our research community is the greatest threat to the advancement of science in pemphigus and pemphigoid. The . . . urges the NIH to maintain mechanisms that recognize the inherent challenges in rare disease research and to preserve funding for pemphigus and pemphigoid specific research.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Pemphigus and pemphigoid research continues to be an area of opportunity for the P/P community. There are more drugs in various stages of trial than any other time in recent history. There is interest in pemphigus and pemphigoid by drug developers; imagine the boost this research area would receive if alternative or opposing viewpoints received funding? Funding pemphigus and pemphigoid research in a new direction answers any hypothesis with valuable information. Either it works or it does not and funding could be directed in the area of promise. Currently, with rare disease patients scattered to all areas of the country, accessing expert pemphigus or pemphigoid physicians is sometimes not possible. This is why the . . . supports telemedicine and its use in the clinical trial process. Funding to evaluate this approach would allow investigators of rare disease treatments access to a larger population.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Its trans-NIH strategic plan should promote lessened reliance on animal models in favor of using more human-relevant, non-animal alternatives; Resources used on animal experimentation would pay much higher dividends in progressing human health if they were directed to more human-relevant research, as data extrapolated across species is highly unreliable due to differences between humans and animals.

Compatibility of the framework with the broad scope of the NIH mission

Opportunities to move away from animal models have never been greater, as human cell lines, stem cells and tissues and computational models can provide effective non-animal alternatives; Researchers would be eager to develop and use more human-focused and humane methodologies if challenged to do so.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-

NIH strategic plan

More Americans than ever before oppose the use of animals in scientific research —50% according to the latest Pew survey. The NIH needs to plan for a future focused on human-relevant models to best increase our chances of improving human health and well-being.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

With the threat of AHRQ and PCORI losing funding, it will be *CRITICAL* and *ESSENTIAL* to have NIH revisit its strategic plan and mission, particularly if one or both lose any of their funding. The health care system is failing and this has a critical impact on the US in so many ways - we must have health services, safety and comparative effectiveness at the core of any strategic plan. These should be synergistic and collaborative with other funding agencies.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

health services, safety and comparative effectiveness New technology assessment

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

I think it is critically important that basic science and translational science are considered equally important than the current trend. Without given equal weight to both, new and clinically relevant

research cannot be conducted. Short term goals sometime seem to outweigh the long term research strategy which has produced very effective translational and clinical products for healthcare. For example, work in Drosophila and C. Elegans has produced groundbreaking foundations for current translational research. I think placing equal weight on both during the current framework will yield better healthcare advances in the future.

Compatibility of the framework with the broad scope of the NIH mission

The future of the NIH and healthcare research depends on young scientists from high school, undergraduate, pre-doctorate, and post-doctorate levels. These programs are underfunded and some type of framework needs to be put in place to help foster the development of young scientists.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

The major factor limiting trans-NIH research themes is the requirement for multiple PIs to have joint publication history. This is a bit too cumbersome and at times limits the ability of an outstanding team to put together projects to create future endeavors for research.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

The need to develop young scientists with new fellowship programs. The need to revamp the R21 grants to include truly explorative projects with little preliminary data. The need revamp the review process to make sure reviewers are evaluating the quality of publications of the applicants rather than simply the number of publications.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

More research is needed on the biological and behavioral effects of violence, which has implications for health disparities and disease prevention.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

biological and behavioral effects of violence

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

biological and behavioral effects of violence

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Current system for funding research favors large, well-established laboratories and focuses on several popular fields or diseases. By doing so, smaller labs and investigators who study more specialized fields or rare diseases have difficulty competing and are often left without funding. It is difficult to accurately predict where the next big breakthrough will come from. NIH limits its potential by emphasizing certain, more common diseases (e.g., cancer, Alzheimer's). Nature is conservative, and many seemingly disparate diseases or conditions share common molecular pathways. NIH should invest more in truly innovative research, and give smaller labs that may have fresh ideas more of a chance to thrive.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

More funds are needed for wound healing research. This will be critical not just for an aging population, but for disaster management, which is likely to be a future necessity, and for military personnel involved in combat situations. Abnormal scarring has received very little attention from NIH, however the impact of scarring is enormous. Optimal functional outcomes after wounds or skin injuries depend on rapid wound closure and reduction of scarring, yet the NIH has funded shockingly few grants studying hypertrophic scarring or keloid disease. While these conditions may not be life-threatening, they significantly impact quality of life and ability to participate in activities of daily living. This field requires more funding to advance the science and enable development of effective therapeutic strategies.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The concept of enhancing stewardship has both positive and negative aspects. On the positive side, it is clearly critical for NIH to take an active role in trying to promote the development and retention of a

biomedical research force, as this has been a major concern due to the recent economic crises. Further, it is critical for NIH to take an active role in promoting scientific rigor and reproducibility. On the negative side, sometimes government oversight/rules can contribute to stagnation and a lack of initiative and flexibility. Thus, it will be critical to determine an optimal balance between these competing demands.

Compatibility of the framework with the broad scope of the NIH mission

The framework is broad enough that it clearly falls within the scope of the NIH mission.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

We did not identify additional concepts that should be included in the trans-NIH strategic plan, other than as described in the responses to the other questions. However, we would argue that some of the concepts from the proposed trans-NIH plan need to be more fully integrated into individual ICOs' strategic plans (such as the premise that advances in basic science are fundamental and need to be supported).

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

A missing theme is the idea that there are critical biological, psychological, and environmental factors that contribute to health conditions of interest to many different ICOs, but few NIH pathways that facilitate targeting general risk factors. The idea of breaking down of traditional disease boundaries is in line with this, but active institutional mechanisms are needed to foster it. This point subsumes, but goes beyond, the need to reduce ICO silo effects. The NIH Blueprint initiative has been helpful in this regard but has tended to focus on the early / more basic science phases of research, with opportunities being missed at a more translational level. Research that addresses environmental factors contributing to a range of health outcomes is often not considered for funding at individual institutes when they are aimed at mediating factors that are not yet at the level of specific health outcomes, leading to a lack of critical research on general risk factors. Also missing is reference to investment in Dissemination and Implementation (D&I) Science. It may be that by the concept of stewardship, NIH means supporting the training of future scientists at the undergraduate and graduate level. If not, it will be critical for NIH to foster training of skills necessary for science that cuts across ICOs, such as quantitative, critical thinking and dissemination skills. Further, to remain competitive in the attraction and retention of the world's brightest scientists, the NIH should accelerate its investment in the health science research infrastructure through the development of a workforce pipeline that promotes the involvement and integration of students early in their academic careers. The R13 mechanism has proven effective in at least one institute (NICHD) in promoting undergraduate engagement in health science through its support of undergraduate attendance at biennial meetings of the International Congress of Infant Studies.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

NONE

Future opportunities or emerging research needs

Another critical issue is that many of the health-related outcomes that the NIH wishes to enhance are either themselves primarily behavioral/psychological (e.g., mental illness, development / remediation of cognitive, emotional, and social skills) or mediated in part by behavior/psychological mechanisms (e.g.,

behavioral risk factors for stroke, cancer, heart disease, diabetes). As such, it needs to be clear that basic science needs to include basic behavioral and psychological sciences as well as basic genetic, molecular, and systems neuroscience. Fundamentally we will not be able to enhance many public health outcomes without addressing behavior, psychological mechanisms, and environment (physical, social, economic). Continued overemphasis on genetics and molecular/systems neuroscience will impede progress.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Two of the three areas of opportunity are directly tied to clinical missions. In the webinar I heard, the moderator stressed that translational research is also an important component of the first area of opportunity, so that would bring us to 3/3! Although I understand that this is the strategic plan framework for the NIHealth, the rising role of targeted research (as opposed to innovation and fundamental research) is getting critical. I fear that we will continue to lose talent and endanger the livelihoods of our future leaders in life science research if this continues.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

research related to aging

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Regarding Myalgic encephalomyelitis (often referred to as Chronic Fatigue Syndrome or ME/CFS) NIH must find ways to address diseases that cross Institute boundaries. ME/CFS has immunological and neurological components, yet it is not assigned to NINDS or NIAID. It is not covered by any strategic plan, nor does it benefit from dedicated funding by a responsible Institute. The goal "Breakdown of traditional disease boundaries" does not sufficiently address this problem.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

?resources used on animal experimentation would pay much higher dividends in progressing human health if they were directed to more human-relevant research, as data extrapolated across species is highly unreliable due to differences between humans and animals; ; ?researchers would be eager to develop and use more human-focused and humane methodologies if challenged to do so; and

Compatibility of the framework with the broad scope of the NIH mission

?more Americans than ever before oppose the use of animals in scientific research —50% according to the latest Pew survey.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

The NIH needs to plan for a future focused on human-relevant models to best increase our chances of improving human health and well-being. We hope that you will take advantage of this important opportunity to voice your concerns about the use of animals in biomedical research and that you will share this information with other animal advocates.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

?opportunities to move away from animal models have never been greater, as human cell lines, stem cells and tissues and computational models can provide effective non-animal alternatives

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

?its trans-NIH strategic plan should promote lessened reliance on animal models in favor of using more human-relevant, non-animal alternatives;

Future opportunities or emerging research needs

see above

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

more emphasis should be placed on the development and use of human-relevant, non-animal alternatives, and that less emphasis is directed on experiments involving non-human animals.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

There is great potential benefit to the concept of turning "enhancing stewardship of the research enterprise by recruiting and retaining an outstanding biomedical research workforce and enhancing workforce diversity" into a true trans-NIH unifying principle. Currently, the major efforts in this area are (with rare exception) borne by the TWD division of NIGMS. Every NIH program and study section should be engaged in meeting this charge in all of their programs, including R01 funding. The major challenge to achieving this is the current lack of any proposal review criteria related to "enhancing stewardship of the research enterprise by recruiting and retaining an outstanding biomedical research workforce and enhancing workforce diversity." It must be appreciated that workforce diversity is cultivated in the labs of individual P.I.'s who are competing for funding. The P.I.'s who are most productive in this regard never have their diversity efforts accrue to their benefit in NIH proposal review. But all labs are not equal in their efforts in this vein, and the NIH needs to retain in its funding portfolio those labs putting in strong effort to cultivate diversity. In summary, an NIH-wide funding mechanism is needed that places high value on outstanding science as well as outstanding efforts to dually utilize those projects to cultivate diversity in the US biomedical research workforce.

Compatibility of the framework with the broad scope of the NIH mission

This framework seems much more compatible with the broad scope of the NIH mission than the current one. This is particularly true of the concept that "enhancing stewardship of the research enterprise by recruiting and retaining an outstanding biomedical research workforce and enhancing workforce diversity" ought to be a true trans-NIH unifying principle for all of its many programs. My concern about the new framework is fiscal. This new vision seems to require reallocation of dollars. I suggest that these dollars can be reallocated via the following: 1. Capping F&A costs at 50% or even lower 2. Fixing P.I. compensation at a specific minimal level per project irrespective of base salary 3. Limiting P.I.'s to one

(or in extraordinary cases two) major NIH grants at any given time. Funding needs to be shifted away from institutional entitlements to exorbitant amounts of free money. These funds need to be shifted into activities that can clearly demonstrate how they help the NIH meet all components of this new strategic plan. If diversity is truly a part of this plan, then this absolutely requires expanding (and not contracting) the number of NIH funded labs at the diversity of research sites in the U.S. Furthermore, NIH study sections must be charged with strictly adhering to new review criteria that encompass the totality of the principles guiding the strategic plan.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

I am not able to comment authoritatively on this question. But I suspect one ought to look very carefully at the strategic plans of NIGMS. They seem to be leading the way on many of the concepts described here.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

The idea that breakthroughs in one field often come from unexpected directions (i.e. a completely different field) is indisputable, and certainly belongs in this strategic plan. Working against this emerging trend, however, is the sub-field specific structure of the NIH study sections. Each study section has its own collective agenda as to what topics are highest priorities within their sub-field. This makes it very difficult for an "outsider" with a new idea to cross over into a study section of a field that the P.I. does not yet belong to. Thus, I believe there is a need to liberate the study section review process from sub-field-specific agendas. Instead they should be organized to simply recognize outstanding science that meets the components of the new NIH strategic plan.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Preventing health harms from climate change should be included as a 4th bullet under the Improve Health Promotion and Disease Prevention priority. The Lancet Commission on Climate Change and Health, the 3rd U.S. National Climate Assessment, and the IPCC AR5 all make clear that, unless adequately addressed, climate change is likely to have a range of dramatic harmful impacts on human health and well-being in the US and around the world. In addition, as clearly noted in NCA3, these impacts will almost certainly exacerbate existing health disparities in the US and elsewhere, and as such,

this new priority will complement the currently proposed priority on implementing evidence-based approaches to reducing health disparities.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

-I am encouraged by and support the emphasis on the unpredictable nature of the basic research efforts. It is critical that investigator-initiated research into basic biological mechanisms in particular not be tied to predicted or putative impacts on a particular disease or even disease class. There is no better recent example of this than the recent discovery of CRISPR/Cas, from my own field of RNA structure and function. This phenomenon was first discovered simply as a neat thing that some bacteria did in order to protect themselves from their own pathogens, and then, after detailed and curiosity-driven investigation of what its components were and how they worked, proved to be a key to unlocking what may yet be a technological revolution. Nobody could have "sold" the "impact" of a grant to study CRISPR by claiming it would have the results it did.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

-In my experience, one of the great barriers to effective health treatments is the lack of comparative effectiveness data -- clinicians are often at sea about whether a new and more invasive, more inconvenient, or simply costlier (and yes, that matters, in a world of finite resources) treatment, which has been proven "effective" versus a placebo, actually holds any advantages over established protocols for which the risk profile is very well known. I am not unaware that this is a political minefield, but if health outcomes are what we are ultimately interested in then ignoring this aspect of patient care is a glaring lacuna in NIH's priorities. And quite frankly, shouldn't scientists of all people be going where the data says we should?

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The potential benefits of this strategic plan are only constrained by the drawback of limited funding. The challenge at hand to improving health and advancing treatments and cures, not only on a national level but on a truly global scale, is totally dependent on the resources we see fit to allocate to this most important endeavor because, “As we limit the span of uncertainty in the cause of death and illness and extend and enrich the span of life, we act in the highest ideal of government, in the service of the governed, and in the best tradition of public, private, and individual enterprise.” John E. Fogarty

Compatibility of the framework with the broad scope of the NIH mission

The framework is totally compatible with the NIH mission to enhance health, lengthen life and reduce illness and disability here and abroad.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

The concept that should be continued and increased is the sharing of information, advances and discoveries that enhance health and reduce illness with and by all ICOs.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Future opportunities are directly related to increased funding and that should be a priority.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

I would like to see more emphasis placed on the development and use of alternatives, and less emphasis on experiments involving animals. Using animals is extremely cruel, outdated, and unnecessary. There is absolutely no justification in this day and age for the continued use of animals in research and testing since widely available modern research techniques exist —such as computer modeling, medical

simulators, in vitro techniques, and tissue engineering—which are educationally superior, scientifically reliable, and humane. Animal testing is becoming a thing of the past. As a nation, we should be advancing science towards ethical and compassionate practices, not utilizing archaic means of the past.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

The fundamental contribution of regular physical activity and exercise to health, prevention and treatment of many diseases cannot be over emphasized. However, there is the misperception on the part of many reviewers of NIH projects that we already know as much as we need to about the benefits of exercise and therefore we do not need to fund more work in the exercise field. However, this could not be further from the truth. In fact, not only do we not know how exercise confers its benefits, but the benefits of exercise are so far reaching and cost-effective, that much more work needs to be done regarding exercise compliance, the interaction of exercise and drug therapy, and predictors of responders so that exercise therapy can be individualized or personalized.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Need more flexibility in substance abuse medical problem research. Focus should not be on HIV/AIDS. Need more on health problems of aging substance abusers. Lower extremity changes from injection drug use. Balance, gait, and falls. Need more on wounds and the effect of wounds on the individual.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

. . . urges the NIH to include nutrition research, an integrated and integrating discipline, as an “Area of Opportunity that Applies across Biomedicine” within the Strategic Plan. While . . . supports the value placed on basic science in the “Promote Fundamental Science” portion of the framework, . . . would like to see equal importance given to human nutrition research with clinical trials in the Strategic Plan. Nutrition research creates a unifying theme across multiple fields thereby promoting teamwork, collaboration, translation and technology-sharing. Crosscutting areas of nutrition research that NIH should highlight under “Improve Health Promotion and Disease Prevention” include nutrigenomics, the gut microbiome, and the concept of developmental programming. Developmental origins of disease influencing a person’s health throughout their life course have been shown to be molded by peri-conception conditions of the parents, oocyte environment, in utero conditions, and even infant/postpartum diet. Nutrition can cost-effectively prevent, treat, and mitigate disease, and therefore improve public health. . . . encourages NIH to maintain their existing focus on public-private partnerships and underserved individuals within the Strategic Plan, and promote the recruitment and support of a diverse and interdisciplinary research workforce throughout their training and early independent career. . . . looks forward to implementation details for the Strategic Plan, as well as the opportunity to provide comments on the draft Strategic Plan.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

. . . urges the NIH to include nutrition research, an integrated and integrating discipline, as an “Area of

Opportunity that Applies across Biomedicine” within the Strategic Plan. While . . . supports the value placed on basic science in the “Promote Fundamental Science” portion of the framework, . . . would like to see equal importance given to human nutrition research with clinical trials in the Strategic Plan. Nutrition research creates a unifying theme across multiple fields thereby promoting teamwork, collaboration, translation and technology-sharing. Crosscutting areas of nutrition research that NIH should highlight under “Improve Health Promotion and Disease Prevention” include nutrigenomics, the gut microbiome, and the concept of developmental programming. Developmental origins of disease influencing a person’s health throughout their life course have been shown to be molded by peri-conception conditions of the parents, oocyte environment, in utero conditions, and even infant/postpartum diet. Nutrition can cost-effectively prevent, treat, and mitigate disease, and therefore improve public health.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

. . . urges the NIH to include nutrition research, an integrated and integrating discipline, as an “Area of Opportunity that Applies across Biomedicine” within the Strategic Plan. While . . . supports the value placed on basic science in the “Promote Fundamental Science” portion of the framework, . . . would like to see equal importance given to human nutrition research with clinical trials in the Strategic Plan. Nutrition research creates a unifying theme across multiple fields thereby promoting teamwork, collaboration, translation and technology-sharing. Crosscutting areas of nutrition research that NIH should highlight under “Improve Health Promotion and Disease Prevention” include nutrigenomics, the gut microbiome, and the concept of developmental programming. Developmental origins of disease influencing a person’s health throughout their life course have been shown to be molded by peri-conception conditions of the parents, oocyte environment, in utero conditions, and even infant/postpartum diet. Nutrition can cost-effectively prevent, treat, and mitigate disease, and therefore improve public health.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

. . . urges the NIH to include nutrition research, an integrated and integrating discipline, as an “Area of Opportunity that Applies across Biomedicine” within the Strategic Plan. While . . . supports the value placed on basic science in the “Promote Fundamental Science” portion of the framework, . . . would like to see equal importance given to human nutrition research with clinical trials in the Strategic Plan. Nutrition research creates a unifying theme across multiple fields thereby promoting teamwork, collaboration, translation and technology-sharing. Crosscutting areas of nutrition research that NIH should highlight under “Improve Health Promotion and Disease Prevention” include nutrigenomics, the gut microbiome, and the concept of developmental programming. Developmental origins of disease influencing a person’s health throughout their life course have been shown to be molded by peri-conception conditions of the parents, oocyte environment, in utero conditions, and even infant/postpartum diet. Nutrition can cost-effectively prevent, treat, and mitigate disease, and therefore improve public health.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The drawbacks of the current framework of NIH are as follows: 1. If you keep doing the same thing you will get the same result! 2. Things cannot change and stay the same. (lack of innovation implementation and application of current whole systems information regarding human development!!) A profound lack of "connecting the dots" has held up a Science based framework for helping across the lifespan. Think I am wrong: look around at our culture and society and compare us with Finland, Norway, etc. 3. Old NIH funding could be likened to "Climate deniers" approach to the body of knowledge about Climate Change.....

Compatibility of the framework with the broad scope of the NIH mission

Begin with the end in mind! Work backwards. This is probably very incompatible with the "framework" of NIH. to really implement a visionary ...future leaning comprehensive framework you have to be willing to not "stay safe"...but to lead....and educate...educate...educate... cross pollination of disciplines and collaboration need to be encouraged and supported between Sciences and Social Sciences...

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

1. First things first: A National campaign of dialogue and education regarding the current state of emergency for our citizens, families, children etc....the connection between childhood, poverty, and adult mental health and the effect on people for their entire lives...this needs to come from the top down..from the White house..and every Governor in the country...we need a National Health and Healing day to promote a new paradigm for thinking about ourselves and one another.. We could do this!! The ship needs to be turned around, righted and put in the best direction for ourselves and our country... Lets get everyone who is connected with NIH across all disciplines to participate and co create this! Leading with the research that demonstrates the connection between childhood and Adult health!!

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Delivery of Community Centered Comprehensive Health care: our models don't work very well New Model anyone?? Maybe we need the Google folks or the IT brilliants to innovate for us.. the theme is: Can we get medicine and Mental health care out of the box and actually changing lives?? How?

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

More, More research on the first 3 years of a child's life from birth to 3 and to 6... The connection between our poor educational system and struggles for adults through out the life span The connection between neurobiology, epigenetics, and the increasing poverty level of our society

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Please promote lessened reliance on animal models in favor of using more human-relevant, non-animal alternatives; resources used on animal experimentation would pay much higher dividends in progressing human health if they were directed to more human-relevant research, as data extrapolated across species is highly unreliable due to differences between humans and animals; opportunities to move away from animal models have never been greater, as human cell lines, stem cells and tissues and computational models can provide effective non-animal alternatives; researchers would be eager to develop and use more human-focused and humane methodologies if challenged to do so; and more Americans than ever before oppose the use of animals in scientific research —50% according to the latest Pew survey. The NIH needs to plan for a future focused on human-relevant models to best increase our chances of improving human health and well-being.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

In the following areas I agree: increase support in clinical application of EB interventions to eliminate health disparities In particular: Advance treatments, cures or management of wounds in particular. With the increase amount of HTN, DM and aging population wounds are becoming a huge quality of life issue. We are not as yet prepared as a health care system to mange this issue.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Analyst ,Target Structural Substance variation

Compatibility of the framework with the broad scope of the NIH mission

inferential, Fungoides(poor) Prior library ,normal /Abnormal Heart , Blood, And Exome Sequence.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

development Diverse Sources To Intellectual Risks ,RESOURCEFUL STUDIES, PLANNING WIDE GENOME AREA, BIO-IMPACT results

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

resources supported in your Laboratory, Major Biomedical/ Bio- behavioral Science

Future opportunities or emerging research needs

paradigm from other supported Area, access technology, Sleep System(HLBS), Disorder

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

n behalf of the . . . , we are pleased to offer the following response to the NIH-wide strategic plan: We

support the heading “promote fundamental science” as currently written. Under the heading of “improve health promotion and disease prevention,” we believe it is important to acknowledge that part of health promotion is recovery from disease. While it is optimal if prevention prevents people from becoming ill, unfortunately, many people will develop disease, regardless of these efforts. Further, once a disease has been treated, this does not mean that a patient goes back to their pre-morbid state. For example, once a patient has been “cured” of sepsis or ARDS in the intensive care unit, the majority will end up having physical, mental or cognitive dysfunction for months or years after the need for inpatient medical care has finished. As such, we would advocate for expanding this section to include an additional bullet point that reads “Restoration of health following acute disease.” Under the heading of “advance treatments and cures,” we believe it is important to acknowledge that treatment and cures frequently occur as a result of collaboration of multiple disciplines across many levels of care. As an example, an outpatient with cancer who receives chemotherapy may become sick enough to be admitted to the hospital where their immunosuppression might make them vulnerable to development of sepsis. Depending upon disease severity, their care might involve specialists in oncology, cardiology, pulmonary, renal, infectious diseases, critical care, radiology, surgery, etc. Further, their care would cross the spectrum of outpatient, emergency room, inpatient ward, and intensive care unit. As such, we would advocate for expanding this section to include an additional bullet point that reads “Addressing illness across the continuum of care.”

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

These responses were developed . . . that seeks to i) expand awareness and promote support for research into the ubiquitous and diverse roles of Intrinsically Disordered Proteins (IDPs) in biological systems and ii) leverage this knowledge to therapeutically mitigate their roles in human diseases so as to improve human health. . . . Investigations of the 3D structures of folded proteins, yielding over 100,000 structures deposited in the Protein Data Bank, have revealed the molecular mechanisms of myriad biological processes and enabled the development of drugs. However, recent discoveries have shown that approximately one third of the Human Proteome consists of intrinsically disordered proteins (IDPs), or proteins that contain intrinsically disordered regions (IDRs), which do not adopt defined 3D structures. Importantly, this “missing” portion of the proteome cannot be studied using traditional methods of structural biology, creating a gap in molecular mechanistic knowledge regarding IDPs/IDRs and their critical functions in cellular regulation and assembly of sub-cellular structures. Consequently, by analogy to the concept of ‘Dark Matter’, we use the term ‘Dark Proteome’ to describe the large portion of the Proteome that is disordered and currently “unseen”. Importantly, alterations of the normal functions of IDPs/IDRs through diverse mechanisms are associated with numerous catastrophic human diseases, including neurodegenerative diseases (Parkinson’s disease, Alzheimer’s disease, ALS, and others), many different cancers, diabetes, cardiovascular diseases, and infectious diseases. The Dark Proteome offers unique, trans-NIH opportunities to target a spectrum of debilitating diseases.

Compatibility of the framework with the broad scope of the NIH mission

Not applicable.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Not applicable.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity

that Apply Across Biomedicine

IDPs/IDRs are now recognized to be ubiquitous and have important and diverse biological functions. Disordered proteins/regions are involved in functions such as cellular regulation and in mediating critical protein-protein and protein-DNA/RNA interactions—hence the concept of ‘functional disorder’. Beyond discrete functional assemblies, IDPs/IDRs drive the formation and functions of numerous complex cellular structures, including chromatin, membrane-less organelles and the nuclear pore complex. Strikingly, estimates indicate that 60-80% of proteins associated with, neurodegenerative disease, cancer, cardiovascular disease, and diabetes are IDPs or have IDRs. The societal impacts of these diseases are significant, and they underscore the importance of understanding the fundamental properties of IDPs and IDRs that underlie their involvement in disease. Innovative molecular methods, that leverage new technologies, must be developed to reveal the mechanisms of IDPs/IDRs and to relate them to their roles in biology and disease. The resulting knowledge, not attainable using conventional approaches, promises to yield advances in human health. We argue that a systematic effort, i) to develop methods and conceptual frameworks to understand the molecular mechanisms and cellular functions of IDPs/IDRs and ii) to identify drug targets and develop drugs against these targets to battle the illnesses associated with IDPs/IDRs, should be a top NIH priority. A trans-NIH research initiative focused on, i) elucidating the fundamental physical properties and mechanisms of IDPs/IDRs, ii) establishing relationships between these features and the associated biological functions, and iii) discovering the full extent of biological processes mediated by IDPs/IDRs within cellular systems, will create new knowledge that can be leveraged to extend healthy life and reduce illness and disability. The involvement of IDPs/IDRs in myriad biological processes and many different human diseases cuts across the scientific interests of the NIH enterprise and fundamental and disease-targeted studies into these currently poorly understood proteins offer opportunities for trans-NIH impact.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

Not applicable.

Future opportunities or emerging research needs

A trans-NIH initiative supporting research on IDPs/IDRs would cut across traditional disease boundaries and NIH Institutes and create unprecedented opportunities for treatment of several debilitating diseases, based on new knowledge and understanding of the basic properties, molecular interactions, and cellular functions of IDPs. 1. Basic science of IDPs/IDRs and other “invisible” protein states. Existing structural biology and biophysical methods must be adapted to understand the dynamic physical properties and interactions of IDPs/IDRs in their functional states. New technologies are emerging to characterize transiently populated “invisible” protein states that promote aggregation and disease. Innovative, multiscale computations have a significant role to play in uncovering ‘hidden’ molecular level interactions of IDPs/IDRs. 2. Establish relationships between the dynamic physical properties of IDPs/IDRs and their cellular functions. Existing methods must be applied, and new methods developed, to study the molecular features of IDPs/IDRs in their functional, cellular settings to understand the mechanisms through which disorder contributes to biological function. 3. Systems-level experimental and computational studies of protein disorder in health and disease. IDPs/IDRs interact with many functional partners and thus have diverse biological functions. Systems-level experimental data must be generated and mined computationally using innovative approaches to understand the broad roles of IDPs/IDRs in signaling networks in normal cells and how these are altered in disease. 4. Focused efforts, across various disease-associated NIH institutes, to leverage basic science advances at the molecular, cellular and systems levels to understand the roles of IDPs/IDRs in a wide range of human diseases and improve health outcomes. These efforts could be institute-centered but should be managed and

common themes integrated from a trans-NIH perspective. 5. IDP/IDR-targeted therapeutics. IDPs/IDRs represent novel drug targets and new drug discovery paradigms must be developed to overcome the challenges associated with their dynamic features and often novel functional mechanisms. Investment in this research area could have tremendous trans-NIH impact.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Overview . . . suggests NIH provide concrete examples of high-impact, biomedical research – perhaps in a table format – to illustrate the current status and meaningful opportunities. Dr. Richard Hodes’ presentation at the 2015 American Geriatrics Society Annual Meeting could serve as a model. In addition, we believe that purchasing power in NIH’s discussion on the “constraints confronting the community in the face of lost purchasing power,” not only needs to include inflation, but also physician salaries, especially those with serious debt burdens. Areas of Opportunity that Apply Across Biomedicine Under the category “Improve Health Promotion and Disease Prevention,” we encourage the specific inclusion of normal aging physiology as part of the “importance of studying health individuals.” Within the “Advance Treatments and Cures” category, . . . encourages adding 1) a longitudinal study of disease outcomes; 2) a study of multi-morbidity; and (3) bio-behavioral intervention clinical trials. Unifying Principles As part of “Setting NIH Priorities,” . . . believes NIH should emphasize the need for outcome measures that extend beyond surrogate measures (e.g., imaging of the thickness of an artery in a trial of a therapy of a lipid lowering drug). NIH should also emphasize the importance of universal health outcomes (e.g., symptom burden, function, and health related quality of life). Under “Enhancing Stewardship,” . . . suggests that NIH consider including a “pipeline” figure or table of programs that recruit and retain individuals to focus on a career in aging. It could begin with students (undergrad/graduate), move to post-docs, early career investigators, mid-career investigators, and conclude with senior level investigators. NIH could also highlight programs that enhance workforce diversity such as the Butler-Williams Scholars Program.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Under the “Promote Fundamental Science” section, . . . suggests NIH emphasize the idea that promoting data availability/data sharing generally leads to increased collaboration and productivity and should be encouraged.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Wound care is not a separate specialty, and is vastly under-represented in current funding priorities. Chronic wounds are not a single system issue, but incorporates the skin itself, vascular supply, biomechanics, neurologic concerns, nutrition, functional mobility, therapeutic modalities, psychology, public health, physiology, microbiology, biochemistry, cellular biology, and so much more. It has not fit into the Institute silos model easily.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

More focus on wound care as a cross-disciplinary field.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Wound care

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The ability to do double blind studies in wound patient remains too costly.

Compatibility of the framework with the broad scope of the NIH mission

Wound healing cross the continuum of healthcare and has become nothing short of the wild wild west in managing the problems. There need for endpoints for high cost products such as Pulse Lavage and VAC need to be determined.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Good data does not exist regarding topical wound care products and healing. The community is overwhelmed with products and it is only a guessing game as to what to use.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an

NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Need an increase in wound healing research. There is an urgent need to determine what the markers are to predict wound outcomes in patients with co-morbidities.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Cancer cells have an altered metabolism that suppresses efficient, aerobic mitochondrial energy in favor of more primitive and less efficient anaerobic glycolysis. It was once thought that this occurs because cancer cells outgrow their blood supply and adapt to low oxygen conditions. However, the same phenomenon occurs when there is adequate oxygen. The reason is the competition for the fuel that feeds the Krebs cycle inside mitochondria. Acetyl-coA, citrate, and glucose are diverted from the Krebs cycle to build new cells: lipids for cell membranes, nucleic acids for DNA, and amino acids for proteins. Instead of burning fuel, the cancer cell is programmed to build biomass for rapid growth. Uncontrolled cell growth is the main characteristic of cancers and this growth is fed by diverting fuel from mitochondria. The principle of tumor imaging with PET (positron emission tomography) is based on cancer's affinity for sugar. It was previously believed that this was because cancer cells merely had high metabolism, but it is really because cancer cells are in rapid building mode. Research in mitochondrial energy will lead to greater understanding of cancer cell metabolism. Apoptosis is programmed cell death and determines whether a cell will continue to live or die. Mitochondria are central to apoptosis, responding to protein signals in the cell, releasing apoptotic proteins, and triggering the death of the cell. Apoptosis research may lead to new discoveries about cancer, embryonic development, and tissue atrophy.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

FOCUS REQUIRED ON INCREASING RESEARCH IN THE DEVELOPMENT OF THERAPIES IN ADVANCED WOUND CARE THERAPIES WHICH ARE NON CYTO TOXIC

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The main thrust of my concerns is that NIH place much more emphasis on the development and use of human-relevant, non-animal alternatives, and that less emphasis is directed on experiments involving non-human animals. I am deeply opposed to the continued unthinking use of animals when other means would be as good or much better. Animal testing when unnecessary is inhumane and wrong and let us catch up to other first world science. My main points are below: - its trans-NIH strategic plan should promote lessened reliance on animal models in favor of using more human-relevant, non-animal alternatives; - resources used on animal experimentation would pay much higher dividends in progressing human health if they were directed to more human-relevant research, as data extrapolated across species is highly unreliable due to differences between humans and animals; - opportunities to move away from animal models have never been greater, as human cell lines, stem cells and tissues and computational models can provide effective non-animal alternatives; - researchers would be eager to develop and use more human-focused and humane methodologies if challenged to do so; and - more Americans than ever before oppose the use of animals in scientific research —50% according to the latest Pew survey.

Compatibility of the framework with the broad scope of the NIH mission

The main thrust of my concerns is that NIH place much more emphasis on the development and use of human-relevant, non-animal alternatives, and that less emphasis is directed on experiments involving non-human animals. I am deeply opposed to the continued unthinking use of animals when other means would be as good or much better. Animal testing when unnecessary is inhumane and wrong and let us catch up to other first world science. My main points are below: - its trans-NIH strategic plan should promote lessened reliance on animal models in favor of using more human-relevant, non-animal alternatives; - resources used on animal experimentation would pay much higher dividends in progressing human health if they were directed to more human-relevant research, as data extrapolated

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Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

PLEASE HAVE A HEART!!! PROTECT ALL OUR ANIMALS!!! Human models are more reliable and safer! Not to mention less horrific, traumatizing, painful and fatal to animals!!! Your trans-NIH strategic plan should promote lessened reliance on animal models in favor of using more human-relevant, non-animal alternatives; Resources used on animal experimentation would pay much higher dividends in progressing human health if they were directed to more human-relevant research, as data extrapolated across species is highly unreliable due to differences between humans and animals; Opportunities to move away from animal models have never been greater, as human cell lines, stem cells and tissues and computational models can provide effective non-animal alternatives; Researchers would be eager to develop and use more human-focused and humane methodologies if challenged to do so; and More Americans than ever before oppose the use of animals in scientific research —50% according to the latest Pew survey. The NIH needs to plan for a future focused on human-relevant models to best increase our chances of improving human health and well-being!!! Thank you!

Compatibility of the framework with the broad scope of the NIH mission

PLEASE Save our animals NOW not later!!!!

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The benefits of using non-animal models in research are endless: * Animal-based tests are questionable at best. Because animals are not human, test results cannot replicate that of humans. * Research modeling is scientific and proven. It is widely used by forward-thinking organizations. * There is the absence of suffering, physically and emotionally, by the animals. * It's the most cost-effective way to conduct research. With no animal-related expenditures, animal care or government reporting requirements, significant cost-savings are realized. * Reputations are improved for those organizations using non-animal research. This could mean more funding. * Best of all, there is no compromising of researchers' values in the inhumane use of animals. Bottom line: This is a win-win for everyone involved.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

I am a member of I don't know how many animal advocacy groups, international human rights groups, as well as NGO international aid groups. I care deeply about humans AND animals. I want to see animal-based models phased out completely and more human-relevant, non-animal-based models used in their stead. Despite all the good that has come out of animal-based scientific inquiry, it is, in my view, unethical and inhumane, and I am completely opposed to it. Please, please redouble your efforts to fund research into alternative, non-animal based models, substrates, and test specimens for NIH-funded medical research.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

I would like to encourage the NIH to include the study of intrinsically disordered proteins (IDPs) in the comprehensive trans-NIH research themes that apply across Biomedicine. IDPs have only become appreciated as major players in biological function within the last two decades. They had previously evaded description because of the inability of x-ray crystallography to capture their structures and because of their susceptibility to proteolysis. Since then it has become clear that ~30% of the human proteome contains long disordered regions, and that these are overrepresented in proteins associated with disease. This fact points to the functional importance of IDPs. They are major targets for posttranslational modification, they play scaffolding roles at the center of signaling networks, and function in signal integration. Importantly, IDPs play broad roles in the pathogenesis of neurodegenerative diseases, different types of cancers, diabetes and infectious diseases. Because molecular disease mechanisms will likely be broadly applicable, IDPs should be studied as a trans-NIH research theme. I thus propose molecular and cellular studies of IDP mechanisms to improve our understanding of normal IDP function in cells, and how this is altered in pathological states. New types of therapeutics that target IDPs should be a natural next development. The proof of principle that this strategy is promising has been provided recently. A trans-NIH initiative to study IDPs would help solve

many critical questions that currently inhibit new developments.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

I would like to ask that any research in the future be directed away from the use of animals and use more in vitro and non-animal means. I am concerned that some results from animal testing are not compatible with human problems being studied.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

increase wound healing funding

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

increase wound healing funding

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

increase wound healing funding

Future opportunities or emerging research needs

increase wound healing funding

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

I am concerned about "orphan" diseases falling through the cracks. My illness, ME/CFS, currently has no assigned institute home. ME/CFS has both neurological and immunological components. We are learning many illnesses cross boundaries as set up in body system - centric approaches. This needs to be addressed.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

This following is a quote from . . . I share her concerns and I could not say it better. "While I agree that burden of disease should not be the only factor in priority setting, it must play a more central role. NIH must do more than select 69 categories from the Global Burden of Disease study. It's a start, but in no way is it sufficient. For example, ME/CFS is a disabling disease that costs the US economy more than \$20 billion per year, but it was not included in the GBD study. No one has calculated a DALY figure for ME/CFS in the United States. And so, left to fall through the cracks, the burden of this disease is not considered in decision making. Furthermore, NIH must create more transparency in its funding decisions. Regardless of whether the 21st Century Cures act passes and mandates such transparency, NIH owes it to the ultimate source of its funding – the American people – to justify the enormous gap between the burden of a disease like ME/CFS and the paltry funding allocated to solving it. A disease like ME/CFS, which crosses multiple body systems, represents a tremendous opportunity for discovery. Unlocking the pathophysiology of this disease could have implications far beyond just ME/CFS. This is an area that could and should be prioritized, but instead it languishes without any focused attention. There are institutional obstacles to progress for diseases like ME/CFS, yet if those could be solved the opportunity to advance science and find treatments is enormous. If the strategic plan includes

“Research Spotlights” as proposed, then I submit that ME/CFS is a case study in opportunity and trans-NIH priorities.”

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Time after time, it has been shown that animal models are an inadequate substitute for humans. If you persist in using animals for research, testing, and education, please adhere to these principles: REDUCE the numbers of animals used; REFINE the methods and tests being used to produce high validity results with the minimum of animal subjects; REPLACE animals used in research and testing with alternatives, such as computer models, cells and tissues, and organs on a chip.]

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

The number of Americans who oppose the use of animals in scientific research has hit critical mass. Opportunities to move away from animal models have never been greater, as human cell lines, stem cells and tissues and computational models can provide effective non-animal alternatives. It's time to employ those alternatives.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Please include wound care specific funding. Specifically in regards to hospital acquired pressure ulcers. Upwards of 11 billion dollars a year is spent on hospital acquired pressure ulcers in the US. Research focusing on the correct identification, prevention, and treatment of these wounds is essential for improved patient outcomes and fiscal responsibility.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

There is new (CLINICAL) evidence showing that LOW frequency (<20 kHz), FDA SAFE and LOW intensity (<100 mW/cm²) ultrasound accelerates chronic wounds healing. These studies should be supported as they have a tremendous importance to reduce healthcare cost (venous ulcers (VU) alone affect over 600,000 patients and have an estimated total direct cost between \$3.5 and \$5.5 billion annually). Diabetic ulcers (DUs), which affect an estimated 15-25% of patients with diabetes. There is a misconception that this treatment is not novel - it is - the reviewers need to be educated; they link ultrasonically assisted wound healing with treatment performed at frequencies that are two orders of magnitude higher (1-3 MHz) and intensity levels that are WELL ABOVE the FDA levels. Wearable ultrasound applicators will be able to improve Quality of Life of patients, reduce cost of treatment and address the issue of chronic wound healing that is NOT solved today. There is no randomized study addressing this low frequency treatment - with proven efficacy the wearable applicators would

revolutionize the standard wound care and introduce new paradigm of patient treatment.

Compatibility of the framework with the broad scope of the NIH mission

The healing of chronic wounds is included in the mission statement of many Institutes,

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

The assessment of the mechanisms of action would permit personalized and customized treatment and would require interdisciplinary teams (engineering AND molecular biology)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Increase wound healing funding

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Please stop using animals for research. Move to alternatives.

Compatibility of the framework with the broad scope of the NIH mission

Please stop the torture of animals in research which is unnecessary now that alternatives are available.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Stop animal research.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Alternatives to animals in research.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

Use non animal alternatives.

Future opportunities or emerging research needs

Use non animal alternatives.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Wound Biomarker research, Biofilms and their relationship to wound degeneration and osteomyelitis,

Compatibility of the framework with the broad scope of the NIH mission

Biomarker and biofilm research would identify wounds in their natural progression to breakdown or healing and allow the practitioner to predict the effectiveness of wound therapies and avoid misuse of expensive advanced therapeutic measures.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Genetic transfer of bacterial resistance and methods of prevention. Topical antiseptics and antibiotics

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Cellular research on wound healing

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Funding for Wound healing Research

Compatibility of the framework with the broad scope of the NIH mission

High

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Wound healing research needs a really push when it comes to funding and I truly believe that there is an high need for quality research for new drug discoveries in wound healing

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Permanent auditory damage caused by noise can be reduced effectively only by omitting the principles of ISO 1999. A concept, based on facts, is available.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

•its trans-NIH strategic plan should promote lessened reliance on animal models in favor of using more

human-relevant, non-animal alternatives; •resources used on animal experimentation would pay much higher dividends in progressing human health if they were directed to more human-relevant research, as data extrapolated across species is highly unreliable due to differences between humans and animals; •opportunities to move away from animal models have never been greater, as human cell lines, stem cells and tissues and computational models can provide effective non-animal alternatives; •researchers would be eager to develop and use more human-focused and humane methodologies if challenged to do so; and •more Americans than ever before oppose the use of animals in scientific research —50% according to the latest Pew survey.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Focus on non-animal testing. Your strategic plan should promote lessened reliance on animal models in favor of using more human-relevant, non-animal alternatives. Resources used on animal experimentation would pay much higher dividends in progressing human health if they were directed to more human-relevant research, as data extrapolated across species is highly unreliable due to differences between humans and animals. Opportunities to move away from animal models have never been greater, as human cell lines, stem cells and tissues and computational models can provide effective non-animal alternatives. Researchers would be eager to develop and use more human-focused and humane methodologies if challenged to do so; and more Americans than ever before oppose the use of animals in scientific research —50% according to the latest Pew survey. Please stop testing on animals. They are all living and sentient beings.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework
opportunities to move away from animal models have never been greater, as human cell lines, stem cells and tissues and computational models can provide effective non-animal alternatives;

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework
Please inform me fully.

Compatibility of the framework with the broad scope of the NIH mission

Please inform me fully.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Please inform me fully.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity

that Apply Across Biomedicine

Please inform me fully.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

Please inform me fully.

Future opportunities or emerging research needs

Please inform me fully.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

This suggestion concerns the subject of reducing administrative burden within the Enhancing Stewardship topic area. The NIH should consider shifting as much as possible of the current application to be received on a JIT basis. I strongly believe that everything except for the Aims, Research Strategy, and Biosketches are unnecessary for the review process and could become JIT. This would substantially reduce the administrative burden on extramural scientists and their institutions for the vast majority of applications whose priority scores are not close to the payline. I would even allow the scientists to submit their applications directly to grants.gov without approval from their institutions, which would further reduce the administrative burden on all of us. The reduced administrative burden should also allow a reduction in the indirect cost rates, which would free up resources and thereby allow more grants to be funded. Because the reduced administrative burden on extramural scientists might result in increased numbers of submissions, it might be prudent to limit the number of submissions per PI. An attractive mechanism for this would be a yearly application limit of a reasonable number (perhaps 3) minus the number of the PI's current grants that have greater than 2 years of funding remaining. This would have the additional advantage of preferentially reducing applications from scientists that already have multiple funded projects and thereby free-up resources to allow funding of additional investigators.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

The NIH should consider funding substantially more R-grants without increasing total expenditures by reducing the time-period of funding of some RO1s, for example to 2 years. This would increase the number of grants that end each year and thereby allow substantially more new applications and renewals to be funded each year. Clearly some grants, such as large clinical trials, would not be appropriate for this but most basic science applications could easily be reduced in scope to

accommodate a shorter funding period. An attractive mechanism to achieve this would be to fund the applications with the best priority scores for the full 4-5 year period and then fund applications in a second tier of priority scores for the shorter period. This would have the additional benefit of reducing the arbitrary all-or-none problem in the current system where spectacular applications that just miss the payline receive zero funding (and are not even eligible for resubmission if they are A1s) while applications with very similar (statistically indistinguishable) priority scores receive full funding.

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

*trans-NIH strategic plan should promote lessened reliance on animal models in favor of using more human-relevant, non-animal alternatives *resources used on animal experimentation would pay much higher dividends in progressing human health if they were directed to more human-relevant research, as data extrapolated across species is highly unreliable due to differences between humans and animals

Compatibility of the framework with the broad scope of the NIH mission

*opportunities to move away from animal models have never been greater, as human cell lines, stem cells and tissues and computational models can provide effective non-animal alternatives

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

*researchers would be eager to develop and use more human-focused and humane methodologies if challenged to do so

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

*more Americans than ever before oppose the use of animals in scientific research —50% according to the latest Pew survey

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

Stop using animals in research, and start using more advanced models that don't use animals in experiments.

Future opportunities or emerging research needs

*more Americans than ever before oppose the use of animals in scientific research —50% according to the latest Pew survey

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Dear NIH, its trans-NIH strategic plan should promote lessened reliance on animal models in favor of using more human-relevant, non-animal alternatives; resources used on animal experimentation would pay much higher dividends in progressing human health if they were directed to more human-relevant research, as data extrapolated across species is highly unreliable due to differences between humans

and animals; opportunities to move away from animal models have never been greater, as human cell lines, stem cells and tissues and computational models can provide effective non-animal alternatives; researchers would be eager to develop and use more human-focused and humane methodologies if challenged to do so; and more Americans than ever before oppose the use of animals in scientific research —50% according to the latest Pew survey.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Americans are caught within a weltanschauung of humanism, which precludes ontological parity with other species. This type of metaphysical-ontological interface with other species does not promote long-term wellbeing of humans, and most definitely destroys other species at an alarming rate. The ones we don't annihilate, are often the ones we torture for information, which is all driven by capitalist greed. We need to take a NEW moral look at our research is not already pre-figured by current moral structures, for they are the very ones that preclude us from thinking in new ways. This means looking outside of the usual universities with ethics professional who engage in moral analysis of NIH research protocols. IN short, the deep assumptions of the whole system need to be reviewed. . . .

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

I am writing to urge you to devote more resources toward the development and use of human-relevant, non-animal alternatives for testing, and place less emphasis on experiments involving non-human animals. The opportunities for improving research through use of computational models, stem cells and tissues and other new technologies have never been greater. These promise much more relevant results than unethical testing on non-human animals so prevalent today.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity

that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

I am writing to urge you to devote more resources toward the development and use of human-relevant, non-animal alternatives for testing, and to place less emphasis on experiments involving non-human animals. The opportunities for improving research through use of computational models, stem cells and tissues and other new technologies have never been greater. These promise much more relevant results than testing on non-human animals so prevalent today.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

More emphasis must be placed on the development and use of human-relevant, non-animal alternatives, and less emphasis must be directed on experiments involving non-human animals. Please consider the following: •the trans-NIH strategic plan should promote lessened reliance on animal models in favor of using more human-relevant, non-animal alternatives; •resources used on animal experimentation would pay much higher dividends in progressing human health if they were directed to more human-relevant research, as data extrapolated across species is highly unreliable due to differences between humans and animals; •opportunities to move away from animal models have never been greater, as human cell lines, stem cells and tissues and computational models can provide effective non-animal alternatives; •researchers would be eager to develop and use more human-focused and humane methodologies if challenged to do so; and •more Americans than ever before oppose the use of animals in scientific research —50% according to the latest Pew survey.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Promote Fundamental Science Basic science is the foundation for progress Consequences of basic science discoveries are often unpredictable Advances in clinical research methodologies stimulate scientific progress Leaps in technology often catalyze major scientific advances Data science increases the impact and efficiency of research. Improve Health Promotion and Disease Prevention Importance of studying healthy individuals Advances in early diagnosis/detection Evidence-based interventions to eliminate health disparities Advance Treatments and Cures Unprecedented opportunities on the basis of molecular knowledge Breakdown of traditional disease boundaries Breakthroughs need partnerships and often come from unexpected directions

Compatibility of the framework with the broad scope of the NIH mission

Setting NIH Priorities – NIH sets priorities by incorporating measures of disease burden, understanding the need to foster scientific opportunity through nimble and adaptable methods, supporting opportunities presented by rare disease research, and considering the value of permanently eradicating a pandemic. Enhancing Stewardship – NIH enhances stewardship of the research enterprise by recruiting and retaining an outstanding biomedical research workforce, enhancing workforce diversity, encouraging innovation, optimizing approaches to guide how decisions are made, enhancing partnerships, promoting scientific rigor and reproducibility, reducing administrative burden, and employing risk management strategies in decision-making.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

its trans-NIH strategic plan should promote lessened reliance on animal models in favor of using more human-relevant, non-animal alternatives; resources used on animal experimentation would pay much higher dividends in progressing human health if they were directed to more human-relevant research, as data extrapolated across species is highly unreliable due to differences between humans and animals; opportunities to move away from animal models have never been greater, as human cell lines, stem cells and tissues and computational models can provide effective non-animal alternatives; researchers would be eager to develop and use more human-focused and humane methodologies if challenged to do so; and more Americans than ever before oppose the use of animals in scientific research —50% according to the latest Pew survey.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

At first blush, the framework appears to lack a clear commitment to implementation and distribution of new insights and technology to the ultimate users - physicians and the larger health care community. Personally, I believe that this has been a long-term, NIH-wide "blindspot" that has had the effect of causing important advances to languish in a few elite labs and medical centers without ever being fully translated to, and integrated with, the day-to-day workflow of health care providers nation-wide and world-wide. Although in recent years we have seen much lip service to "translational research" this has rarely encompassed a comprehensive understanding and approach to the broader problem of translating new discoveries and technology into devices, protocols, agents etc. that can be distributed widely to the health care community at large. Despite some small efforts such as the SBIR/STTR program, a focus on the problems and real research issues related to converting lab-developed technology into user-friendly, safe, economically viable products seems to have been implicitly left up to "the market". As a basic scientist who has attempted to address this issue through creation of a spin-off company, I have seen first hand how the oft quoted "bench to bedside" trail still has significant gaps that need to be bridged before industry is willing to assume the financial risk of commercializing any but the most lucrative of new technologies. This is a gap that NIH needs to address and it should be part of the new framework.

Compatibility of the framework with the broad scope of the NIH mission

With the addition of modifications suggested above, I believe that the framework would then truly meet NIH's mission to improve health care and the well-being of the US population because it would address ALL the problems encompassed by the "bench to bedside" philosophy.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

The comments above should apply to all ICO strategic plans and to NIH as a whole.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

See above

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

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Future opportunities or emerging research needs

NIH should identify target issues and create funding opportunities to motivate and focus research and development on late-stage translational problems that can prevent the dissemination and broad utilization of new discoveries and technologies that otherwise might not make it out of the lab.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Thank you for the opportunity to comment. I urge you to develop a trans-NIH strategy that relies less on animal models and more on human-relevant, non-animal alternatives. Please redirect resources used for animal experimentation to human-relevant research; data extrapolated across species is highly unreliable due to differences between humans and non-humans. Please stop using animal models and incorporate more general use of human cell lines, stem cells and tissues and computational models as non-animal alternatives. Please urge researchers to develop and use more human-focused, responsible methodologies.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

This strategic plan should promote lessened reliance on animal models in favor of using more human-relevant, non-animal alternatives. More Americans than ever before oppose the use of animals in scientific research, and opportunities to move away from animal models have never been greater. Human cell lines, stem cells and tissues and computational models can provide effective non-animal alternatives. Moreover, resources used on animal experimentation would pay much higher dividends in progressing human health if they were directed to more human-relevant research, as data extrapolated across species is highly unreliable due to differences between humans and animals. The NIH needs to plan for a future focused on human-relevant models to best increase our chances of improving human health and well-being. I hope that you will take advantage of this important opportunity to promote lessened reliance on animal models in biomedical research.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Please place more emphasis is placed on the development and use of human-relevant, non-animal alternatives, and that less emphasis is directed on experiments involving non-human animals. its trans-NIH strategic plan should promote lessened reliance on animal models in favor of using more human-relevant, non-animal alternatives; resources used on animal experimentation would pay much higher dividends in progressing human health if they were directed to more human-relevant research, as data extrapolated across species is highly unreliable due to differences between humans and animals; opportunities to move away from animal models have never been greater, as human cell lines, stem cells and tissues and computational models can provide effective non-animal alternatives; researchers would be eager to develop and use more human-focused and humane methodologies if challenged to do so; and more Americans than ever before oppose the use of animals in scientific research —50% according to the latest Pew survey.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

- its trans-NIH strategic plan should promote lessened reliance on animal models in favor of using more human-relevant, non-animal alternatives;
- resources used on animal experimentation would pay much higher dividends in progressing human health if they were directed to more human-relevant research, as data extrapolated across species is highly unreliable due to differences between humans and animals;
- opportunities to move away from animal models have never been greater, as human cell lines, stem cells and tissues and computational models can provide effective non-animal alternatives;
- researchers would be eager to develop and use more human-focused and humane methodologies if challenged to do so; and
- more Americans than ever before oppose the use of animals in scientific research —50% according to the latest Pew survey.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

There is a gross inadequacy of funding that goes to helping us prevent, identify and address social determinants of health like violence and abuse. The lack of funding research addressing violence and abuse has significant impact upon health.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

We applaud the proposed framework's acknowledgment that disease burden per capita is an "important" but should not be the "only" factor in determining NIH priorities. HIV affects young populations and, because of the chronic nature of the infection, those affected can have many decades requiring management of the infection and its long-term complications. Research investment also must follow and prioritize scientific opportunity that can have the greatest impact and contain and halt the spread of deadly life-threatening infectious diseases. Additionally, when it comes to infectious diseases, including HIV infection, the calculus of disease burden cannot be limited in scope to disease prevalence in the United States alone. Infectious diseases transcend our borders, and investment in containing and eradicating transmissible infections is critical to the public health and security of our nation. The recent Ebola outbreak and the rise of anti-microbial resistant strains of flu, gonorrhea and other communicable diseases underscore the potential for an infectious disease outbreak anywhere in the globe to present a threat to the United States. We also commend the framework's statement that the NIH prioritization process should consider the value of the potential of eradicating a costly and debilitating epidemic. NIH research is directly responsible for saving millions of lives through remarkable advances in HIV treatment and prevention, and is on the road to a cure and an HIV vaccine. Ending the HIV/AIDS epidemic would benefit tens of millions of people across the globe and strengthen U.S. global humanitarian and development interests.

Compatibility of the framework with the broad scope of the NIH mission

We appreciate the framework's mention of the importance of "evidence-based interventions to eliminate health disparities." As noted in the recently updated National HIV AIDS Strategy, HIV in the US disproportionately impacts Blacks and socially disadvantaged communities, and research must prioritize addressing those populations and their specific needs. Additional behavioral research is necessary to support implementation of interventions that can effectively reduce health disparities in key populations as well as social science-based research to address structural factors associated with HIV infection.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

The NIH Office of AIDS Research (OAR) coordinates the scientific, budgetary, legislative, and policy elements of NIH HIV research. The OAR, in its role as a planning and coordinating body, exemplifies the type of cross-cutting trans-NIH planning mechanism that could serve as a model for key NIH research priorities.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

We recommend that the framework more directly address NIH involvement in implementation research. Implementation science should be viewed as an integral component of the NIH's focus on translational research as it is critical to effectively translate discoveries into high-impact interventions through implementation of available biomedical prevention tools and treatment strategies. The framework notes the importance of breaking down traditional disease boundaries. HIV/AIDS research has exemplified the cross-cutting nature of research on specific diseases, fueling biomedical advances and breakthroughs that have yielded significant benefits far beyond the AIDS pandemic. AIDS research methods and findings have been used to study and treat other serious conditions, such as cancer, and hepatitis B and C virus. In basic science, AIDS research has paid extensive dividends to our understanding of many other areas including immunology, virology, microbiology, molecular biology, and genetics. AIDS research continues to lead to discoveries relevant to other infectious, malignant, neurologic, autoimmune, and metabolic diseases, as well as to the complex issues of aging and dementia.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Looking to the future, we also support and encourage an even stronger emphasis on the plan's inclusion of cross-NIH objectives to support a robust and diverse biomedical research workforce. We must cultivate, recruit, retain and incentivize new investigators, particularly minority investigators from populations that experience significant health disparities, to continue to advance the U.S. biomedical research enterprise.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

framework should consider revisiting the peer review system. Essentially it is largely broken for many reasons including a large no. of applications, inexperienced reviewers on occasions who have little knowledge of the field and do not understand the relative importance of different applications. The review process is often poor with critiques that are unfounded scientifically and clearly do not reflect the quality of the application. when scores get tight on founding reviewers are encouraged to spread the scores inappropriately. Priorities must be set so as not to destroy the future of the scientific enterprise. Currently it often takes several years between the time of funding and first application which means simply that the lab personnel can not be sustained. Bridge funding must be made possible on a more generous basis which engages home institutions. they must also contribute.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

gene therapy has reemerged as an important approach to medical therapy. why doesnt the NIH recognize this again with institutional grants. In many cases this is the only treatment option especially for important brain degenerative diseases. Partnerships with industry should be encouraged.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Emerging Research Opportunity on noncoding RNAs in biology and disease . . . With the advancement of next generation deep sequencing, it is now established that up to 90% of human genome is transcribed, and the majority of these transcripts are noncoding (nc) RNAs that do not encode proteins. ncRNAs can be classified as short ncRNAs such as microRNAs, long ncRNAs and other classic RNAs. The regulation and function of the majority of these ncRNAs, especially long ncRNAs, in development, regeneration, disease and evolution, are still largely underappreciated. Due to the abundancy of ncRNAs, ncRNA research represents an unprecedented need and opportunity in understanding the mechanism of biological processes, identifying new disease markers and therapeutic targets. Studying the mechanism

of ncRNA function will uncover additional layers of genome regulation, which could revolutionize our traditional view on life and biology. For example, our studies and others have found that some gene functions that were previously attributed by proteins may be actually attributed by ncRNAs, while ncRNAs that were previously thought to be noncoding may encode micropeptides. Without ncRNA study, the advancement of the novel mechanism of life and biology may not be adequate. On the other hand, the combination of ncRNA and genome-wide protein/DNA study, as well as the novel CRISPR technology, may facilitate a new wave of breakthroughs in biological research.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

These bullet points do not represent a cohesive plan designed to address the changing context of research funding in the United States. The plan does not include innovative approaches to addressing relatively flat NIH funding. Nor does the plan address how NIH will hasten the time from basic science discovery into practice that improves the health of the United States. The plan does not explicitly address how funding will help to achieve the triple aim of improved population health, care or reduced health care costs. The plan does not leverage emerging methods, PBRNs, big data, or use of electronic health records.

Compatibility of the framework with the broad scope of the NIH mission

The plan does not address the central problem of shortening the time between basic science discovery and incorporation into clinical practice. Specifically, the plan fails to address two critical constraints that hinder translation of scientific evidence into clinical practice. This represents a critical gap given the rapid shift towards value-based payment in health care. The first constraint results from too few pragmatic clinical trials that are designed to test efficacious interventions under ‘real world’ conditions. This undermines generalizability of findings during a critical time in health care. The second and larger constraint results from too little implementation research, i.e. the science of translating pragmatic evidence into clinical practice. The plan does not address how evidence-based interventions to eliminate health disparities will be implemented. Doing so successfully requires implementation research to ensure the approaches reduce (rather than amplify) health disparities. The NIH Strategic Plan needs to address both of these constraints. Ensuring sufficient pragmatic and implementation research requires dedicated funding, training for early investigators and current study sections in relevant methods, coordination with other federal agencies that currently fund similar research, e.g. AHRQ (D&I), CDC (both), PCORI (Pragmatic CER), the VA/DoD (both), and even CMMI (both). A viable plan ensures appropriate coordination of federal research agencies on how to address these twin constraints during an era of constrained budgets. The NIH plan needs a viable strategy for accelerating implementation of scientific evidence into practice. This requires not only support for implementation research (knowledge) but also incentives (motivation) for organizations to conduct implementation research and embed best practices into care.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

The NIH Strategic Plan neglects to improve accountability among major recipients of NIH funding, i.e. Academic Medical Centers (AMCs), for becoming genuine translational research leaders by example, i.e. in conducting implementation research within their own health care systems. Implementation research and integration of best scientific evidence into practice requires new paradigms for how research is conducted within AMCs (see AAMC-IOM Round Table on Value & Science Driven Health Care). This new research paradigm requires breaking down silos between research and operations, new incentives, new

training programs, and new funding streams. Funding requirements are needed to ensure accountability. Accountability for conducting implementation research within health care systems affiliated or owned by AMCs could be improved by explicitly linking large research awards, (e.g. Rs, Us, Ps, CTSAs, etc) to evidence that the institution is conducting meaningful research in this area. Incentives could be further ratcheted up by linking evidence of past implementation research to future indirect F&A costs.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

I have a power point I am putting together for critical thinking class. I have been involved for many year in CMHN, NIH, NIMH, SAMSHA, the WRAP grants, Peer Support Cert, inactive. It is a way to look at reform incorporating changing demographics, economic determinants, Wraparound initiative and whole health care. Will put any medically related in the hands of the client/team, reducing litigations, elimination loop holes, cracks and crevices. Incorporates collaborating, job creation, and future health and economics in demographic change that are inevitable. With ease of evaluation, research, and data information for studies, effectiveness, and efficiency. I look forward to hearing back from you if interested. It is approx. a 3 hour presentation of approx. 17 slides. Thank you for your consideration.

Compatibility of the framework with the broad scope of the NIH mission

Addresses them thoroughly.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

TBD

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

TBD

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework
(*Submitter left answer blank*)

Compatibility of the framework with the broad scope of the NIH mission
(*Submitter left answer blank*)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

The NIH has generally failed to prioritize research that focuses on social determinants of health. There is now strong evidence that violence and abuse, exposure to a substance abusing parent, etc have powerful adverse impact on one's health trajectory over the life course. Given this knowledge, it is imperative that NIH support studies that seek to identify and effectively respond to these issues.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

It is important to be explicit about supporting dissemination and implementation/translational research, and research in which academicians partner actively with communities.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan
(*Submitter left answer blank*)

Future opportunities or emerging research needs
(*Submitter left answer blank*)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework
The translation of novel technology to clinical practice remain difficult due to financial and regulatory hurdles. NIH should consider enhancing the support of collaboration between academic centers and industry to bring advances in diagnostic and treatment technologies to clinical practice.

Compatibility of the framework with the broad scope of the NIH mission
(*Submitter left answer blank*)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan
(*Submitter left answer blank*)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine
(*Submitter left answer blank*)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

The use of mobile digital devices and the internet to decentralize healthcare services from hospitals and clinics to individual home and work environment is a great opportunity that should be catalyzed.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The proposed ideas will broadly improve the health of Americans by improving NIH's cost efficiency and accelerating research, translation, and patient care. My ideas fall into the following broad categories: 1) improve health education of the American population 2) streamline and modernize NIH extramural peer review and granting programs 3) increase funded research innovation 4) increase the quality of NIH administration and intramural research

Compatibility of the framework with the broad scope of the NIH mission

All of these concepts align with the NIH mission

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

1) Increase and improve NIH educational outreach: a) current NIH efforts (institute websites, tweets, etc.) are not interesting to general population, especially young people, only interesting to scientists. b) internet/social media is a wealth of misinformation (anti-vax, anti-GMO, Ebola misinformation, etc), lives could be saved. c) I suggest an authentic public program to speak to general population that is interesting and entertaining to lay population (begin by using a charismatic individual cf. Neil Tyson Degrasse) d) avoid using government communications personnel, outsource media production. 2) Increase cost efficiency of extramural funding by: a) dramatically overhauling peer review and grant application programs (goal: provide applicant yes/no answer in 1 week, not several months, this is 2015. b) initiate dynamic database of "minuteman" peer reviewers c) publically recognize reviewers, they work hard for basically minimum wage reviewing grant applications 3) Accelerate biomedical innovation: a) provide more opportunities for small grants for out-of-the-box thinking (high risk high reward but more nimble than the Common Fund) b) increase funding for innovative businesses (for example, a new type of SBIR for established prolific biomedical inventors in industry) c) increase emphasis on innovation - increase NIBIB funding - NIBIB has by far most patents per grant dollar, but lowest grant dollars. d) Increase SBIR funding - ~\$7 million/R01 patent, but ~\$150K/R43 patent.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

4) Improve Efficiency and Accelerate NIH Intramural Administration and Research: a) Recruit external people more effectively, improve the HR system (hiring at NIH is hit and miss, hiring process is poor compared to industry). Make concerted effort to seek out and hire best people, use recruiters. Hiring high quality people makes a difference. b) Make it easier to fire or demote incompetent people c) Improve benefits that are aligned with the mission of NIH, for example, fitness, diet, and wellness. It is counterintuitive that corporations often offer employees free gym membership, but the National Institutes of Health has meager fitness/wellness benefits. There are only 1 or 2 little gyms on campus and the employees have to pay to use them. d) NIH could also initiate research studies on employee volunteers for new fitness/wellness/diet programs as a model for large corporations.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The framework's focus on developing both basic and clinical science, as well as the use of novel methodologies and technology is a strong aspect of this framework. Another strength is the focus on developing priorities that are based on measures of disease burden. Areas of potential consideration in framing the opportunities under improving health promotion and disease prevention include more attention to the issue of population health, and not just an individual-level focus. More attention to policy and macro-environmental influences, including institutional and system factors is needed. More attention to research on treatment dissemination and translation of findings into practice would also be valuable. Challenges to be considered are balancing "innovation" criterion used in grant reviews with continued use of well-established methods that may still lead to advances and new discoveries, and how innovation may be defined.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The . . . supports the framework for the NIH-wide strategic plan and applauds the efforts of the Advisory Committee to the Director. We firmly believe that maintaining a high-level non-disease specific strategic vision is the appropriate approach. There is a need for a broad array of research to improve health, and the areas of opportunity articulated in the framework appropriately include fundamental science, disease prevention and advancing health care. We are pleased that one of the areas of opportunity that apply across biomedicine includes an emphasis to support evidence-based interventions to eliminate

health disparities. While we are supportive of the plan we strongly encourage the Advisory Committee to recognize that while there is a need for basic mechanistic research, concomitant efforts to support interventional studies, behavioral and social science, public health research and population-based research also are needed. Ensuring a balance between basic, clinical and translational research across the NIH would ensure continued focus on fundamental discovery, but also underscore the need to push those discovery more aggressively into the translational pipeline.

Compatibility of the framework with the broad scope of the NIH mission

The proposed framework and unifying principles offer a sufficiently broad array of areas within which every ICO could create its own strategic decisions – the lack of emphasis on disease-specific themes is a strength and would underscore the need for team science and cross-ICO collaborations.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

While recruiting and retaining an outstanding biomedical research workforce is mentioned as one of the broad underlying principles, it would be important to single out the need for continued NIH investment in career development and training of future scientists. Having a greater number of flexible and innovative programs such as those made available by the BEST awards would be highly desirable. We also encourage a more robust dissemination plan to provide information to the public, medical and scientific communities and policymakers about research and interventions. Rapid communication of scientific discoveries through social medical groups of interest may speed the development of new science and public adoption.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

One theme that has not been captured in the areas of opportunity is maximizing community engagement in research through big data and other efforts to harvest information to advance biomedical research.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

. . . supports all of the components identified in the areas of opportunity that apply across biomedicine. However, we would like to point out that there is a lack of bioinformatics genetic analysis infrastructure at most research institutes and research intensive universities. With the whole genome analysis of subjects being obtainable at low cost there is an explosion of big genetic data and a limited supply of analysis centers.

Future opportunities or emerging research needs

Future opportunities or emerging research needs include: • Crowdsourcing science experiments such as #SciFund Challenge are opening the way for scientists to connect with and have support from the public. Having about a more science-savvy and engaged world benefits everyone – and may have a place even in the federal sector. • Health effects of pending climate change related to global warming.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The . . . agrees that the three proposed Areas of Opportunity provide a sound framework for pursuing the basic science that is fundamental to NIH's work. Promoting Fundamental Science will allow us to

explore the basic processes that underpin both health and disease over the entire lifecourse. Improving Health Promotion and Disease Prevention is critical to many aspects of maternal and child health, including all aspects of child development; fortunately, children are usually healthy, but further supporting healthy development is crucial to lifelong health. Advancing Treatment and Cures provides a broad umbrella for examining disease, starting with preconception and maternal health and through birth, childhood and beyond. The . . . urges NIH to embrace the unpredictability of basic science in expanding human knowledge and providing new avenues for exploration. We agree that advances in methodologies stimulate progress, because new methods offer previously unavailable insights. Leaps in technology are just one aspect of speeding up the pace of progress. Data science is increasingly influential in research, and NIH should dedicate significant attention to working with other parts of the government to design electronic health records that are also useful for research purposes. Another area that merits major attention is the division of efforts between intramural and extramural research. The . . . stands ready to offer our considerable research expertise in addressing these issues over the coming years.

Compatibility of the framework with the broad scope of the NIH mission

The . . . believes that proposed framework of the Strategic Plan is fully compatible with the broad scope of the NIH mission. We would note, however, that NIH should consider whether recent years have bred excessive multiplicity of silos among and within Institutes. Some degree of consolidation could provide the opportunity for increased interaction among different disciplines and better interactive research. The efficiency of the underlying support mechanisms within NIH is useful, but the establishment of guarantees of freedom for unorthodox approaches will be key to progress. Science is inherently inefficient, because it must by necessity explore many avenues that ultimately prove fruitless in the process of discovering those of utility. There cannot be guarantees of success without explicit tolerance of failure. NIH study sections have become increasingly risk-averse and the perceived consequence is approval of iterative proposals rather than bold approaches that may change fundamental understanding.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

The National Institute of Child Health and Human Development Scientific Vision: The Next Decade, issued in 2012, provides a critically valuable roadmap to pursuing excellence in maternal and child health. One key theme of that report that has great utility for the overall Strategic Plan is its emphasis on transdisciplinary science (“Conduct of Science”). The Vision document states that NIH must pursue, “both novel ways to remove current systemic structural obstacles to such research and enhanced rewards for its pursuit.” It then goes on to discuss the need for opportunities for transdisciplinary research to be created proactively and deliberately; the importance of fostering development of researchers because such work requires, “a different skill set, experiential background, and way of working”; the critical nature of partnerships with the private and nonprofit sectors; and the need for the transdisciplinary mindset to infuse the ways we “study, frame, and measure health outcomes” in maternal and child health. We urge you to incorporate these ideals and principles into the overall NIH Strategic Framework. Having just completed the establishment of a network of five transdisciplinary Prematurity Research Centers across the nation, the . . . is deeply interested in promulgating this model as a new approach to examining complex, multifactorial health conditions. We would be pleased to share our ongoing insights into the benefits and challenges of this work in hope of enabling NIH to pursue transdisciplinary models more rapidly. A key advantage of transdisciplinary research is a guarantee of freedom to explore the unlikely. In this situation, the traditional structures for grants and their administration can become obstacles to progress. We urge you to consider ways to foster

transdisciplinary approaches so that intelligent naiveté can offer novel insights. The structures of the ICOs, focusing on specific organ systems or stages of life, may restrict transdisciplinarity intramurally

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

The . . . believes that the Framework should explicitly embrace innovation and, within reason, both risk and tolerance of failure. Innovation may very well come from sectors outside those traditionally associated with NIH. NIH must be more nimble, less risk-averse, and less conservative while also being a responsible steward of taxpayer dollars. In this regard, the breakdown of traditional disease boundaries will be vitally important. Insights into a given disorder or condition may come from a completely different field. The . . . Prematurity Research Centers have, in just the few years since the first was established, already uncovered numerous promising new avenues of inquiry as a result of transdisciplinary collaboration. We urge the NIH to commit itself through the Framework to the pursuit of novel approaches like these. While orientation to diseases is a fundamental theme of the NIH and underpins much of its structure, it may be necessary to examine some diseases not directly, but in a retrograde manner. Given a rare disease, we need to discover what prevents the healthy majority from becoming ill. Given a common disease, studying the rare individuals who do not become ill may offer a clue to the cause. Once again, the division of research by disease or body part may prove an impediment rather than a useful organizing principle.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

The field of maternal and child health presents a virtually limitless array of future opportunities, partly because research on these populations has been pursued tentatively in the past, and somewhat more energetically only in recent years. For example, the fundamental biological processes involved in conception, pregnancy, parturition and postnatal recovery are very poorly understood. As a result, deviations in these processes, such as preterm labor, are almost complete mysteries. Without a basic understanding of the fundamentals, we are hampered badly in our attempts to prevent or treat these conditions. The . . . also foresees opportunities in many other areas of maternal and child health. Maternal immunization has the potential to reduce infant morbidity and mortality dramatically, both in the U.S. and around the world. Research into mental health could begin to address the terrible toll of disorders like maternal depression and addiction that persists through pregnancy. Non-communicable diseases have surpassed infectious diseases as the leading causes of morbidity and mortality for both women and children in many cases. It is our fervent hope that the Framework will provide a vision for addressing these and many other of the most pressing issues in human health.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Challenges - getting minority healthy adults to participate in the study. Eliminating health disparities or even reducing the number of disparate issues would be a step forward.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

- Importance of studying healthy individuals: COMMENTS As a volunteer participant (observational) in the Women's Health Initiative (WHI) research study, I tried multiple times to recruit family and friends to become participants. Not a single one agreed to participate because, and I quote, "I don't want to be a guinea pig in anybody's study." What plans do you have in place, or will have, prior to the recruitment phase, that will attract minorities who will participate? An appeal to African American churches might draw attention to the need for minority participation It would be prudent to show minority representation in all media releases as well as a statement of participant personal benefit to be derived. FYI publications distributed should contain language that is understandable to most under-served individuals.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

There is a significant problem in how we (biomedical researchers) and our research are perceived by the general public. This is primarily due to a lack of attention or skills in communicating complex scientific concepts to the layperson. Some focus on doing that well, to promote the public view of biomedical science, would be a significant benefit to the entire scientific community.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Expand funding opportunities for exploratory translational research beyond the current 2 year, R21, mechanism. All Institutes should offer grants that can be extended beyond the 2 year limit if the milestones are met. Translational neuroscience research is funded at two levels: the 2 year R21 and the large, get ready-for the clinic, P01. We need something in between to fund preclinical studies. Similarly, the BRAIN initiative is not funding small to medium size grants.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

It is well framed research plan. We need more work to be done. We are doing basic and clinic research for the past several decades but the outcome is increasing prevalence of obesity. We need to identify the risk in free living population. I want NIH to encourage National Health Survey at different population levels at different age groups to identify the risk and the issues behind the prevalence of obesity. Programs like physical activity in schools and its impact need focus. Hospitals, institutions need to encourage to involve in research. Public acceptance program research is more important than standardized studies because it is not acceptable in our day to day life. Agreed more research is required laboratory work on mechanisms and clinical trial but why failed to prevent the obesity?. We need success in our efforts. Encourage free living population studies, observational studies and impact of different nutrients on risk factors of obesity and we need prevention than cure/treatment.

Compatibility of the framework with the broad scope of the NIH mission

Encourage psycho social factors impact on the current broad scope of the NIH mission.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Involve industry, local and public health organizations for strategic plans but not their influence on research.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Need to encourage quantitative research than qualitative research. Include biotechnology in biomedicine research.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

It is a group work. Cross functional is more important for any success eventhough it is not applicable to NIH strategic plan. Group networking is important. I prefer to encourage multi center studies with different disciplines involved in research to be included in Biomedicine research.

Future opportunities or emerging research needs

Interventional research on different nutrients showing promising effects in basic research Free living population studies, epidemiological research, National Health Survey research Psychosocial and behavior responses in different population School health programs and surveys Impact of physical activity in schools, institutions and hospital as a part of their interventional program. Involve multidisciplinary research approach Cross functional network in research Media research is also important Consensus meeting to find research gaps

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

There is a major weakness in the proposed plan structure, in that it assumes that the Institutes cover all diseases in their own strategic plans. However, there are diseases like ME/CFS which have no assigned Institute home. Under the current framework, ME/CFS and other orphan diseases will be left to fall through the cracks. Instead, NIH must find ways to address diseases that cross Institute boundaries. ME/CFS has immunological and neurological components, yet it is not assigned to NINDS or NIAID. It is not covered by any strategic plan, nor does it benefit from dedicated funding by a responsible Institute. The goal "Breakdown of traditional disease boundaries" does not sufficiently address this problem. There is, of course, an ongoing role for body system/disease centric approaches. But NIH must grapple with the challenges of diseases which cross boundaries, and must either assign responsibility to existing institutes or create a new structure that can address the diseases that currently fall through the cracks.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

This strategic plan has allowed no room for the voices of patients. While FDA has sought to expand the role of patient voices in its decision making, and PCORI's mission is focused on patient views and preferences, NIH has taken no steps in this direction. This is NIH's loss. Patients and caregivers have

valuable information that can inform research design and priority setting. Even basic research can be improved and informed by including patients' views. Creating large cohorts of healthy and sick individuals, such as in the Precision Medicine Initiative is valuable, but it is not sufficient. Patients can contribute to hypothesis generation, selection of outcomes measures, and identification of treatment targets. NIH must come to terms with the role patients can play in biomedical research. Incorporating these views in a systematic way would strengthen NIH and its research, regardless of the disease or Institute involved.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

While I agree that burden of disease should not be the only factor in priority setting, it must play a more central role. NIH must do more than select 69 categories from the Global Burden of Disease study. It's a start, but in no way is it sufficient. For example, ME/CFS is a disabling disease that costs the US economy more than \$20 billion per year, but it was not included in the GBD study. No one has calculated a DALY figure for ME/CFS in the United States. And so, left to fall through the cracks, the burden of this disease is not considered in decision making. Furthermore, NIH must create more transparency in its funding decisions. Regardless of whether the 21st Century Cures act passes and mandates such transparency, NIH owes it to the ultimate source of its funding – the American people – to justify the enormous gap between the burden of a disease like ME/CFS and the paltry funding allocated to solving it. A disease like ME/CFS, which crosses multiple body systems, represents a tremendous opportunity for discovery. Unlocking the pathophysiology of this disease could have implications far beyond just ME/CFS. This is an area that could and should be prioritized, but instead it languishes without any focused attention. There are institutional obstacles to progress for diseases like ME/CFS, yet if those could be solved the opportunity to advance science and find treatments is enormous. If the strategic plan includes "Research Spotlights" as proposed, then I submit that ME/CFS is a case study in opportunity and trans-NIH priorities.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

"Promoting scientific rigor and reproducibility" is listed in the framework, but I think that's something that should receive greater emphasis and specific direction. A surprising amount of published data is not reproducible, which not only damages scientific credibility by the public, but misleads future research and wastes resources. Ultimately, journals and reviewers have the most power to combat this, but the NIH can do more to help as well. There are several specific things that I would like to see receive greater emphasis. 1) Double-blind data acquisition. This is a given in most clinical research but from what I have seen, applies to only a minority of basic research. Many experiments are performed by a single person from start to finish who is either partially or fully aware to which cohort each sample belongs. This could be improved by demanding a description of double-blinded methodology in grant applications wherever feasible, as well as leading by example for intramural projects and publications thereof. 2) Statistical education. When I was a graduate student not long ago, at a relatively prestigious institution, our formal training in statistics was minimal, and most was learned through mentors and colleagues or through self-teaching. Unfortunately, those mentors and colleagues were often incorrect about proper statistical methodology. This could be improved by having stronger minimal statistics education requirements among NIH-supported graduate programs, and possibly demand for more descriptive explanations of

statistical methods within grant applications. Another option would be to provide or recommend consulting statisticians to researchers at programs with limited resources. 3) Task force/focus group. I explained some of my ideas, but really I think this should be a major focus of the NIH, and a group of people dedicated to finding helpful strategies for dealing with the problem of irreproducible data would be well-worth the investment.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Please add language consistent with the translation and implementation of scientific discovery to Areas of Opportunity. It remains a major area in which we lag and threatens to reduce true, meaningful, applied scientific progress.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

As above.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

As above.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Creating funding mechanisms to extend traditional ones and test implementation strategies as opposed

to requiring stand-alone proposals to test implementation strategies. Community-based Participatory Research (CBPR)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

My greatest concern is the low percentage funding rate for NIH grant applications and the fact that this is 1) driving many good minds away from research and 2) eating up massive amounts of time for those who persist in applying and re-applying and trying and trying again, all potential time-wasting that could have been spent actually DOING USEFUL RESEARCH rather than TRYING TO OBTAIN FUNDING.

Compatibility of the framework with the broad scope of the NIH mission

These sorts of re-thinks of long-range goals and plans can be useful. But NIH needs to be willing to undertake some significant or even major changes. If the attitude is that we are the best right now so let's be very cautious about changing anything, then we will not succeed in "making the best better" (the 4-H club motto that I grew up with!).

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

I firmly believe that the number of grants per investigator or investigative team need to be limited, an easy way to simultaneously increase the number of scientists and groups each pursuing their own individual ideas. Yes, there are some things that need "big science", so let's give a few "big grants" for that kind of big science. More and more there are people who have the luxury of full-time for research, meaning also full-time for grant writing, who then become adept at the grantsmanship game and garner 3 - 6 or even more grants, R01s plus PPGs plus Center Grants plus R21s for their senior postdocs. Each researcher who has more than one grant ends up keeping that many other potentially good researchers and research ideas from ever being tested. It is my understanding that there is relatively compelling research showing that the "bang per buck" is greater for smaller labs than for larger labs. Even if that were not the case in terms of publications or other metrics, I believe the more minds working on science the better. Let's limit NIH funding to some much lower reasonable number, all sources combined; and not let big labs thwart this by having the lab leader write grants in the names of their junior scientists; and get lots more good minds pursuing their good ideas. After two grants, there should be some major hurdles to get any more, and some extremely strong justification, and some extremely compelling evidence that those extra grants are in fact advancing science better than the same money could be doing if spent in a different lab with different ideas and approaches.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Any sort of truly viable metrics that help NIH prioritize and determine where and when its funds are being spent wisely and efficiently. Is 6 grants to one lab truly better than one grant to 6 different labs? Is the lab with the largest number of papers really advancing science further than another lab with fewer papers but of greater importance? Were there really significant advances in the first 5 years of funding that justify another 5 years of renewal? Or is this just helping the rich get richer and keeping new ideas and other people out of the game? Opportunities are not only "on the basis of molecular knowledge", but also on the basis of new technologies that are not molecular per se; these include things like amazing new imaging modalities, instrumentation, techniques, materials science, computational and modeling. Molecular is for sure important, but it seems too limiting for such a global document.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

All seem relevant

Future opportunities or emerging research needs

Just last night I was contemplating whether much of the money spent on NIH-funded research might be better spent on more urgent and direct needs -- providing medical care for those who need, providing healthy meals to those who do not have them, providing pure water where it is not available, promoting safe behaviors, etc. Sure, a cure for a given cancer would be great, and would save some thousands of lives per year in the US. But providing basic needs to those without them might save many thousands more lives. OK, not in the NIH domain and mission perhaps. But I do feel VERY STRONGLY that DHSS and perhaps including NIH itself need to do much more to PROMOTE HEALTH and PREVENT DISEASE and not just keep looking for after-the-fact treatments.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

I think the three-part "Areas of Ppportunity" framework is great, particularly in its incorporation of fundamental research as a key component. However, I see a disconnect between this and the "Setting NIH Priorities" section. Here, three of these points focus on disease, while the other ("adaptability") doesn't provide strong motivation for giving fundamental research a prominent place in the prioritization scheme. I think it would be useful to think about ways in which the "Setting NIH Priorities" section could be revised to allow more explicitly for the support of research that is not focused on particular diseases, but instead emphasizes biological principles and mechanisms that operate in healthy systems.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

As it stands, the Framework provides a sensible starting point and is designed to complement the many

outstanding programs for research and training created by NIH's 27 Institutes, Centers, and Offices (ICOs). We are pleased that the NIH-wide plan does not intend to usurp the planning functions of the individual ICOs. On-going programs that support investigator-initiated research have been the principal driver for progress in the biomedical sciences, and we hope that new initiatives are not launched at the expense of these time-tested mechanisms. In these challenging times of constrained investment in research, it is important to consider the broader research context. The "Overview" discussion of the research landscape, including an analysis of "the constraints confronting the community in the face of lost purchasing power," is important. Progress in the biomedical sciences, and the application of this knowledge to the improvement of human health, demand that we address these issues, and we hope that this perspective guides the planning process.

Compatibility of the framework with the broad scope of the NIH mission

The . . . We appreciate the opportunity to provide comments and suggestions on the Framework for the NIH-wide strategic plan. With the opportunities for discovery and the demand for funds greatly outstripping the current research resources, priorities must be set carefully. We commend efforts to incorporate outside viewpoints in the strategic planning process. As it stands, the Framework provides a sensible starting point and is designed to complement the many outstanding programs for research and training created by NIH's 27 Institutes, Centers, and Offices (ICOs). We are pleased that the NIH-wide plan does not intend to usurp the planning functions of the individual ICOs. On-going programs that support investigator-initiated research have been the principal driver for progress in the biomedical sciences, and we hope that new initiatives are not launched at the expense of these time-tested mechanisms. In these challenging times of constrained investment in research, it is important to consider the broader research context. The "Overview" discussion of the research landscape, including an analysis of "the constraints confronting the community in the face of lost purchasing power," is important. Progress in the biomedical sciences, and the application of this knowledge to the improvement of human health, demand that we address these issues, and we hope that this perspective guides the planning process. The "Areas of Opportunity that Apply Across Biomedicine" listed in the Framework provide an appropriate guide for identifying trans-NIH themes. The topics listed reflect broadly accepted goals and complement the existing ICO programs and plans. We are pleased by the recognition of the value of fundamental science. We look forward to working closely with NIH as designs for specific initiatives are brought forward.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

None

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

None

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

None

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

In light of the claim for an overall socio-environmental communicational model for mental illness, the principles of the Scientific Method are necessarily employed: namely, (1) propose a hypothesis, (2) make predictions from that hypothesis, and (3) test the accuracy of the predictions within an experimental setting. According to Step (1), the major hypothesis has initially been established; namely, mental illness represents the transitional interplay of the double bind and counter double bind maneuvers in relation to the vices of excess within an all-encompassing socio-environmental context. According to this radical interpretation, mental illness represents a concerted effort to transition into the realm of excess, shown in the grand schematic depicted below. + + VICES OF EXCESS MENTAL ILLNESS (Excessive Virtue) (Transitional Excess) + MAJOR VIRTUES LESSER VIRTUES (Virtuous Mode) (Transitional Virtue) _____ 0 NEUTRALITY STATUS _____ – VICES OF DEFECT CRIMINALITY (Absence of Virtue) (Transitional Defect) – – HYPERVIOLENCE HYPERCRIMINALITY (Excessive Defect) (Transit. Hyperviolence) The extreme degree of exaggeration typically required to make the point ultimately accounts for the bizarre (and often highly emotional) nature of such a dysfunctional form of interaction. Indeed, as has long been surmised, mental illness represents a subconscious set of tactics aimed towards achieving a specific advantage within a given dysfunctional socio-environmental relationship. This preliminary interpretation is further compounded by the affiliated class of counter double bind maneuvers, along with the respective tendency towards verbal disqualification, such as characterizing the neuroses and schizophrenia. A chronic repetition of such agitated behavior is often observed, allowing such syndromes to be precisely classified over the course of treatment within a clinical setting. please see attachment-- also <http://www.communication-breakdown.net>

Compatibility of the framework with the broad scope of the NIH mission

Skipping ahead to Step (2), the predictions based upon this hypothesis necessarily invoke the formal communicational factors under consideration. Here, the 64-part grouping of schematic definitions collectively models the predicted classifications of mental illness: in particular, the reciprocating interplay of the double bind and counter double bind maneuvers. Jumping ahead to the remaining Step (3), these theoretical predictions are subsequently tested within a clinical environment, as stringently compared to a broad range of clinical observations of mentally ill patients. The logistics involved in conducting such an overall clinical study prove exceedingly daunting, compounded by the risks of introducing subliminal bias into the procedure. Indeed, despite what clinicians care to admit, clinical diagnosis is more of an art than a science, scarcely an entirely objective endeavor. An alternate accepted strategy involves consulting the established literature within the field, for the groundwork often has already been laid in pre-existing studies. A comprehensive survey of the relevant literature, indeed, has turned up a wealth of relevant research particularly suited to the task. In particular, German clinician Karl Leonhard's detailed terminology of the psychoses (in conjunction with terminology contained within the DSM-IV) makes for an extremely precise match with the specifics predicted for the transitional socio-environmental model of mental illness. This innovation conveniently makes use of preexisting systems of terminology, directly avoiding the introduction of new complements of terms into an already complex field. Furthermore, the majority of Karl Leonhard's observations were made in Germany before 1959 (the pre-pharmaceutical era), an established system of clinical observations that formally bypasses any risk of circular logic, issues directly affecting any study conducted within a more current time frame. please see attachment-- also <http://www.communication-breakdown.net>

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Leonhard's chief experimental paradigm referred primarily to inheritance patterns, as suggested in the title of his major work: *The Classification of Endogenous Psychoses* (where endogenous is defined as arising from within). This interpretation followed the traditional model of mental illness at that time; namely, physical syndromes that affect specific brain circuitry: as further associated with distinctive inheritance patterns. Here, Leonhard continues in a long line of German Classificationists, a pupil of neurologist Karl Kleist, who, in turn, was mentored by the renowned Carl Wernicke. According to such an established tradition, Leonhard's extensive interviews with the families of psychotics were chiefly conducted to identify the affiliated hereditary patterns leading to the occurrence of mental illness within the family. In his later years, Leonhard further broadened his focus to include psychosocial and socio-environmental factors, although this occurred long after his complex terminology (and supportive observations) were already firmly in place. In truth, Leonhard's elaborate system of observations are considered a masterpiece of insight and intuition in their own right, well placed to stand apart from any system of theory designed to explain them. Returning to the ongoing analysis, the most exciting aspect of this fortuitous correspondence in terms involves Leonhard's extensive clinical observations and case studies: providing a particularly tight correspondence with the 64 slots predicted for the transitional model of MI Narcissistic Personality ?..... Obsession Neurosis Confabulatory Euphoria ?..... Confab. Paraphrenia Enthusiastic Euphoria ?..... Proskinetik Catatonia Non-Participatory Euphoria ? Silly Hebephrenia Borderline Personality ? Phobia Neurosis Suspicious Depression ?..... Fantastic Paraphrenia Self-Torturing Depression ?..... Negativistic Catatonia Non-Participatory Depression ?..... Insipid Hebephrenia Dependent Personality ?..... Compulsion Neurosis Pure Mania Expansive Paraphrenia Unproductive Euphoria ? Parakinetic Catatonia Hypochondriacal Euphoria ? Eccentric Hebephrenia Avoidant Personality ?..... Anxiety Neurosis Pure Melancholy ? Incoherent Paraphrenia Harried Depression ? Affected Catatonia Hypochondriacal Depression?..... Autistic Hebephrenia please see attachment--for more details also <http://www.communication-breakdown.net>

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

In keeping with the modern emphasis on Information Technology, the AI computer is certainly destined to figure prominently in the mental health facility of the future. In particular, the potential AI implementation of the power schematic definitions for mental illness further predicts the prospects of a new class of AI mental health therapist: as outlined in US patents #6,587,846 and #7,236,963. Through such specific programming, the AI computer would potentially decode the bizarre symptomology of mental illness, ultimately emerging as the cornerstone for a broad number of expanded treatment options. The AI clinician would instantaneously be able to detect any ongoing patterns of dysfunctional communication, allowing for continuously updated diagnostic parameters. Equally definitive treatment options would surely follow, leading to a continuously modified therapeutic environment, effectively minimizing any major payback to the patient. The extraordinary computational speed predicted for such an AI therapist could potentially allow for moment-to-moment adjustments, a feat that would boggle the mind of even the most gifted human clinician. please see attachment—

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

N/A

Future opportunities or emerging research needs

This all-inclusive format appears eminently suited for consideration, representing a highly creative and completely original new psychological interpretation. It integrates the terminology of the virtues and values (Positive Psychology) employing the paradigm of Communication Theory (Counseling

Psychology). It further distinguishes the realm of criminality and hyperviolence (Forensic Psychology), as contrasted within an overall philosophical context (Value Ethics). This new system also proposes an underlying behavioral foundation for the entire system (instrumental conditioning), as well as significant technological applications with respect to recently granted US patents for ethical artificial intelligence. Indeed, this grand-scale integration with respect to the range of psychological disciplines leaves out very little of substance within the field, providing an overall theory of coherence across many fields with great potential impact for revolutionizing the field as a whole. Indeed, much research has typically gone towards the "disease" model of mental illness, with the current genetic - psychopharmacological models of susceptibilities dominating the research field. The current model of communicational factors is not mutually exclusive in terms of this standard picture, in turn, serving in a complementary role in relation to the overall puzzle of mental illness. please see attachment-- also <http://www.communication-breakdown.net>

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

I think the emphasis on Improving Health Promotion and Disease Prevention is very important and should be the key to the entire plan. Eliminating health disparities should include involvement of the communities and individuals at risk through community-based participatory research. Evidence-based interventions should focus not only on eliminating health disparities but on reaching the total population and should include not just individual level interventions but environmental and policy interventions as well as interventions at multi-levels of the socio-ecological model.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Dissemination and implementation research Community-based participatory research While reducing health disparities is extremely important and should definitely be a focus, interventions should not be only for the purpose of eliminating health disparities, but to prevent disease and promote health in the entire population and should focus not just on individuals but organizations, communities, environments and policies.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Dissemination and implementation research Community-based participatory research Multi-level interventions and interventions that reach not just individuals but organizations, communities, environments and policies.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Dissemination and implementation research Community-based participatory research

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

There is a fundamental contradiction between the "Areas of Opportunity" and the "Setting NIH Priorities" sections. The "Areas of Opportunity" section states, rightly, that "consequences of basic science discoveries are often unpredictable", and "breakthroughs need partnerships and often come from unexpected directions". However, the "Setting NIH Priorities" section focuses largely on identifying priorities by focusing on specific diseases ("measures of disease burden", "opportunities presented by rare disease research", and "the value of permanently eradicating a pandemic"). If "basic science is the foundation for progress" and advances often come from unexpected and unpredictable directions, then prioritizing funding based on immediate disease relevance is not likely to be helpful. (One example of many: microRNAs were discovered based on NIH-funded research on the timing of the formation of the *C. elegans* vulva throughout larval development. Where would funding this research have fallen if the priorities were as stated in the proposed framework?) This framework needs to better match the NIH priorities to the areas of opportunity identified. If basic science is prized for the ability to produce progress in unexpected directions, then an NIH priority must include supporting excellent basic science into fundamental biological mechanisms, regardless of immediate disease relevance.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

I fully agree that (1) Basic science is the foundation for progress, and (2) Consequences of basic science discoveries are often unpredictable. NIH should put more efforts on basic science. There was too much effort on translational research, which is not so fruitful. NIH should also focus on common mechanisms underlying the genesis and progression of neurological diseases. Dysregulation of immune system and glial activation could be common causes. We have made great progress in revealing neurocircuits in the brain. However, this knowledge is insufficient to develop new therapies, if we do not understand how immune system regulates neuronal functions in disease conditions. Given the complexity of disease mechanisms, we should consider poly-pharmacy to target both neuronal and neuronal mechanisms. Prevention of neurological diseases such as AD, PD, and chronic pain is as important as the treatment.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Partnerships, combining different models and/or approaches, are both efficient and effective

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Research for advances in technology ("High-Tech") has outpaced advances in research of behavioral medicine and particularly the integration of psychology with hands-on somatic medicine ("High-Touch"). New paradigms are needed for research areas that appear to be stuck possibly in part due to a lack of flexibility regarding the concepts underlying our understanding of disease processes. An example for

that is the lack of progress in finding better ways for treating low back pain, one of the most common conditions encountered in primary care. High-Tech medicine has not provided much insight into feasible treatment options for such a common medical condition.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

New ideas are often created outside of medical science, for example in the spreading practice of hands-on somatic psychology approaches (that is catching increasing attention from our patients), and await rigorous examination from science. Science itself may need to expand its conceptual framework to be able to discuss new paradigms.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Multi-disciplinary approaches, e.g. to managing chronic pain or PTSD, are provided by separate providers for pharmaceutical or technology-based approaches versus hands-on physical approaches (touch-based or exercise-based) and these again separate from psychology-based approaches. Opportunities for understanding an integrated phenomenology are missed. Outside of medicine, approaches are developed that attempt to integrate these disciplines in a way that appear to expand the underlying conceptual framework for pain. One reference attached.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

More Mitochondrial Research is Needed: In . . . book, "The Science of Fitness: Power, Performance, and Endurance" coauthored with . . . (Elsevier/Academic Press), we focus on mitochondrial biology as a unifying theme to explain human vitality, athletic power, nutrition, chemical toxicity, the aging process, and disease prevention. . . . is the best case study in mitochondria because he had the best metabolism of his era winning the Tour de France three times, but later was diagnosed with a mitochondrial myopathy due to lead poisoning from a shotgun injury, ending his racing career. Mitochondria multiply in response to physical training, but are also sensitive to an array of toxins including common medications. Mitochondria are thought to have a central role in PTSD (brain injury) and Gulf War syndrome (smoke toxicity). In my speech, I argued that mitochondrial biology is the latest branch of medicine, underlying many common and preventable diseases and that more fundamental research is desperately needed.

Compatibility of the framework with the broad scope of the NIH mission

Mitochondria are the major unifying principle in all of biology and medicine. Mitochondria supply 95% of cell energy by converting food and body fat (using oxygen) into the ATP energy that the heart, brain,

organs, and muscles can actually use. Mitochondria are 17 times more efficient than anaerobic glycolysis in generating energy. It is essential to have strong and numerous mitochondria to be healthy. Mitochondria are endosymbiotic residents in our cells with their own DNA related to ancient bacteria. Mitochondrial genetics are fascinating since mitochondria are inherited maternally and change slowly over the eons, allowing tracing of human migration, proving the Asia to the Americas land bridge and tracing the mitochondrial Eve back to Africa. In our current age of obesity (adults and children), type 2 diabetes, and metabolic syndrome, exercising to stimulate and multiply our mitochondria has never been more important. When people get fit and lose weight, all fat burning takes place inside of mitochondria. Mitochondria occupy up to 1/3 of the volume of cardiac tissue and therefore cardiac output and damage from heart attacks depends on viable mitochondria. Mitochondria power the brain and the latest theories about the causes of Alzheimer's disease and Parkinson's disease point to mitochondrial energy in brain cells. Mitochondria not only underlie these common diseases, but also many varied genetic disease of metabolism (often misdiagnosed in children). The latest theory of aging is called the Mitochondrial Theory of Aging based on free radical damage and mitochondrial DNA damage. Common mitochondrial toxins include: trans fats, certain antibiotics, and statins.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

NIH: Basic mitochondrial research and drug applications FDA: testing of current and new medications for mitochondrial toxicity DOD: mitochondrial explanations for human performance, PTSD, and Gulf War syndrome HHS: Prevention of obesity, type 2 diabetes, metabolic syndrome, and neurodegeneration by strengthening mitochondria SSA: Understanding the biology of aging with the Mitochondrial Theory of Aging. How to slow the aging process and prolong independence by maintaining muscle mass and mitochondrial mass. NASA: effects of microgravity on loss of muscle mass (typically 25% loss) and mitochondrial power (typically 50% loss) with implications in sedentary lifestyles on Earth.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Mitochondrial energy is often taken for granted, but there are many things that can go wrong with mitochondria: mitochondrial atrophy from inactivity, mitochondrial toxicity from common medications (for example statins block cholesterol and coenzyme Q10 synthesis in the same synthetic pathway), occupational exposure toxicity (heavy metals, pesticides, herbicides), negative effects of trans fats on mitochondrial membranes, malnutrition and vitamin deficiencies (common in low income diets with high calories but low nutrients). Since mitochondria are in all animals, research with standard lab animals is possible to study the myriad of enzymes which make up the Krebs's cycle and electron transport chain in mitochondria, which generate a proton battery of energy inside each mitochondrion. The most complicated enzyme in all of biology (ATP synthase) is powered by this mitochondrial proton battery as it churns out ATP energy.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

When I spoke before US Congress on April 16, 2015 at the Mitochondrial Caucus on behalf of the . . . , the other guest speaker a pioneering mitochondrial researcher, . . . , said that other countries such as Russia and China are way ahead of the USA in mitochondrial research. For example, . . . found a mitochondrial gene that explained why some Chinese soldiers function better at high altitude in Tibet. DOD and military applications could make better performing soldiers who would have more strength, endurance, and fatigue resistance. I am a radiologist and the organ toxicity of the iodine contrast and gadolinium contrast we use is now thought to be at the mitochondrial level.

Future opportunities or emerging research needs

I contend that mitochondrial biology is the latest branch of medicine, unifying the many fields of medicine and disease prevention by understanding and maximizing cell energetics. Evidence for my contention is that the US government recently made mitochondrial science the latest (41st) disease category for research funding. The problems we face now and in the near future are sedentary lifestyles, obesity, over medication, toxicity, loss of independence, an aging populace, and neurodegenerative disorders. All of these problems have mitochondria as their underlying fundamental cause...and cure. Thank you for your consideration, . . .

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

One drawback to the current framework is that it is very biologically driven and omits the behavioral aspects of disease, disease prevention, and disease treatment. This should be explicit and applies particularly to "Improve Health Promotion and Disease Prevention." Another drawback is a lack of any attention to replication. Given the current serious problems in clinical trials, promoting replication is key to true advances in treatments and cures. The NIH review system which requires innovation is currently biased against replication studies.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Behavioral aspects of disease, disease prevention, and disease treatment Replication studies

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Behavioral aspects of disease, disease prevention, and disease treatment Replication studies

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

I want to comment specifically on the question of funding for obesity research, which is currently very inadequate and could be addressed in these new initiatives. Although burden of disease is noted as one factor in setting priorities for NIH funding, the magnitude of obesity-related deaths (nearly 400,000 per year attributable to obesity) means that it should be one of the top-funded diseases and yet it is not. Compared to diseases like eg AIDS, funding for obesity is tiny in absolute terms, and yet it kills annually more than 300 times the number of people. Creating a fairer way to balance the competing interests of different diseases would result in a huge increase in obesity funding, which is desperately needed given

the enormous public health impact of this disease and the continuing increase in rates of obesity in all segments of the population.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Challenge 1: To achieve the goals of precision medicine, researchers, clinicians, and the pharmaceutical industry will need "population models" of mice, rats, and other model species. These models must have a realistic level of genetic complexity. Animal models must "grow up" and incorporate not only sex differences, but also differences in genetic background. Such "population models" exist for mice and rats (BXD family, Collaborative Cross, HXB family of rats). These cohorts incorporate millions of natural sequence variants. These cohorts can be used to test the limits of precision medicine. Challenge 2: We need better tools for synthesis of research data sets and to build more statistically sophisticated models of genome-phenome-and-environment. Current data are highly fragmented and hard to integrate other than at a high semantic level. It would be far far better to generate structurally coherent omics data sets for cohorts and populations. GTEx is one such example, but we need the equivalent for mouse and rat. The BXD family, the Collaborative Cross and the HXB rat cohorts are all great experimental infrastructure for long term collaborative research that can be integrated at the level of data. Challenge 3: We need resources that enable more efficient replication of data and results. Populations of isogenic and "immortal" strains and F1 hybrids of mice and rats are an excellent resource for the long term analysis of GeneXLaboratory and GeneXTreatment effects. The BXD family has now been used for over 40 years for this purpose. More investigators need to use these common resources.

Compatibility of the framework with the broad scope of the NIH mission

Precision medicine will remain a blunt tool until we have experimental populations of model organisms with the same level of complexity of humans, but with the added benefit of having many replicates per individual (isogenic "clones" of F1 hybrids and inbred strains). Many issues in precision medicine will benefit greatly from a "model population" resource rather than just a "model mouse". A unitary model mouse may be a great tool for testing gene function, but it is not necessarily a great tool for understanding disease process across many genotypes. The replication problem traces may often trace

back to the use of single genetic backgrounds.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Generation of more globally coherent population data sets. Framingham set the stage for human clinical work. We now also need Framingham for mice and rats (and perhaps even non-human primates). Ideally, each genome would be represented by many individuals (as is true for isogenic F1 hybrid mice and rats).

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Including "Advances in clinical research methodologies stimulate scientific progress" as a subcategory under "Promote Fundamental Science" is misplaced. Clinical research concerns the category "Advance Treatments and Cures", and by its very nature applies fundamental science discoveries to treat illness. It is harmful for basic research to have clinical research encroach on discovering the basic mechanisms underlying biological processes. Since funding could well be tied to categories on this framework, the inclusion of clinical research in fundamental science would necessarily reduce funding for true fundamental science, which already is being eroded by the increased emphasis on research tied to specific diseases. The "Advances in clinical research methodologies stimulate scientific progress" should be moved to "Advance Treatments and Cures" where it belongs.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Just as studying healthy individuals is important for Improving Health Promotion and Disease Prevention, studying and applying daily temporal dynamics in many biological parameters is important for Improving Health Promotion and Disease Prevention. Such temporal dynamics contribute dramatically to the production and severity of diseases from cancer to diabetes, as well as to the treatment and prevention of these diseases. This is certainly an overarching theme that applies to all of the areas listed in the framework, and should be listed as such.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Just as studying healthy individuals is important for Improving Health Promotion and Disease

Prevention, studying and applying daily temporal dynamics in many biological parameters is important for Improving Health Promotion and Disease Prevention. Such temporal dynamics contribute dramatically to the production and severity of diseases from cancer to diabetes, as well as to the treatment and prevention of these diseases. This is certainly an overarching theme that applies to all of the areas listed in the framework, and should be listed as such.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

With the emergence of efficient genome editing technologies, non-model organisms should be used to study the molecular and genetic basis of biological processes. Deriving basic biological principles using genetically and anatomically complex systems such as mice is daunting, whereas less-complex model systems that have phenotypic and reproductive advantages for studying biological processes should be promoted.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

1. Engaging public and advocacy groups in disease research. Define, incentivize individual partnership opportunities in disease research programs, clarify entry points and enrollment into gene mutation-specific databases to accelerate progress in phenotyping human gene variants. 2. Facilitate gene data sharing from clinical diagnostic platforms and commercial enterprises to public platforms. Make all gene testing paid by public dollars publically accessible. 3. Engage pharma in discussions on priority research areas involving biomarker development.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

Plans to capture massive amounts of individual biometric data from individuals with diagnosed disorders to validate drug response. At present, most patient outcomes are evaluated subjectively by physicians and not analyzed as a group. Electronic medical record allows mini Phase 3 trials to be widely performed even within a single practice group, but when combined, outcomes can be efficiently analyzed in much larger cohorts at lower cost. Partnerships with pharma to build these platforms.

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

It is important to consider and include the diverse populations on our United States in our evaluation and development of solutions to current health issues. Chronic diseases are greatly influenced by behavioral patterns. These patterns are developed by the unique social, historical, and cultural context in our diverse communities in which we live, work, and play. Further, the indigenous Peoples of the Nation have unequal burdens of health that require special consideration.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Integration of the social sciences, with the biological sciences. The inclusion of business strategies and commercial partnerships for dissemination of evidence-based solutions needs to be encouraged and promoted.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Methods of dissemination of programs and practices that accelerate and embed new approaches.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Please include a media campaign to restaurants owners indicating that the number of people seeking gluten free meals will be increasing as more people are diagnosed. Indicate that there are apps (Find Gluten Free - GF) that people use to go through their life. People go to restaurants where they can eat gluten free. It is important to have research & diagnosing people as a strategic plan, however, the people that are newly diagnosed struggle to adjust. Please help us and the large number of people to follow be able to adapt more easily by helping eating establishments clearly understand that it is in the best interest of their "bottom line" for them to become gluten friendly. Please help them understand that a large group of people may decide to eat at their place of business, if they offer gluten free, out of consideration of one person's eating restrictions.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-

NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Under the category of recruiting and retaining an outstanding biomedical research workforce (a unifying principle), consider adding a trans-NIH training platform for future physician scientists. The current T35 structure is institute-specific and institute-constrained. Most medical students do not have an interest in one specific area of biomedical research. AN NIH-wide T35 mechanism would permit students to participate in a short-term research training program with the best and most appropriate mentor, independent of the funding institute. This platform would go a long way in stimulating interest in research in our "not-yet differentiated" medical student population. The NIH needs to make every effort to replace our dwindling population of physician scientists.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Infectious disease prevalence, in particular those (many) that are assisted in transmission by a vector or (other species) intermediate host, is extending into new geographic areas as a consequence of climate changes. Such diseases are 'moving targets' and will require persistence (into the extended future) of research to mediate their negative health effects. This group includes several parasitic diseases.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

fine overall framework - would add per below

Compatibility of the framework with the broad scope of the NIH mission

Excellent

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

I believe that specifically recognizing the crosscutting opportunity in imaging science in addition to molecular frameworks would serve the strategic plan well. The area is a bridge between clinical medicine, disease processes and physiology (normal and abnormal) and much like molecular information increasingly creates the data driven interpretations for treatment and prevention.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Fundamental algorithmic decision support based on multiparametric data sources including molecular, genomic, imaging, clinical information

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

all applicable

Future opportunities or emerging research needs

per above

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The overview appears fine, but success will be the details. For example, under Enhancing Stewardship it states "Recruit/retain outstanding research workforce." As detailed in the attached published article, there is inadequate supply of skilled clinical researchers. Medical schools, residencies and clinical fellowships are doing an inadequate job in training clinical researchers. The time that academic faculty have to learn and conduct clinical research has been cut in half in the last 2 decades. Based on the increasing emphasis that medical universities place on patient service income, the situation is unlikely to improve and will probably worsen. This is not a problem that the NIH can solve on its own, but it can be part of the solution by focusing more resources on training the next generation of clinical researchers, encouraging medical universities improve the situation (e.g., using indirects to improve training and the environment for clinical research), and acting as advocates to improve the situation. The attached document outlines the scope of the problem and suggests solutions. I am glad to discuss further details.

Compatibility of the framework with the broad scope of the NIH mission

Very compatible.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

The issue raised above about the state of clinical research is certainly one across the NIH.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

No comment.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

The issues raised above about clinical research.

Future opportunities or emerging research needs

Funding opportunities and advocacy for clinical research training.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Basic research is essential, but there needs to be an emphasis on mammalian models, and mammalian species other than rodents. Many models are useful, and occupy a graded series of positions of trade off between cost and relevance. Large animal models need to be developed. Rodents are poor models of many human diseases and processes. Invertebrate models are much worse in those areas. All too often, use of alternative mammalian models is discouraged for budgetary reasons. The high relevance of these alternate mammalian models warrants their use, and administrative measures need to be taken to ENCOURAGE their use, not discourage them.

Compatibility of the framework with the broad scope of the NIH mission

Failure to recognize and reward the value of mammalian models will keep the NIH from realizing major breakthroughs in understanding and preventing human disease. Some esoteric areas of study should

receive a low priority. Study sections need to be populated with experienced reviewers, and instructions need to be given to emphasize relevance to public health--those studies can and should be funded by NSF. For example, studies of the control of fly excrement may be interesting to some scientists, but I would question the relevance to public health (and these have been funded by the NIH). Studies of mechanisms that are specific to some invertebrates, while interesting, have much lower immediate relevance to human health than the study of biological processes in mammalian models. Just as NIH does not support planetary science, there are biological areas of study that should received lower priority. Planetary science is fine, just not an NIH priority. So too, some areas should not be priorities.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Need to fix the peer review process. Need to populate study panels with qualified scientists. The quality of peer review is much degraded in recent years.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Areas to be considered: enhancing the reproducibility of research findings, enhancing the predictivity of animal and in vitro models, reducing wasteful research, reducing conflicts of interest, reducing fraud, enhancing open data availability and data sharing, promoting rigorous controls in antibody-based methods,

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

enhancing the reproducibility of research findings, enhancing the predictivity of animal and in vitro models, reducing wasteful research, reducing conflicts of interest, reducing bias, reducing fraud, enhancing open data availability and data sharing, promoting rigorous controls in antibody-based methods,

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an

NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

enhancing the reproducibility of research findings, promoting expertise in trial design, statistics and bioinformatics, promoting translational approaches and collaborations between basic and clinical researchers, promoting clinical applications of basic research,

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Exposure to radio frequency (RF) and microwave (MW) radiation have continued to increase since the 1940s. A growing population is sensitive to this radiation and have symptoms that have been classified as electrohypersensitivity (EHS). These symptoms are due to long-term, continuous stress on the body that results in premature and rapid aging. Exposures continue to rise with Wi-Fi, cell phone antennas, broadcast antennas, mobile phones, wireless baby monitors, wireless gaming boards and will continue because the currently FCC guidelines are ineffective and based solely on a thermal effect. Estimates of those who are sensitive to electrosmog are between 3% (severe sensitivity) to 35% (moderate sensitivity). In the U.S. and this could account for a population between 10 and 100 million people. Cancer risk is also elevated among those exposed and appears to be due to a compromised immune system and cancer promotion rather than cancer initiation. Sperm motility and survival are also altered in the presence of microwave radiation. The environment influences health. Living in an environment with constant and increasing exposure to microwaves and radio frequencies is a bad idea and just as we learned that lead, tobacco, DDT, asbestos affects health, so does RFR and MWR. Research in this field is both urgently needed and essential if we truly believe in promoting healthy lives. RF and MW radiation are emerging toxicants in the environment and affect children and those with compromised immune systems and interact with other environmental toxins synergistically. Failure to act in a timely fashion and to acquire the research that will lead to safer ways of using this technology is not an option especially for a society that values human health and quality of life.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework
(*Submitter left answer blank*)

Compatibility of the framework with the broad scope of the NIH mission
Compatible

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan
(*Submitter left answer blank*)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine
The current framework lacks any mention of reproducibility and the need to improve it. When only 6 of 53 "landmark" studies can be replicated by independent researchers, the whole field of biomedical research has a serious credibility issue, which could be easily exploited by an "anti-science" congress to defund science. Particular areas of concern include cell lines, protocols, poorly defined and characterized antibodies.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan
(*Submitter left answer blank*)

Future opportunities or emerging research needs
Funded hypothesis driven research should be complemented by funded technology development research. Presently technology development is usually developed within the context of hypothesis driven research, rather than being developed for its own sake. Given that "Leaps in technology often catalyze major scientific advances" it would seem that funding such potential "leaps in technology" would be a good idea.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework
It remains critical to re-invigorate and promote Fundamental Science, as proposed in the "Areas of Opportunity" listed above. However, reviewers continue to promote lower enthusiasm for applications in which the translational nature is not immediately apparent and in which clear relevance to specific diseases is not outlined/generated/promised. This puts applications related to Fundamental Science at a disadvantage. It also forces applicants, if they want to have the work met with enthusiasm and supported, to fit their proposals into the constricting framework of specific disease or translation, even when the research is too new and novel to be assigned a specific disease area. Creating a separate category(s) for fundamental research, unrelated to specific disease or biological system, would 1) draw reviewers who can appreciate such research, unrelated to specific diseases, 2) create a framework where other proposals are also of similar focus and thus, easier to compare. This would provide much needed support for returning Fundamental Science to the place it warrants in the NIH portfolio.

Compatibility of the framework with the broad scope of the NIH mission
(*Submitter left answer blank*)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

There is a critical need to incorporate into the framework an emphasis on the social determinants of health. Family and community contexts, in particular, play critical roles in the health of individuals. We still need to understand better, for example, the mechanisms by which a stressful family environment influences a wide range of health outcomes in utero, early childhood, and into adulthood; and how community norms and infrastructures catalyze or inhibit behavioral changes at the individual level. The combined influences of family and community context on health needs further attention. Observational/behavioral research of this kind could then inform the design of "social and/or economic interventions" that address many environmental "root causes" of poor health.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Impact evaluations of "social and economic interventions" on the health of individuals; in particular, how various economic incentives, with and without training in gender rights to change social norms about gender, mitigates various forms of violence in families, a major contributor to a risky family

environment for women and children.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The biggest issue is not lack of framework, it's a combination of lack of funds and inadequate peer review. I'd be willing to bet that some researchers out there already have submitted (and had rejected) proposals that, if put into action, would prevent or cure Alzheimer's, successfully help tobacco users quit, and prevent cancers. But because the gatekeeper/reviewer system is inadequate, these solutions might never see the light of day. I've been on study sections for more than 20 years and have seen many innovative proposals die simply because they **were** innovative. It ties in to overwhelmed reviewers not being thorough, a drive to push through the reviews as quickly as possible, and reviewers' inner fear that if something they're reviewing gets funded, they themselves won't be able to get proposals funded.

Compatibility of the framework with the broad scope of the NIH mission

They are compatible. I just don't see that the framework solution addresses the real problems. Will this solve the problem where the rubber meets the road? I am skeptical. What I see is a researcher submitting a proposal in more than 20 iterations, using different funding mechanisms over the years, addressing and readdressing reviewers' concerns, and finally getting some grant funding years after the project was timely. How can science and health progress this way? How can technology meet current needs?

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

There's an ongoing need to bring in better reviewers, give them more time to do reviews, encourage them to think and act independently of each other, and stop this freight-train approach that runs over half the submissions to get through the review process quickly. It has become common and expected for reviewers to parrot each other and all say the same (often inaccurate) things, because they aren't reading carefully, and some aren't reading much at all. One reviewer makes a comment in the study section, and the other reviewers say they agree and add it to their "reviews." This is how science falls apart under peer review. A framework won't fix this. Adequate funding for proposals and for the review process will begin to fix it. Additionally, there's a major disconnect between the review process and the express needs and plans of the institutes. Whether a proposal is sufficiently responsive to a PA or an RFA is ignored by reviewers, who are oblivious to the institutes' goals. Once during a break at a study section where every proposal tied to a given institute had been dismissed with bad scores or no score, someone from the NIH institute (I knew him slightly) approached me and said, "The reviewers seem to think this is THEIR money." That violated the concept that reviewers aren't supposed to mention funding, but it

reflected the perception that the reviewers perceived themselves as gatekeepers with a holy charge to keep most proposals from being funded. In that regard, the review process is keeping institutes from setting and carrying out plans. Stated goals in RFAs and PAs are ignored. In search of the Fatal Flaw, the reviewers often are at cross-purposes to the institutes.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

"With the new NIH wide strategic plan the institutes will continue to create their own disease-specific plans." Not all diseases are assigned to an individual institute, leaving some diseases in the lurch with regards to funding and accountability. ME/CFS is one that gets swept under the NIH carpet. Despite the plethora of literature supporting immunological and neurological components to ME/CFS, many of which are described in the recent IoM report, the disease is still not assigned to NINDS or NIAID. As an NIH orphaned disease it is not included in any strategic plan, and it doesn't receive any dedicated funding from a responsible Institute. What changes will the NIH make for ME/CFS in its new wide strategy in order to equalize the current imbalance that exists between the tremendous burden of a disease like ME/CFS and the comparatively small funding it currently allocates to solving such an enormous puzzle? This oversight in funding and accountability must be addressed in the NIH goal "Breakdown of traditional disease boundaries".

Compatibility of the framework with the broad scope of the NIH mission

The NIH mission is to mission to support research in pursuit of fundamental knowledge about the nature and behavior of living systems, and the application of that knowledge to extend healthy life and reduce illness and disability. The goal of this NIH-wide Strategic Plan is to highlight major trans-NIH themes and aims to outline a set of unifying principles to guide NIH in pursuit of its mission. The proposed NIH Wide Strategic Plan states that it will "Incorporate Disease Burden as an Important, but not the Only Factor." How is it possible to effectively reduce illness and disability without focusing efforts on those diseases that cause the greatest illness and disability? While the Precision Medicine Initiative is focusing on diseases with the greatest burden, this 5-year NIH-wide Strategic Plan states that disease burden should be incorporated but not the sole factor. Incorporation of disease burden is not nearly enough consideration. How else can this agency prioritize funding and focus if not based on the burden of individual diseases? How can a plan focus on prevention, treatment and cures if it hasn't first identified the diseases with the greatest economic burden and patient populations most in need? ME/CFS is a disabling disease that costs the US economy more than \$20 billion per year, but it was not included in the Global Burden of Disease (GBD) study. No one has calculated a daily figure for ME/CFS

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

In considering major cross-cutting themes this wide strategic plan has not considered the one constant which crosses all themes, the patients, who in many ways can contribute to the process of research design, priority setting, basic research, and drug and other treatment trials. In the case of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) the most severely disabled home/bed bound patients are not included in the literature because they are too sick to travel and/or participate. They and other patients should drive the 5-year NIH-wide Strategic Plan. The FDA has begun to focus on the patient, as has PCORI. Even the NIH's own Precision Medicine Initiative is doing this by engaging a million or more Americans to further the understanding of health and disease. With so much money and so many resources being poured into the NIH-PMI, shouldn't its (top-down) 5-year NIH-wide Strategic Plan explicate the PMI by including patients in its strategic plan?

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Enhancing Stewardship: Reducing Administrative Burden The NIH should consider utilizing a national database platform like NDAR for diseases with high burden and unmet needs like ME/CFS. NDAR is a biomedical informatics system and research data repository developed by the National Institutes of Health (NIH). NDAR provides the infrastructure to store, search across, and analyze various types of data. In addition, NDAR provides longitudinal storage of a research participant's information generated by one or more research studies. Utilization of an NDAR-like platform for diseases like ME/CFS would significantly reduce research costs and redundancies and would speed the process of research.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

It wasn't listed as an area of opportunity, but advance research opportunities for Rare Diseases is included in the list of priorities. Again, why focus resources on something that is rare and affects the fewest amount of people? Why is advancing research opportunities for rare diseases even be considered a priority for a high level plan? Although studying rare diseases might inadvertently uncover something more globally useful, preventing, treating and curing diseases affecting larger groups should be the priority. Rare diseases should fall under the individual institutes.

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Agree with the notion of fostering cross-disciplinary work and creating more integration across the institutes in that regard. Please see other ideas for specific suggestions.

Compatibility of the framework with the broad scope of the NIH mission

This framework is consistent with and supportive of the mission.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

There are a number. The BRAIN initiative, the OAR and efforts to increase the number of clinically trained individuals doing basic and translational research, particularly human centered research are some examples. If the National Childrens' study is resurrected in response to congressional mandate, this would be another example. If so, it needs to have much greater rigor and scrutiny and less of an entitlement mentality. Autoimmune diseases would also be ripe for a cross-institutional approach that links disease specific autoimmune funded efforts to broader platforms supported by NIAID.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

See previous

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

We strongly support the need for foundational basic science work, which though unpredictable, is the essential underpinning for new knowledge and technologies by which to discover and foster the development of new preventive, diagnostic, predictive and therapeutic approaches. Support of such unfettered knowledge discovery is a mission for which no other entity is so important or has contributed so much as the NIH. The erosion of siloes and support of cross-disciplinary and cross-disease work is crucial for future success. The next generation of scientists needs to be trained across disciplines and be not only comfortable with but predisposed to working in this way. Fostering the development of such scientists will require a concerted effort to be inclusive and to further strengthen efforts to increase the rate at which those seeking to enter the scientific workforce can get their first independent funding and be given a sufficient period of support that they can take risk and work across siloes. Consider setting up more transition to independence mechanisms. Consider a mini-MERIT award mechanism for extension of the first independent award. Such a mini-MERIT award might allow scientists whose first grant is particularly meritorious to seek ~3 year extension of a typical RO1, based on accomplishments in their first 3-4 years of the R01. The extension should be reviewed based on productivity and forward vision for the next phase that showed innovation and risk-taking. Such awards would complement the Innovator awards run out of the Director's office to bet on promising/great people early in their careers with interesting ideas rather than having them confront the standard innovation averse IRG process for 1st renewal. Continue to foster efforts to support basic research on humans and new tools (organoids, better imaging and analytics) now make it much more feasible to work effectively in such systems.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Re: Promoting fundamental science, consequences: I find this area to be of great value to public health and other branches of health. Attention should be devoted to an in-depth study of the impact of CRISPR on relevant aspects of genetic research.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

With regard to health promotion issues, please identify specifically healthy older/aging individuals as well as younger and middle aged individuals in the areas of opportunity.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework
(*Submitter left answer blank*)

Compatibility of the framework with the broad scope of the NIH mission
(*Submitter left answer blank*)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan
(*Submitter left answer blank*)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine
(*Submitter left answer blank*)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan
(*Submitter left answer blank*)

Future opportunities or emerging research needs

It is now well established that fungal infections cause nearly 1.5 million deaths each year and are a major worldwide cause of morbidity and mortality. Unlike diseases like TB, fungal infections are a major problem in US hospitals. Yet, our emphasis on combating fungal infections remains badly inadequate. To significantly reduce deaths due to AIDS, we must address fungal infections. There is an urgent need for better diagnostics and therapeutics and a greater understanding of disease development and prevention of drug resistance. The NIH needs to lead the world in this area and it must increase its presence. The attached "Road map" from the Global Action Fund for Fungal Infections (GAFFI) is relevant to this critical domestic and global health issue. Fungal infections need to come out from the shadow and be confronted to save lives.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

A breakthrough innovation and Challenge for the neurosciences invokes the first Periodic Table for the Human Forebrain; which enjoys similar advantages to the dramatic influence that the Periodic Table of the Elements has enjoyed with respect to Chemistry and Physics. This respective neural counterpart imparts a crucial sense of systematic order and purpose to the fragmented state of affairs currently prevailing within the neurosciences. more at www.forebrain.org ** . . . (1977). The Development of the Forebrain as an Elementary Function of the Parameters of Input Specificity and Phylogenetic Age. J. U-grad Rsch: Bio. Sci. U. C. Irvine. (6): 274-294.

Compatibility of the framework with the broad scope of the NIH mission

This new framework explains the pattern underlying the wide variety of cortical parcellation schemes that have emerged over the course of the preceding century. In hindsight, these ultimately accurately reflect this observed style of specificity of inputs, wherein permitting a number of crucial functional predictions in relation to the organization of the human neocortex. The first major system of cortical

parcellation was proposed by German anatomist K. Brodmann in 1909. This enduring system used Arabic numerals to specify roughly 50 distinct areas in the human cerebral cortex (as schematically depicted). A complementary parcellation system was further introduced by Austrian researcher Constantin von Economo in 1923 employing a lettering system of notation. The dual parameter grid depicted in Fig. 1 (of attached file represents a modified version of an original representation reproduced from an earlier journal article by the author (. . ., 1977). The initial journal diagram represented the first measured endeavor towards quantitatively ordering subdivisions of the forebrain into a globally coherent pattern. The currently modified version of the dual parameter grid aspires to designate the first "Periodic Table for the Human Forebrain," analogous to the similar influence the Atomic Periodic Table enjoys respect to Chemistry and Physics. The respective neural counterpart imparts a crucial sense of systematic order and purpose to the fragmented state of affairs currently prevailing within the neurosciences. As such, it provides the long-anticipated link between the "hard" physical science of neuroanatomy with its "soft" correlates to behavioral psychology. A more detailed review of cortical growth ring theory provides further welcome validation for the dual parameter paradigm.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Through the aid of this break-through "periodic table" for the human forebrain (employing elementary exteroceptive, interoceptive, and proprioceptive input categories) an intimately detailed pattern of correspondence can be established with respect to the instinctual principles of behavioral psychology. Here, the human forebrain formally expands upon the basic stimulus/response (sensory/motor) reflex arcs implicit within the neuraxial spinal cord and brainstem. The intermediary neurons of the neuraxis mediating interoceptive sensations interposing emotional correlates within the sequence of exteroceptive stimuli and subsequent behavioral response, as schematically reflected in the operantly conditioned sequence. The nervous system never completely replaces basic circuitry, rather further modifying it: as evident in the vast expansion of the human forebrain based upon the visual and olfactory senses. Therefore, by applying these behavioral principles on an evolutionary scale clear on up to humans, it ultimately proves feasible to propose a grand unified synthesis of behavioral psychology with its corresponding "hard science" referent within the neurosciences. The forebrain appears to have adaptively evolved as a dedicated motivational analyzer that attaches motivational significance to exteroceptive stimuli (such as vision and hearing) in preparation for appropriate action by the motor areas that also mediate proprioceptive feedback in terms of such operantly conditioned behaviors. Indeed, this behavioral dynamic exhibits many parallels to the black-box paradigm of input/output characteristics. The human forebrain (similar to the hypothetical black-box) still hides many of its secrets; although unprecedented progress is clearly in order with respect to the dual parameter grid.

www.forebrain.org

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Each unit-square of this chart graphically represents the coordinate set of unique age and input parameter levels. The individual unit-squares of this theoretical grid systematically and compass each of the experimentally determined thalamic subdivisions on a one-to-one basis. This point-for-point correspondence accounts for essentially every thalamic subdivision, yet is virtually free of any duplication across adjacent unit-squares. The minimal redundancy observed in the older thalamic growth shells appears to be the result of the hesitancy on the part of some researchers to subdivide regions of already diminutive proportions. Besides being listed by name within each unit-square, the thalamic classifications of Hassler's system are designated through their exact position with the

schematic grid. This Cartesian coordinate paradigm of the human thalamus reduces the great complex of this elaborately structured region to an elementary level of quantitative simplicity. This precise coordinate style of system for the human thalamus had not been achieved prior to the original proposal of the dual parameter grid (. . ., 1977). This original model has undergone a number of further modifications, achieving its final format in Fig. 1. see attachment and www.forebrain.org

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

This innovation is Fully compatible

Future opportunities or emerging research needs

The theoretical establishment of such an all encompassing age parameter format has further ramifications with respect to the overall pattern of forebrain connectivity. The identical number of age levels in both the thalamus and the cortex indicates that only correspondingly numbered growth shells and growth rings are reciprocally connected by the thalamic radiations. In theory, a thalamic cell on a discrete point within the time-differentiation continuum directs its main projection to cells of the cortex derived at the same phylogenetic age. Similarly, cortical cells that emit feedback projections destined for the thalamus analogously respect this age level restriction. These intersegmental considerations restrict the intrinsic interconnectivity of the thalamo-cortical loop the strictly to identical sets of age levels. Yakolev's (et al, 1966) documentation of the limbic and insular projections of the three most ancient thalamic age levels appears to corroborate these theoretical age level restrictions the. Cortical citations for the newer age levels of the thalamus by Hassler (1959) similarly seem to verify this contention, even though Hassler did not technically considered his hexapartition levels as separate age levels. In addition to this age levels type of consideration, the thalamo-cortical loop is further subject to an alternate style of input functional restriction. As stated previously, the thalamic radiations serve to relay the entire complement of forebrain inputs to each of the age levels of the cerebral cortex. . By utilizing both age and input parameter criteria, the cortical parcellation schemes of Brodmann and von Economo correlate on a one-to-one basis with the dual parameter grid. This strict unit-square correspondence accounts for virtually every major subdivision within both parcellation schemes.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

When I read "research in pursuit of fundamental knowledge about the nature and behavior of living systems, and the application of that knowledge to extend healthy life and reduce illness and disability" I felt I should share, that my personal study during more than 30 years of international public health practice convinced me that the "global health community" continues to make a fundamental error in accepting the static nature of the health systems concept as defined by WHO. Health systems are large scale social systems, and it is time we apply the science of living systems to our understanding of their evolutionary nature. I am convinced that if we challenge the ICOs to join hands in exploring this concept by borrowing from fundamental life sciences a great deal of ideology that influences current thinking in health systems might be questioned on scientific grounds to the benefit of our joint capabilities to evolve systems that improve dramatically their efficiency in "extending healthy life and in reducing illness and disability"

Compatibility of the framework with the broad scope of the NIH mission

no comments

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

I know at least from my collaboration with CDC projects that the following would apply: suggestion :living health systems; see insertion. Promote fundamental science: ?Basic science is the foundation for progress ?Consequences of basic science discoveries are often unpredictable ?Advances in clinical research methodologies stimulate scientific progress ?Life sciences inspire novel thinking about living health systems ?Leaps in technology often catalyze major scientific advances ?Data science increases the impact and efficiency of research

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

It is clearly important to study healthy individuals to determine interventions that prevent the onset of disease. It is equally important to study individuals with chronic conditions, particularly those who are elderly. Aging can be loosely defined as the increasing accumulation of chronic diseases. These cut across the NIH. Interventions that may be effective for the primary prevention of individual chronic diseases may be ineffective, or even harmful, for older individuals with increased chronic disease burdens. An effective approach for increasing health span requires study of the interrelationship of these conditions. It also requires the assessment of strategies to slow the accumulation of additional chronic diseases among individuals who have already encountered one or more of these conditions. There is increasing enthusiasm for using electronic medical record databases to supplement prospective experimental designs. And, there is great potential in these data sources, however there is no current method to account for the wisdom inherent in clinical decision-making and patient preferences. These factors demonstrably reduce the variability within electronic medical records and lead to over-estimates of the precision of estimates and associations and to spurious findings. Studies based on these records fall far short of the weight of evidence provided by well-designed controlled clinical trials.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

The US population is markedly changing: it is older, heavier, ethnically more diverse, and reflective of greater disparities in wealth. The development of the most effective and cost-effective prevention strategies should target the population of the future, not the past.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity

that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

The behavioral and cultural nature of health and health care in the US and abroad. The scientific, basic and applied, study of the structure of relations among socio-structural, cultural, and psychological factors influencing behavioral and biological phenomena relevant to health, locally and globally, is fundamentally necessary to enhance health outcome in general and health disparities in among minority and socially disadvantaged populations in the U.S. and globally.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

It amazes me how little funding there is and how little attention NIH gives to theory development or even use of the limited theoretical integrative frames available for research and intervention, We all know the tremendous importance of behavior in addressing the most pressing health problems, particularly those related to chronic disease and health disparities. Still, the scientific study of the powerful role of culture and its interaction with social-structural and psychological processes relevant to health care and outcome are mostly ignored. More over, the little funding allocated to this are goes to comparisons among ethnic or socially disadvantaged group instead to basic and applied research dealing with such powerful factors influencing health, from the interactions of culturally diverse patients with a health care system based mainstream cultural assumptions and policies that more often than not ignore the role of cultural factors that usually impact health behavior and biological phenomena that, when scientifically investigated, by multidisciplinary teams, could do so much to enhance the health care and outcome not only of minorities but also the mainstream population.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

See above.

Future opportunities or emerging research needs

See above

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Overdue for Program return to a CONTRACT Funding mechanism, to leverage "best talent available" as in the early days of the Artificial Kidney and Artificial Heart programs . Scientists & Engineers in private companies, in contract R&D labs, and in Military/DOD laboratories should be encouraged to propose and compete for scarce funding now reserved to academia as a supposed "entitlement". All Contracts should include a pre-negotiated "Statement of Work", a Timeline with Milestones, and a requirement for open publication (in a Technical Report, if not a Journal) of ALL findings--including negative findings that will be of high value to subsequent projects.

Compatibility of the framework with the broad scope of the NIH mission

Delivery of benefits and products more swiftly to the tax-paying public, rather than re-cycling the problem descriptions to keep Federal funding isolated to RO1 grants that never terminate. No need for duplicated studies and "re-invention of the wheel" now occurring because "blind alleys" are not disclosed.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Encourage, not inhibit or forbid, clearly labeled "Conflict of Interest" studies and publications...It is NOT good practice to require that scientific/engineering competitors evaluate "dispassionately" emerging concepts/products that require the tender loving care of the originators.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Insist that materials utilized in EVERY investigation be completely analysed and described. It is improper to employ substances knowing only their Tradenames and not their actual compositions or surface chemistries. A particularly egregious example of poor NIH decisions in research funding, is paying for investigations of dental composite resins of undescribed make-up.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

Investigations of phenomena in wet, salty environments (like the ocean) that are very environmentally important but not focused on blood, saliva, and other biological fluids of relevance to health and disease.

Future opportunities or emerging research needs

Relation of living cells' passive spreading and related biomechanics to cell function and activity.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The attached Appeal calls on "governments (to) fund training and research on electromagnetic fields and health that is independent of industry and mandate industry cooperation with researchers." On May 11, 2015, 190 scientists from 39 nations submitted the International EMF Scientist Appeal to the UN, the WHO, and all world leaders. This petition (<https://emfscientist.org>) calls for government-sponsored research on electromagnetic fields (EMF) and health. As of July 31, 2015, 207 scientists from

40 nations signed this statement. All signatories have peer-reviewed publications on EMF and biology or health. EMF—a term that includes frequencies along the electromagnetic spectrum—is generated in the radiofrequency bands (RF/EMF) by popular wireless devices like cell phones, cordless phones, baby monitors, tablets, Wi-Fi enabled computer equipment, cell phone towers/antenna arrays, radio/television broadcast facilities, and wireless smart meters, among others. EMFs are also emitted in the extremely low frequency band (ELF/EMF) by electrical appliances, electrical wiring, and power lines; and in the intermediate frequency (IF) range by electronic devices that generate high frequency transients on electrical wiring. Non-ionizing electromagnetic fields are the fastest growing forms of environmental pollution. Numerous scientific publications have found that EMF affects living organisms at levels far below international exposure guidelines adopted by the US and most industrialized nations. Current guidelines set exposure standards for high-intensity, short-term tissue heating thresholds, considered not applicable for the long-term, low-intensity, chronic exposures we typically experience today. According to published, peer-reviewed research, the effects of low-intensity EMF include: increased cancer risk, cellular stress, free radical formation, increased permeability of the blood brain barrier, and genetic damage. Other potential effects include learning and memory deficits, neurologic/neurotransmitter disorders, reproductive effects, and negative impacts on general well-being. Moreover, there is growing evidence of harmful effects on plant and animal life.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

See above.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

See above.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

As the National Institutes of Health develops its 5-year Strategic Plan to advance its mission, the . . . strongly recommends one major theme be incorporated into your vision: that more emphasis is placed on the development and use of human-relevant, non-animal alternatives, and that less emphasis is directed on experiments involving non-human animals. There are serious scientific flaws in thinking animals can accurately mimic human biology: • Differences between species make extrapolation of data across species highly unreliable. • Small genetic differences between humans contribute to health, disease prognosis, progression, prevention and response to treatments, so which humans are we expecting animals to model? • It is not justifiable, ethical or scientifically valid to continue to use animals as stand-ins for humans when researchers could instead be encouraged to develop and work with human-relevant models. With the availability of human cell lines, stem cells and tissues, computational models and, most importantly, researchers eager to accept the challenges of developing more human-focused and humane methodologies, opportunities to move away from animal models have never been greater. Now is the time. Millions of dollars of taxpayer money have been spent on the acquisition and care of live animals to be used for NIH-sponsored research. These resources would pay much higher dividends in terms of progress in human health if they were directed to more human-relevant research. As the NIH plans for the next five years, it must accept that animal models are inherently flawed as predictors of what is safe and effective for humans. It is time to refocus our efforts and our monetary resources on more human-based models to best increase our chances of improving human health and well-being.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

An emerging stream of research provides a new approach for evaluating and improving strategic plans. It is now possible to determine the potential usefulness of a strategic plan before it is applied in practice. Importantly, this is a highly objective approach that is more reliable than the traditional approach of relying on intuition. To help NIH develop the most effective strategic plan possible, we offer the use of our methodology which is expected to double the effectiveness of strategic plans. That is to say, double the potential for the plan to reach higher goals at lower cost with more predictable success. This includes the ability to ensure functional, synergistic linkages between strategic plans of ICOs; transparency to improve ease of management and accountability; and providing multiple options for reaching goals. It has long been accepted that the structure of conceptual systems such as theories, mental models, and strategic plans is related to the successful use of those systems. For example, theories and laws of physics contain more structural connections than theories of the social sciences. And, theories of physics are more reliable in practical application. We use a suite of analytical techniques under the general label of Integrative Propositional Analysis (IPA). Using IPA, we evaluate strategic plans. For their breadth of understanding, depth of understanding, number and direction of feedback loops, measurability of variables, causality, and other measures of structure. In short – we help you evaluate and improve the structure of your strategic plan. For a brief and partial overview, please

see: <http://meaningfulevidence.com/wp-content/uploads/2014/12/Strategic-Planning-3.0-October-27.pdf> Working online or onsite, we can use IPA to help NIH evaluate, integrate, and objectively improve its strategic plan to more reliably support the advance of science in the US and around the world.

Compatibility of the framework with the broad scope of the NIH mission

This is a process to improve the compatibility of multiple frameworks.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

The science of conceptual systems is an emerging stream of research and practice. A conceptual system may be understood as a theory, model, policy model, mental model, and other related conceptual constructs that help us to understand and engage the world. Because the focus of this field is the objective understanding and improvement of policies and theories, it is deemed a "science multiplier." While the methods here are useful across all fields, the benefits will be greatest in the fields that are the least developed. Generally speaking, these would be in the social/behavioral sciences including fields such as psychology, sociology, business, policy and so forth. Importantly, the approaches here are very useful for supporting collaboration within public and/or scholarly venues as well as supporting interdisciplinary work and identifying high leverage research opportunities (by clarifying gaps in extant theory). The science of conceptual systems may be advanced more rapidly so that it may better serve the advancement of science by funding projects including: * Developing new methods for objective evaluation of conceptual systems. * Studies comparing various policies to support dialog by public and scholarly groups. * Improving literature Reviews for doctoral candidates * Studies where conceptual systems are objectively evaluated and compared with their real world benefits. These may include: historical (e.g. comparing policies enacted over time), laboratory (e.g. providing participants with varying theories and observing results), computer modeling (e.g. comparing success of agents with differing schema), applied (e.g. comparing strategic plans of organizations - how they are developed, structured, implemented - and their success/failure). * Collaborative and interdisciplinary efforts to integrate multiple theoretical perspectives and generate a theory that is greater than the sum of its parts (this may be particularly interesting/useful in the systems sciences). * Development of a "periodic table" of theories as a resource for researchers and practitioners

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

I AM INCORPORATING . . . COMMENTS. There is a major weakness in the proposed plan structure, in that it assumes that the Institutes cover all diseases in their own strategic plans. However, there are diseases like ME/CFS which have no assigned Institute home. Under the current framework, ME/CFS and

other orphan diseases will be left to fall through the cracks. Instead, NIH must find ways to address diseases that cross Institute boundaries. ME/CFS has immunological and neurological components, yet it is not assigned to NINDS or NIAID. It is not covered by any strategic plan, nor does it benefit from dedicated funding by a responsible Institute. The goal “Breakdown of traditional disease boundaries” does not sufficiently address this problem. There is, of course, an ongoing role for body system/disease centric approaches. But NIH must grapple with the challenges of diseases which cross boundaries, and must either assign responsibility to existing institutes or create a new structure that can address the diseases that currently fall through the cracks.

Compatibility of the framework with the broad scope of the NIH mission

Given NIH's statement about the importance of using research to extend healthy life and reduce illness and disability, it is incumbent on NIH to place a higher priority on all diseases that create profound illness and affect millions of people, such as ME/CFS. It is inconceivable that a disease with impacts like ME/CFS has been so ignored. The Institute of Medicine report should be an essential guide.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

I AM INCORPORATING . . . COMMENTS. This strategic plan has allowed no room for the voices of patients. While FDA has sought to expand the role of patient voices in its decision making, and PCORI's mission is focused on patient views and preferences, NIH has taken no steps in this direction. This is NIH's loss. Patients and caregivers have valuable information that can inform research design and priority setting. Even basic research can be improved and informed by including patients' views. Creating large cohorts of healthy and sick individuals, such as in the Precision Medicine Initiative is valuable, but it is not sufficient. Patients can contribute to hypothesis generation, selection of outcomes measures, and identification of treatment targets. NIH must come to terms with the role patients can play in biomedical research. Incorporating these views in a systematic way would strengthen NIH and its research, regardless of the disease or Institute involved.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

I AM INCORPORATING AND EXPANDING ON . . . COMMENTS. While I agree that burden of disease should not be the only factor in priority setting, it must play a more central role. NIH must do more than select 69 categories from the Global Burden of Disease study. It's a start, but in no way is it sufficient. For example, ME/CFS is a disabling disease that costs the US economy more than \$20 billion per year, but it was not included in the GBD study. No one has calculated a DALY figure for ME/CFS in the United States. And so, left to fall through the cracks, the burden of this disease is not considered in decision making, a tragic failing. Furthermore, NIH must create more transparency in its funding decisions. Regardless of whether the 21st Century Cures act passes and mandates such transparency, NIH owes it to the ultimate source of its funding – the American people – to justify the enormous gap between the burden of a disease like ME/CFS and the paltry funding allocated to solving it. A disease like ME/CFS, which crosses multiple body systems, represents a tremendous opportunity for discovery. Unlocking the

pathophysiology of this disease could have implications far beyond just ME/CFS. This is an area that could and should be prioritized, but instead it languishes without any focused attention. Indeed, if you look at the research plans of the Open Medicine Institute/Foundation, the Solve Me/CFS Initiative, Stanford University, and other institutions, you will see that they are seeking funding for cross-cutting innovative research that transcends the study of ME/CFS. If the strategic plan includes “Research Spotlights” as proposed, then I submit that ME/CFS is a case study in opportunity and trans-NIH

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Promote Fundamental Science (Advances in clinical research methodologies stimulate scientific progress) and Improve Health Promotion and Disease Prevention (Evidence-based interventions to eliminate health disparities)

Compatibility of the framework with the broad scope of the NIH mission

It is under the NIH mission about fundamental science and prevention strategies

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Obesity and aging which speed up each other and both of them come with different and maybe common second diseases. To speak narrow and according my direct study field, aging come with muscle aging which recognized as muscle mass and strength loss, muscle wasting and shortly sarcopenia, and sarcopenic person also face with body fat increasing more than homogeneous people as their aged. Interestingly, sarcopenia prevalence among obese person is higher. Young to middle aged obesity is different of age related obesity which should completely defined.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Defined age related obesity which at least can be inherently obesity, childhood obesity, mature obesity, adult and middle aged obesity, age related obesity, and disease related obesity, each related obesity recognition signs, special study tools, prevention strategies in early diagnostic and functional and practical treatment strategies.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The current framework includes grant opportunities for non-profit entities and for established small businesses, but does not adequately address the need for support of early start-up businesses that arise from research. Current grant mechanisms (SBIR/STTR grants) are appropriate for established small businesses with existing revenue-producing products. However, new businesses with promising medical products and a sizeable potential market can't move forward because the risk to private or industry

investors is too great. A mechanism for small businesses (start-ups with only "friends and family funding") is needed to REDUCE THE RISK for commercial investors. This could be accomplished through funding for short-term development needs, e.g. performing biocompatibility studies, establishing product manufacturing for an innovative device, addressing regulatory requirements, etc. A program similar to BrIDGs, but for Devices could address this issue. (BrIDGs is for Drug/Biologic/Chemical development.) Alternatively, the SBIR/STTR mechanism could be modified to allow for start-up companies that have very little funding, but have great talent, a great product, significant market for that product, and IP. A BrIDGs counterpart for addressing biocompatibility, prototyping, etc. could make a significant difference.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

I object to characterizing all NIH research as "biomedicine." This leaves out public and population health. Not everything related to health is "medical." The health promotion/disease prevention section only discusses individuals, yet great strides have been made based not on individual behavior or "medicine" but based on research regarding the broader institutional factors that contribute to health and disease. Also concerned about the heavy emphasis on basic science, which leaves out implementation science, community based research, and health policy research. Since the greatest advances in many fields, including tobacco (greatest preventable contributor to death and disease) have come from policy measures, this is a huge omission. I'd like to see included research on the institutional factors that contribute to health and disease. I don't understand what is meant by "employing risk management..in decision making." What kind of risk? Political? I'd also like to know what "enhancing partnerships" means. For example, partnerships with tobacco companies or other entities with economic stakes in the outcomes of research would be very problematic. What ethical guidelines would apply to such partnerships?

Compatibility of the framework with the broad scope of the NIH mission

The framework leaves out a big chunk of research related to health.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Institutional factors in health and disease causation, prevention and treatment
Population health
Preventive health policy research
Health communication
Community action research/community engagement

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Global health policy

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The framework would be stronger if it included another area of opportunity under "improve health promotion and disease promotion" --- "Partner with the National Library of Medicine, libraries, local public health agencies and organization to disseminate health information to the health professionals, public health workers, and the public." Also, the health promotion and disease promotion, should also "support best approaches to increase access to quality health experiences." The framework identifies most areas of opportunity, but overlooks the importance of how climate change is affecting public health and how the NIH can play a role to support emergency preparedness.

Compatibility of the framework with the broad scope of the NIH mission

It's important for the NIH to continue to support the National Library of Medicine and National Network of Libraries of Medicine's role to use libraries as a vehicle to reach the public with health information/messages: "in directing programs for the collection, dissemination, and exchange of information in medicine and health, including the development and support of medical libraries and the training of medical librarians and other health information specialists."

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Increasing access to technology in areas faced with the digital divide presents the opportunity to bring health information to medically underserved areas faced with health disparities. With increased access to technology and resources from NIH and the National Library of Medicine, National Network of Libraries of Medicine, the public can make informed health decisions. One of the greatest factors influencing an individual's health is time: time to exercise, time to plan healthy meals, time to get to health appointments, and time for recreation. According to womenshealth.gov, nearly two-thirds of the caregivers of older adults are women, and, as we know, women often play the primary role in childcare, as well. The NIH should work with other government entities and with corporations to advocate for family friendly policies in the workplace, increase access to healthy food, increase access to recreation, and increase support for local public health agencies and health related community based organizations. Funding for organizations like the NN/LM Evaluation Center help identify best practices for health information outreach and community engagement. Libraries can play an important part of facilitating access to health information in medically underserved areas faced with the digital divide. The National Network of Libraries of Medicine can serve as a conduit to relay important messages from NIH to academics via health sciences libraries, health professionals via hospital libraries, and the public via public libraries. Climate change presents emerging research needs and emergency preparedness needs. Funding resources like the NLM's DIMRC, Disaster Information Management Resource Center, may help the country be better prepared to respond to weather related health hazards. The country is faced with such high rates of gun violence. The NIH should advocate to create a safe environments, reduce access to guns, and increase support for mental health/community supports.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

I do not understand the high-faluting language of this request. All that I have to say is that I contracted Chronic Fatigue Syndrome 19 years ago and research and public and government interest has been nil. My life has been ruined, decades of it stolen by a serious disease. NIH -- thanks for your report that was yet another voice in the wilderness telling the truth about CFS. Now it's time for you to put money into research. Any day now, you or someone you love may get this disease and begin a life of living death. Will they (or YOU) wait 19 years for nothing to be done in terms of serious, committed research and work toward a cure?

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Please also include funding for an expansion of the NLM for them to be able to continue to hold and acquire print materials. Thank you.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The NIH investment in large program project grants is depleting the amount of money available for investigator initiated grants. At . . . , investigators are expected to bring in a minimum of 2 R01 grants. We were reminded yesterday by the CEO of . . . , that failure to do , could result in a reduction of our salaries, and if not remedied within some institutional deadline, would result in the loss of our lab space. Please invest MORE in R01 grants, otherwise investigator initiated basic science could die out, because institutions like mine, will have thrown us out.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an

NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Please see attachment which contains general recommendations for developing a research agenda for integrative mental health care. The comments are excerpted from "Integrative Mental Health White Paper: Establishing a New Paradigm through Research, Education and Clinical Guidelines" that can be accessed at the following web address:

http://www.wpic.pitt.edu/education/CPSP/1%20%20VF1%20%20INIMH%20White%20Paper_FINAL%20DRAFT_July_2012.pdf

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The focus on basic science and on cross-disease initiatives is very important for research to advance future knowledge about health.

Compatibility of the framework with the broad scope of the NIH mission

The framework is compatible with NIH's mission.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity

that Apply Across Biomedicine

An important area that is missing under "Advance Treatments and Cures" is the role of patients' health behavior and self-management of illness. A potential additional bullet would be "importance of patient engagement and health behavior as health reform encourages people to take more ownership of their own health care"

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

N/A

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The framework succinctly point at key opportunities and principles to guide NIH. Nonetheless, it is important to specify that "basic science" is not limited to biochemical mechanisms, but includes a broad range of levels of analysis, from biochemical mechanisms to behavior to society.

Compatibility of the framework with the broad scope of the NIH mission

It is compatible.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

The framework should promote novel and creative approaches to data and modeling that may address difficult topics, such as the complexity of individual behavior, social interaction, disease transmission, etc.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

See attached article.

Compatibility of the framework with the broad scope of the NIH mission

See attached article.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

See attached article.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

See attached article.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

See attached article.

Future opportunities or emerging research needs

See attached article.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

These comments incorporate additional information included in the July 20th ACD presentation and are offered from an Enterprise Risk Management (ERM) perspective. HHS is requesting each OPDIV to implement ERM at the OPDIV level. A strategic plan is a crucial component of successful ERM and the development of NIH's Strategic Plan will be a huge benefit to implementing ERM at NIH. However, NIH top enterprise risks can also be considered to inform the development of a strategic plan and avoid unknowingly complicating future ERM efforts. Although NIH has not yet undergone an effort to formally name its top enterprise risks, a list of potential choices can be gleaned through awareness of topics with the greatest amount of public visibility and areas of focus by the ACD. These potential enterprise risks could be used as one lens through which to view the draft plan. If NIH's top enterprise risks cannot be "seen in" or "relate to" NIH's Strategic Plan, then resources may be misdirected away from optimally achieving strategic plan goals. Specific factors to consider are included in the attached document.

Compatibility of the framework with the broad scope of the NIH mission

I believe the proposed framework adheres well to the currently stated high-level NIH Mission and Goals. It provides usable categories that can encompass the multiple facets of NIH research without a need to cite specific organs or diseases. That said, the proposed inclusion of examples and "research spotlights" moves the plan back towards the original weakness that did not resonate with the ACD.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

No comment.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

No comment.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

The citing of specific examples within the Areas of Opportunity section may unintentionally give the illusion of being NIH's top priorities and risks when these have not yet been officially determined.

Alternate approaches to consider are included in the attached document.

Future opportunities or emerging research needs

Where does the issue of the future availability of a qualified biomedical workforce outside of NIH fit in this picture? Under Enhancing Stewardship, the phrasing of "recruiting and retaining an outstanding biomedical research workforce and enhancing workforce diversity" does not appear to encompass the need for a qualified grantee workforce. If the intent was to include that aspect as well, the phrasing should be expanded to make it clear. Although I am excited to see "employing risk-management strategies in decision making", I am uncertain if it is accurately reflecting the intent. Is it a matter of "employing risk management data and strategies in decision-making" or "employing risk management data in strategic decision-making?" Where do you see positioning the clinical center, the NLM and the IRP to continue meeting emerging research needs? I can easily see this being reflected in Enhancing Stewardship as they support all three Areas of Opportunity. Similarly, what about the availability of adequate facilities? Facilities are definitely a support mechanism but could have a huge impact on future efforts as research advances and evolves. Even having enough space for management functions is important. While I realize that the focus of the strategic plan should be scientific in nature and there is already a slight nod to supporting management functions, the plan seems to dismiss the value of ensuring support functions are adequate to future research needs.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Within the current framework, consideration to develop a reporting structure (for public access) providing an overview of discoveries (by disease type) made from funded studies is required. These could include discoveries on disease mechanism, drug, drug-target, diagnostic method, positive/negative clinical responses, etc. which could provide beneficial information to public looking for answers pertaining to their disease conditions or understand how their tax dollars are helping their well being. Additionally, such information will help them to contact law-makers and funding agencies voice their support or draw attention to unmet causes.

Compatibility of the framework with the broad scope of the NIH mission

Reducing administrative burden is critical in grant review process. Proposal can be scientifically evaluated and scored solely based on the basis of merit (and if possible, blindly). Applicants can be scored, based on Q/A sheets and the scores can be stored for certain period, Institutions can have floating scores. Once qualified proposals are selected, applicant and institutional scores can be integrated for final review.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

For funding cross disciplinary research studies, funding for any selected project can originate from more than one institute (depending upon the percentage of each discipline, addressed in the studies, for example 50% cancer, 25% aging, 25% genomics). Such approach can reduce financial burden on any individual institute and allow sharing credits between institutes.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

Many institutions have acquired several capital equipment through NIH funded programs, sometimes remain underutilized or never utilized. NIH can offer assistance to institutions willing to pool underutilized NIH funded resources and commit access to other NIH funded investigators, which can substantially reduce costs on the individual grants.

Future opportunities or emerging research needs

This being an era of "big-data" and researchers are constantly adding vast volumes of data, most of the data remain under utilized, meaning they either focused on a subset of results or just provided an overview, and the rest are ignored. Sometimes there could be data generated from multiple platforms, multiple models, kinetics etc from diverse groups, if not analyzed to fullest potential, it would be a colossal waste of time, resources and funds. NIH can pick select disease models, and develop multistage funding mechanisms seeking investigators, student/postdoc to forge alliances and develop translatable hypothesis from preexisting big-data as Phase I, and validate the hypothesis in Phase II and eventually proceed to clinical studies in Phase III. This could be made as multistage funding application (Phase I-III), minimizing the risk of failure.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

There is a need to flatten the research enterprise, reduce administrative burden, and stimulate collaboration with entities doing research with venture capital. The 27 institutes and centers create an administrative nightmare. Redundancy in research effort is good. Redundancy in administration is wasteful.

Compatibility of the framework with the broad scope of the NIH mission

The important areas are covered but the current governance of the research enterprise is unmanageable. A prime example is the \$1.3 Billion spend on planning the National Children's Study. It this isn't a wake-up call to the NIH enterprise nothing will ever be. We need a report on what went wrong and how this will be avoided in the future.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

We need a cadre of USPHS uniformed officers whose special expertise is to serve as research liaisons. They would assist to span the boundaries of basic science, translational science, and public health. There is too much silodom at NIH.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

How do you put the patient at the center of the research effort?

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Flatten dramatically.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

It is encouraging to see "Fundamental Science" listed as one prong of the mission of the NIH, but in my experience over the last decade, the NIH has been drastically underfunding basic research. I hope that this is going to change. As noted in your statement, results are unpredictable, and giving researchers leeway to adjust their research trajectory as a project progresses and data points in new directions, is a critically needed improvement.

Compatibility of the framework with the broad scope of the NIH mission

The NIH has put too much emphasis on translational research in the last decade. Translational research should comprise no more than 1/3 of funded projects.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

The NIH needs to redouble its efforts to fund basic scientific research that may not have clear translational potential. Basic research is the cornerstone of advancing biomedicine, and most of the NIH budget should be directed there. Pharmaceutical companies are not going to do basic research, so it is up to the NIH and NSF to fund this type of research.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

There is a major weakness in the proposed plan structure, in that it assumes that the Institutes cover all diseases in their own strategic plans. However, there are diseases like ME/CFS which have no assigned Institute home. Under the current framework, ME/CFS and other orphan diseases will be left to fall through the cracks. Instead, NIH must find ways to address diseases that cross Institute boundaries. ME/CFS has immunological and neurological components, yet it is not assigned to NINDS or NIAID. It is not covered by any strategic plan, nor does it benefit from dedicated funding by a responsible Institute. The goal "Breakdown of traditional disease boundaries" does not sufficiently address this problem. There is, of course, an ongoing role for body system/disease centric approaches. But NIH must grapple with the challenges of diseases which cross boundaries, and must either assign responsibility to existing institutes or create a new structure that can address the diseases that currently fall through the cracks.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

This strategic plan has allowed no room for the voices of patients. While FDA has sought to expand the role of patient voices in its decision making, and PCORI's mission is focused on patient views and preferences, NIH has taken no steps in this direction. This is NIH's loss. Patients and caregivers have valuable information that can inform research design and priority setting. Even basic research can be improved and informed by including patients' views. Creating large cohorts of healthy and sick individuals, such as in the Precision Medicine Initiative is valuable, but it is not sufficient. Patients can contribute to hypothesis generation, selection of outcomes measures, and identification of treatment targets. NIH must come to terms with the role patients can play in biomedical research. Incorporating these views in a systematic way would strengthen NIH and its research, regardless of the disease or Institute involved.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

While I agree that burden of disease should not be the only factor in priority setting, it must play a more central role. NIH must do more than select 69 categories from the Global Burden of Disease study. It's a start, but in no way is it sufficient. For example, ME/CFS is a disabling disease that costs the US economy more than \$20 billion per year, but it was not included in the GBD study. No one has calculated a DALY figure for ME/CFS in the United States. And so, left to fall through the cracks, the burden of this disease is not considered in decision making. Furthermore, NIH must create more transparency in its funding decisions. Regardless of whether the 21st Century Cures act passes and mandates such transparency, NIH owes it to the ultimate source of its funding - the American people - to justify the enormous gap between the burden of a disease like ME/CFS and the paltry funding allocated to solving it. A disease like ME/CFS, which crosses multiple body systems, represents a tremendous opportunity for discovery. Unlocking the pathophysiology of this disease could have implications far beyond just ME/CFS. This is an area that could and should be prioritized, but instead it languishes without any focused attention. There are institutional obstacles to progress for diseases like ME/CFS, yet if those could be solved the opportunity to advance science and find treatments is enormous. If the strategic plan includes "Research Spotlights" as proposed, then I submit that ME/CFS is a case study in opportunity and trans-NIH priorities.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Under Enhancing Stewardship a far greater emphasis needs to be placed on employing scientific methods to study the effectiveness of HOW the NIH carries out it's job. For instance, NIH should employ data analysis on Scientific Peer Review strategies to ensure we are doing our utmost to ensure scientific peer review of applications is using appropriate methods. Peer Review really needs a large bolus of

money going into the IT systems used by staff involved in extramural review (IMPAC II, eRA). These systems are very old (early to mid 90's?) and have multiple layers and functionalities patched onto the system. While the system works, much of this functionality (and potentially its security) is years behind current technology. This increases staff burden, time and effort by PI's and Institutes, and time and effort by volunteer Peer Reviewers. It also would allow for easier Data Analysis and research into funding and peer review. Much of the groundwork was done by the Evergreening of Peer Review workgroup (would just need to be updated) - however, most recommendations were not adapted because of a lack of funding for these vital IT systems.

Compatibility of the framework with the broad scope of the NIH mission

Improving How NIH does it's work should be added to Enhancing Stewardship

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

NIH should look into funding scientific research into the best ways to fund research.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Areas of consideration: human nutrition for chronic disease prevention and optimal wellness. Nutrigenomics is also another important area needing advancements, as this will help personalize nutrition further with evidence based work. Nutrition and candida studies would be beneficial since anti-fungal medication many times do not work long term and this contributes to other chronic underlying problems. Food phytochemicals and beneficial components for optimal wellness.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an

NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Animals raised in standard laboratory cages are extensively deprived of the cognitive and affective stimuli essential for normal brain development. Lack of variation in the conventional environment of the lab animal also contributes to depressed immunocompetency and wound resolution. Drug trials show that most animal models poorly represent human conditions. NIH needs to squarely address the adverse sequelae of animal constraint. It's costly to move away from small animal cages to larger ones but more costly when research from caged animals inadequately represents human biology, or even the biology of a free mouse or non-human primate.

Compatibility of the framework with the broad scope of the NIH mission

Basic science needs to develop alternatives to the study of animals in highly confined cages. These studies are often not representative of free humans, or even wild mice and non-human primates.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Study of wild sentinel organisms should be included in the NIH strategic plan.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Study of wild sentinel organisms should be included in the NIH strategic plan.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

"Health Promotion/Disease Prevention" Section 1. Suggest adding "prevention" into the framework here. 2. As you study "healthy individuals," suggest you make it a priority to extrapolate findings into community-wide, population-based meta data for testing evidence-based interventions on larger groups.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-

NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Translating science into application for improving population health

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

I strongly support the current framework as written. In particular, the framework has the following strengths, which I would like to see unchanged in the final strategic plan: - A strong statement of support for basic science. I could not agree more strongly that "Basic Science is the foundation of progress." I would like the final plan to emphasize this or a similar statement. It would be useful for the final plan to specifically address how NIH will support basic science by setting funding priorities and by providing appropriate instructions to grant review panels. - I also applaud the acknowledgment that the outcomes of basic science research are often unpredictable. The recent development of CRISPR/Cas9 genome editing technology (originally found by studying bacterial immunity to phages) is a beautiful example of this. That the outcomes of basic science research are unpredictable is not an indictment of basic science; on the contrary, it is an argument for funding a large and diverse collection of basic science projects.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework
(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission
(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

The approach taken seems to be patient/individual centric, rather than population focused. I believe that the second heading should be "improve population health promotion and disease prevention". The other piece I do not see is focused on the deterioration of the global environment and its effect on health. Finally, while disparities are very important, elimination of them can be accomplished by either improving health among those groups that are not doing as well as others, or vice versa, i.e., worsening health among those doing better. So the goal should be to improve the health of everyone, along with the focus on eliminating disparities.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Assessing the impact of the demographic, epidemiologic, and nutritional transitions across populations, including preparation for these changes, and lessening their negative effects.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The three areas of opportunity are well-thought and clearly stated. Without basic knowledge of life processes acquired through fundamental science, there cannot be true progress in medicine. Promoting healthy habits and preventing disease are natural initiatives to reduce the psychological and financial burden of disease. Advancing treatments and cure is the final and essential component of the process to ensure that NIH can fulfill its mission to "extend healthy life and reduce illness and disability."

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

The Areas of Opportunity are clear and comprehensive. A trans-NIH strategic plan must, however,

integrate the three areas of opportunity. Individualized medicine would seem to integrate the three areas by requiring fundamental research, facilitating disease prevention, and advancing disease treatment. Advances in equipment and methods for life-long ambulatory monitoring of physiological processes will provide the baseline knowledge needed to clearly identify disease and to understand its progression. I suggest that the Strategic Plan Framework should include strong support for studies on biological rhythms as part of the strategy of crib-to-grave medical care.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Where is Health Disparities? Have we abandon trying to address the issues of disproportionate outcomes in some of ur most vulnerable populations? I worked at NIH for 30 years, across 7 Institutes, before I retired in 2013, and some of the same questions that we were looking at in 1983, are still on the table now. We need strpng and committed funded program, working across Instiutes to address some of these health issues. Though NIH is set up based on diseases, people suffer from CO-MORBIDITIES and therefore NIH needs to be more creative and supportive in fostering that concept. Look at issues of geographic issues and have Institutes to come together along with our other federal partners to see what and how we can work together to ADVANCE SCIENCE TO LEAD TO OVERALL IMPROVEMENTS IN PUBLIC HEALTH OUTCOMES. NIH should develop a plan to engage its retirees to assist them in some way to move these issues forward - retirees already have health insurance and etc and many of them would work for a nominal cost -- CHEAP LABOR from INDIVIDUALS YOU HAVE INVESTED IN TRAINING FOR YEARS! Think about it, untapped resources.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Promoting fundamental science is essential to advancing biomedicine. Without fundamental science, applied science will be blind and inefficient. Applied science needs fundamental science in order to know in which direction to go. Improving health promotion and disease prevention is the key to ameliorating disease. Just as with any other problem, waiting to tackle problems is bound to make the problems worse and the cures more expensive.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

The main and obvious omission is reference to behavior. Behavior is an important (possibly the most important) determinant of disease processes across the diseases. When the Strategic Plan focuses on cross-disease continuity, and when it recognizes both the importance of fundamental science and the necessity of health promotion and disease prevention, it seems essential to mention behavior.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

I have concerns that NIH is spending money less effectively than in the past. I would cite two problems. (1) giving out too many large grants and leaving good scientists and small grants unfunded. (2) trying to over-manage science from the top down (e.g. picking prioritized topics that become over funded while more innovative and thoughtful projects are unfunded. Scientific funding would be better spent by basic grassroots changes such as (1) improving the quality of scientists on review panels (use smart senior, even retired scientists more). (2) level the playing field so that grants are reviewed on quality alone, not on the institution submitting the proposal. (3) make sure that review panels are balanced in perspective. A review panel with too many genomics scientists will inevitably fund genomics grants when more funding should go to physiology and biochemistry grants.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-

NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

1. Vitamin D deficiency and the importance of monitoring for 25(OH)D levels, replacement with sufficient D3 to achieve levels for prevention of medical and psychiatric disorders (40-60 ng/ml) and the early screening of pregnant women, babies, children, adolescents, adults, and elderly. 2. Deprescribing drugs that are not effective, have adverse effects, and drug interactions to reduce the cost of care and hospitalizations. 3. Substance use/abuse across the country for treatment 4. Dental care that is affordable and available to all US citizens

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

I am urging you to focus the grants on getting treatment and services including talk therapy to those with serious mental illness. These grants should NOT be used for the worried well or for health people. Over 10 million Americans suffer from very serious mental illness

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

If we want to invest in preventive medicine, early diagnosis, health literacy, and bending the health care cost curve, we must invest in the health of children. If there is to be anyone left in the U.S. who is sophisticated and patient enough to understand that unpredictable basic science is a wise, if not risk-free, investment for the ultimate health and well-being of mankind, we must also invest in educating the lay public and training and nurturing the physician-scientist workforce in this regard. The palpable defeatism of the latter and anti-intellectualism of the former are, at least in part, the fault of us, the scientific community. We must fix this before there are none of us left.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

i see nothing in this framework that emphasizes the importance of individual investigator-initiated research. The framework is perfectly compatible with a continued emphasis on big science at the expense of the RO1 pool - a trend that I think is slowly eviscerating American science. A commitment not just to fundamental research (an ill-defined concept in the framework so far) but to individual investigator-initiated research as the backbone of biomedical science is essential.

Compatibility of the framework with the broad scope of the NIH mission

It's so vague so far that I suppose it has to be compatible.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

The importance of model organisms A vision of bench to bedside as a circular rather than linear process. In other words, it is not just basic research that leads to clinical advances; it is also that observations of human disease by attentive, curious, scientifically trained physicians lead to advances in fundamental understanding of biology as well.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Co-morbidity between diseases A gradual movement away from a phenotypic disease focus that emphasizes organs and tissues towards one that emphasizes fundamental biological pathways and processes that are involved in disease. There is some of this in "Breakdown traditional disease boundaries" but I think it needs to be much more specifically stated.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

Not obviously

Future opportunities or emerging research needs

Bone and skeletal disorders Fibrosis Any neurodegenerative disease you can name. The paucity of funding for those disorders is a national disgrace.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The NIH does a great job at funding fundamental research and promoting health and disease prevention, but is weak in the area that really matters Treatment and Cures. A treatment product i.e a FDA regulated device, drug or biologic. It is something ONLY a for-profit business can organize and make available to the public and not a university or a not-for profit. Only 2.5% of the NIH budget is actually allocated to creation of real products and services. 1. A study done internally at Rice University found that of the billion or so NIH dollars coming into the Texas Medical Center, less than 1% was realized as an actual product or service. That is a poor score. Commercialization should be given equal weightage as fundamental and preventative research. 2. FDA regulated translational research is done by for-profits at non-profits. So clearly translational research dollars should go to small business. 3. NIH should ensure that research done is 'FDA regulated' with a pathway to approval either 510k, 513(a)(1) or PMA. FDA

pathwayless translational research does not result in a product or treatment. 4. The failure of small businesses who do take the risk is due to inadequate funding by the NIH aptly called the 'valley of death'. Why do this? Is it really necessary to go hat in hand and sell years of hard work and IP to vulture capitalists and private equity? They mark up products by 1000x and encourage off label use. This whole aspect is soul killing at its best. THE CURRENT FRAMEWORK LACKS THE EXECUTION PIECE, OR WHERE THE RUBBER MEETS THE ROAD. UNLESS SOMEONE ACTUALLY TAKES THE RESEARCH AND MAKES A PRODUCT, GETS FDA APPROVAL, SCALES UP MANUFACTURING AND SELLS IT, THERE IS NO TREATMENT OR CURE MADE AVAILABLE TO THE PUBLIC.

Compatibility of the framework with the broad scope of the NIH mission

The NIH's mission is to help create products and services for patients. The journey starts with basic research, but ultimately has to have some real world use. Over time I have seen this discussion morph into who is getting what from the non-profits, who are the recipients of 97% of the NIH budget. NIH grants basically fund the non profit sector. Small businesses are the muscle that pull this cart with less than 3% of the budget and get these ideas into concrete solutions, FDA approved and into the hands of doctors. Small businesses live in the real world, pay theirs bills and taxes, and have to close their doors for good when the money runs out, unlike the non-profits. The NIH should seriously consider increasing the percentage to 50% of NIH allocated funds from 2.5% to small businesses. Increase the length of grant support to 8-10 years with emphasis on FDA regulated translational research, which takes a lot of money and time but results in a real world devices, drugs or biologics.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

1. NIH does not pay for patent fillings in SBIR Grants. It is an unallowable expense. Why pay for the research, require patents to be reported in iEdison, but not pay for the patent protection? Patent protection is really important for commercialization. Think about it. NIH pays for for the walls and ceiling, just not the floor. Why? 2. Why does NIH pay for unregulated translational research that does not end up as a product? Who benefits from that? Big pharma of course. Their approved products, get used off label without FDA approval with a wink and a nod from all concerned. Most NIH translational research is with approved products. Why? 3. A phase IIB SBIR should NOT require a matching amount from outside investors. Why is it assumed that a small business's success is based on outside investment? Diverting precious time and effort towards fund raising and bringing in investors on the cheap at an early developmental stage actually creates conflict and may destroy the small business as the founders are made to exit. Remember how Steve Jobs was thrown out of Apple almost destroying it. 4. There does not have to be a valley of death and if NIH could support small businesses to viability. It would change the dynamic and priorities from return on investment (investor centric) to helping people survive (patient centric). Founders are usually motivated to do good and create value, while investors are only interested in money.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

I applaud the emphasis on the importance of basic science research. It is far too premature to turn solely, even largely, to translational research since we still need to learn a great deal about normal physiology and disease pathophysiology before such translation can be truly effective.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

1. It is important to emphasize the crucial role played by investigator-initiated research. NIH should place a greater focus on this, with less focus on RFAs and contracts. RFAs and contracts are appropriate under some circumstances but I believe are being used too much at the present time. 2. My hypothesis is that the focus on RFAs and contracts is being driven, in part, by a lack of faith in the review process. In other words, extramural program scientists are frustrated with the science coming out of CSR and hence are trying to extract the best research from the community in other ways. 3. This argues for greater attention to improving CSR. Too many study sections are comprised of individuals who are not leaders in their field. 4. Finally, on a separate note, it is essential that grants be awarded based on merit, with no "penalty" to well-funded individuals. We want to avoid an "Occupy NIH movement"--the NIH equivalent of Occupy Wall Street. For NIH to truly derive the maximal scientific productivity from its budget, grants must be given on merit. The absurd opposite extreme would be to disband CSR and simply award a single capped-budget R01 to every individual with a full-time tenured faculty appointment in the US. That would "spread the wealth" but be disastrous for the nation's research enterprise. Let's avoid that absurd outcome and stick with quality and productivity.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

My comment involves the extensive inefficiency of the grant review process. Doctoral level researchers waste millions of hours every year applying for NIH grants that never receive funding; the NIH and external reviewers waste millions of additional hours reviewing unfindable proposals. The whole PROCESS could be made much more efficient for all involved if grant proposal were staged; brief proposals, perhaps focusing on innovation, should be evaluated prior to a request for submission of a

full grant when appropriate. This would winnow down the most promising ideas much more quickly. Applicants would waste much less time pursuing unpromising ideas and NIH and reviewers would focus their valuable time reviewing the most exciting ideas.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The framework works o.k. for supporting fundamental research but is antithetical to some of the core principles of innovation. I represent a private foundation . . . that funds medical research. We have conducted a detailed review of the types of projects and scientists being funded by NIH in the area of tick-borne diseases. The controversy in this field clearly indicates that a lot of work needs to be done to cure Lyme disease and other tick-borne diseases. While some of the fundamental research that NIH has funded in this area is extremely valuable, there is a complete void of funds being directed to a team that will solve the whole problem. In order to truly innovate, it is critical to fund a team of scientists with a proven track-record for large-scale innovation (not scientists who have a track record of advancing the field by millimeters at a time). This team must work on multiple paths in parallel because the paths will likely inform each other and create synergies. And the team must receive a large multi-year grant (read: high-risk) in order to hire and retain the best talent. This is how you drive innovation. I know this because I lead a team of 100 engineers at a solar R&D lab owned by . . . , and all we do is innovate.

Compatibility of the framework with the broad scope of the NIH mission

The NIH talks about supporting innovation, but as far as I can tell that is in name only. The framework needs fundamental changes as discussed above in order to achieve its mission. Part of the problem is that NIH grants utilize a peer-review process and this process will usually dumb down the list of grantees to those that are safely incremental and in the middle of the fairway. Truly creative thinking does not stand much of a chance with peer review, especially if the peer group does not include a majority of scientists that have a proven track record of major innovation in their field. Think of it this way: would private industry utilize a peer review process to solve problems? No. And the reason is because industry understands that out-of-the-box thinking combined with deep knowledge of fundamental principles is how you solve problems. A democratic process where everyone has to agree is antithetical to problem

solving. Thus, the framework is NOT compatible with the NIH mission.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

The NIH needs to figure out a way to allocate a portion of the money to fundamental science and a portion of the money to high-risk, high-reward innovation. I strongly recommend that the NIH create an innovation team and take some classes on the topic. Hire innovation consultants. Study innovation. If you want to achieve this part of your mission, then you need to understand what innovation is. I have reviewed research proposals from almost all of the scientists working on tick-borne diseases and the group of those proposals that I would fund vs what the NIH would fund has almost no intersection. As an expert in the innovation process--hundreds of millions of innovative products that I invented have been sold to date--I strongly suggest that the NIH try to figure out why there is almost no intersection between what I would fund and what NIH would fund. To summarize: 1) You need to study the process of innovation; 2) You need to figure out how to allocate a significant portion of your funds to non-peer review, high-risk, high-reward projects; 3) You need to figure out how to fund teams of scientists with a track-record for major innovation (not incremental progress) that take on the mission of curing the disease, not just incrementally advancing the field, and the teams have to work on multiple paths simultaneously; and 4) You need to figure out how to fund research that may not fit neatly into traditional categories.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an

NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Further clinical evaluation of medical efficacy of marijuana and its component parts (e.g., cannabidiol) for a variety of conditions and diseases

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

the terms "biomedical" and "biomedicine" are limiting. We nurse scientists are concerned with 'health' as are our medical colleagues. Therefore, let's use the term "bio-health" to be more inclusive. This could lead to fewer disparities in the long-run, if we had a more inclusive term, which would reflect the role of nursing; i.e., advocacy, looking at behaviors, as well as only medical issues.

Compatibility of the framework with the broad scope of the NIH mission

the mission is inclusivity--collaboration-- of health sciences . Let's use terminology which reflects this.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

"bio-health". thank you for this inquiry, a demonstration of consensus building!

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

We have a new, pressing, growing and unmet national health need: the compilation, organization,

homogenization and stewardship of the genetic sequencing data that is currently being obtained for research and clinical purposes. There is no entity of sufficient size other than the NIH that can provide this function. Without it, the genetic sequencing data is often worthless, and will remain so until we can compare the data to very large populations and thereby understand how to interpret the data currently classified as "variants of unknown significance". Otherwise I think the document is great.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

see above

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

I am a parent and a spouse of individuals with serious mental illnesses. As an active community mental health advocate and commentator, I have carefully educated myself on our current understanding of mental illnesses and their treatment. Much of the focus of psychiatric and psychological practice, therapies, and research has been focused on "the unhappy well" to the detriment of those with serious mental illnesses. This reflects the general human preference for "picking the low hanging fruit" as the problems and issues of serious mental illnesses are much less tractable. Therefore, I strongly urge that the strategic plan adopt an overall strong focus on serious mental illness. I find the entire section "Improve Health Promotion and Disease Prevention" troubling. There is little to no evidence that investing in studying healthy minds or early diagnosis/detection is pertinent to addressing the needs of those vulnerable to or already the victims of serious mental illnesses. I strongly urge that the strategic plan actively discourage such unfruitful endeavors within the five year scope of the plan. Additionally, the largest disparity in the mental health field is the lack of focus on funding for treatment and research relevant to progress on serious mental illnesses. This is most glaring in the institutionalized avoidance of treating those with anosognosia. (Waiting to treat the mentally ill who can not recognize their own illness until they ask for help, is the equivalent of waiting for a dead man to plan his own funeral.) Therefore, I most strongly urge that in addressing health disparities funding basic research on serious mental illnesses be one strategic focus and addressing the issues of anosognosia be another .

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Areas look find but unclear about the balance between basic and applied research. I am in addiction treatment and one of the big, correctable problems, is that a lot of what is known to help is not being applied, so in this area there is a lot of public health benefit that can result from applying what is known. Many of the barriers are attitudinal and have to do with funding decisions. An excellent example is the judge in NY who ordered a patient stably maintained on methadone to detoxify and he died of an overdose 2 weeks later.

Compatibility of the framework with the broad scope of the NIH mission

OK if attention paid to applied vs basic research; balance may differ according to area.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Documentation of the degree to which what is known to work is being used

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Nothing to add to above comments

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

Be careful about who is chosen for study sections. Have seen some very bad grant reviews

Future opportunities or emerging research needs

There is a lot of interest in using EHRs to reduce costs of clinical trails. The best studies using "big data" seem to come from countries that have national health systems with centralized records. Studies on advantages and limitations of our current health system as it relates to the ability of EHRs and "big data" to get meaningful answers to important questions might be worth a try.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The framework as stated completely overlooks the challenges of dissemination and implementation of NIH funded discoveries. This is a trans-NIH challenge. Advancing the science of HOW to effectively disseminate and implement findings so that they improve the health and lives of the people who could most benefit is crucial. Especially the challenge of doing this at scale, not just in 40 or 50 hospitals across a small region, but in thousands of hospitals, ICUs or primary care clinics across the U.S.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-

NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Using advanced complex network science principles to understand HOW to spread and implement NIH funded research findings and evidence into the communities and settings where the individual patient receives care.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

I would recommend that two words be added to the bullet under "Improve Health Promotion and Disease Prevention"... "Importnace of studying healthy individuals and populations." For example -- within every modern population, there is an SES gradient in health. But in the United States this gradient is larger than in other rich countries, and it is increasing just in the last few decades, and the size of the gap varies across regions. We may be able to learn something by comparing healthy and diseased and disabled individuals within a population, but it would likely be more productive to use multiple levels of analysis, including above the level of the individual organism -- why are the health consequences of failing to complete secondary school so much more severe here than over the border in Canada? Both basic science and translational research could benefit from a population perspective.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

More attention should be paid to children. The foundation for future chronic diseases is laid during the first 20 years of life. Lifestyle and nutrition have a major impact at this age and also determine future healthy or unhealthy behavior. Japan has the highest life expectancy in the world, while the USA is # 40 behind many other countries. Japanese children should be compared to children of Japanese immigrants in the US, other children in the US of high and low economic status (in all 4 groups). Nutrition and life styles should be determined and predictive biomarkers developed..

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

There are no provisions made for patients with this condition. This is scandalous as it is estimated that there is a minimum of 7,000 (seven thousand) people with ME/CFS in NORthern Ireland alone. This figure is likely to be much higher if diagnosis was offered. We need more training and more consultants. Thank you

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

This could be our error, but we are not seeing any clear study of the effects of medical and environmental issues on the human brain or neurosciences, as part of the whole picture. Our foundations have a variety of world experts who strongly believe that it's this very lack of integration that has kept us from progressing in our knowledge. We keep looking at the proverbial elephant through the microscope, and missing the full force of a much larger picture.

Compatibility of the framework with the broad scope of the NIH mission

Again, we would revamp the mission to understand that what effects man's body, systems, organizations and environments, also effects man's brain functionality. And what effects our brains will ultimately determine which responses and courses of action we will even recognize, or study, let alone grasp as significant. We need to build a path across studies, and look at ALL of the options available, and how they might interact with one another. For example, drugs that are tested for one purpose, frequently turn out to be useful for something entirely different. Furthermore, if a large portion of the positive effects of drug studies turn out to be nothing more than placebo, and not dependent on the drugs themselves, only without endangering our bodies from side effects, then why wouldn't be take the placebo effect seriously and use it, in a variety of other circumstances? What constitutes a placebo effect on our environment, and do plants and animals respond to the placebo effect as well?

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

As stated.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

There are so many. We wrongly assume that various aspects of sciences, such as of our bodies, our planets, our environments, and our functionalities are too disparate to cross over disciplines and / or boundaries. This is a limiting assumption that prevents us from learning all we need to know. Balance is a key ingredient in most parts of our world, whether in living things, or chemistry, as all things seek to react to each other, seeking some middle group where they may settle comfortably.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

It has been our experience that the sum of the parts is always greater than the whole. And we have further learned that this strategy applies to parts of our bodies, our systems, our environments and beyond. What this means is that it is only by combining, conjoining and bonding various groups together that we begin to fully comprehend the capabilities of individual parts. And this process itself depends on the concept of interaction, or reciprocity. That is, as soon as information, for example, is shared, then the second group has the opportunity to reinterpret what the first group has said, and the first group may then add their own response to the responses of the second group, and so on. This is where scientific studies fall down flat, when they do NOT allow multiple groups to interpret and reach

conclusions about the same data or results, yet from different perspectives, and NOT necessarily by simply redoing the same experiments. That is, redo something with a new variable each time. Science is NOT always as stagnant as we believe, and things can and do change over time. Sometimes, the most helpful thing that a neuroscientist can do, for example, is to talk to an environmental expert and a medical doctor about his findings, then determine if there are any traits, patterns, or similarities across the groups that might offer deeper explanations of commonalities, or of opposite extremes, which may also offer relationships that we forgot to explore.

Future opportunities or emerging research needs

Why do we humans insist on isolating pieces so severely? Why not start by separating things into larger groups, and then just looking to see how the groups might relate, interact with, or pertain to each other? Then move things around and try again? Why not keep asking questions, testing and trying, until we either prove, or disprove things, rather than making assumptions that we cannot prove relationships without reducing things to their lowest common denominators? It strikes us that science is mostly afraid to take risks, for fear that we cannot reproduce the same results, or if we do, we won't know why. Science needs to accept that there are many relationships in our world that we simply may not fully comprehend or control, and yet, they may still work, and be highly effective for solving certain problems. We simply won't always have all the answers. And, why is this a problem, if we're getting positive results anyway?

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Fibromyalgia and Chronic Fatigue Syndrome affect millions of people, disabling previously healthy and productive people and causing both suffering and great economic loss. Despite this, NIH provides little funding for this conditions. I urge increased research, both basic research into the underlying causes and treatment research.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

I am delighted to see attention to "Importance of studying healthy individuals" To this I would urge adding, as a separate bullet in the framework: "Importance of studying primary prevention health activities and interventions" Particularly in the areas of non-pharmaceutical interventions. For example, there is insufficient attention to the evidence base for early physical activity in younger children (Pre-K - 5th) in terms of impacts on risk for chronic disease development and behavioral issues requiring medication, use of potentially addictive substances (nicotine, alcohol) attainment of educational milestones, resilience and mitigation of adverse childhood experiences (ACES) and future economic attainment.

Compatibility of the framework with the broad scope of the NIH mission

Primary prevention research is highly compatible with the NIH mission of "Turning Discovery into Health". Health is not Healthcare. It is a highly appropriate role for governmental funding and interest as these interventions seldom have a remunerative market opportunity to incentivize private investment in the research. They also the key driver (and therefore potential preventor) of our poor health and high healthcare costs as a nation. It is very difficult research to do, due the difficulty of describing or proving counterfactuals and it is critically important to the chronic disease health challenges of our time. It is also critical to moving upstream to health and quality of life rather than healthcare and cure. Such research is also, at least financially, counter to the interests of the structure of the healthcare industry as it currently exists but should, if present efforts are fruitful over time, be aligned in the future.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Again, I would urge adding, as a separate bullet in the framework: "Importance of studying primary prevention health activities and interventions" This is a cross cutting concept of course, it is also foundational to our nation's health as individuals and a population.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine**Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan**

Primary prevention

Future opportunities or emerging research needs

Primary prevention

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework
(*Submitter left answer blank*)**Compatibility of the framework with the broad scope of the NIH mission**
(*Submitter left answer blank*)**Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-**

NIH strategic plan

Education and training the next generation of basic and physician scientists and providing the resources and guidance to support them as they embark on their investigative careers. I don't see this mentioned directly in the strategic plan and this should almost trump all other activities - without a new generation of engaged and competent investigators all of the research activities under the sun will be for naught...

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Capitalizing on clinically driven information e.g. clinical phenotyping, clinical exome and genome sequencing - There will be a wealth of data generated through private and third party payers - how to leverage this data that is being generated at no cost to the NIH for research purposes and harmonizing this utility across medical and research centers in the US should be a priority

Attachments: *(No attachment)*

Datetime submitted: 2015-07-23 17:42:45.51

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

We need more research and options for newer, better, more effective medications with less severe side effects for the treatment of severe mental illness in particular --preferably in the form of injectables that last more than two to four weeks in order to achieve optimum care, maximum compliance. This will alleviate costly hospitalization, costly jail and court time and costly loss of wages to family members who are caregivers, in addition to the loved one who is ill. New medications with a potential cure could revitalize our local economy by eliminating the need for redundant, ineffective, poorly funded programs/ services and save the taxpayers money and grief, especially in business associated neighborhoods where homeless individuals" live".

Compatibility of the framework with the broad scope of the NIH mission

Whatever your mission, it should have a positive, recovery based outcome for all people with severe mental illness in particular, at all stages of the illness without exclusions, and follow up programs to help reintegrate them into the communities where they live.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The premise that basic science is the foundation for progress in medicine is incorrect. The vast majority of medical innovations that have increased lifespan have been observational in nature. Examples include the microbe approach to ulcer disease, the development of antibiotics and anesthesia and the use of imaging for surgery and diagnosis. The emphasis on "data science" as a factor in medical progress is likewise unsupported by the facts.

Compatibility of the framework with the broad scope of the NIH mission

The science-directed approach provides biologists with an excuse to ignore translational aspects of medical research, and should be left to the National Science Foundation.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Recent bio-engineering advances in interventions such as image-guided surgery have become very mainstream and are now taken for granted in diseases of the spine and gut. The development of nano- and micro-robots and their integration with medical imaging is an exciting opportunity for reducing the morbidity of therapies, and should also be included.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

I don't understand the above category

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

I don't know what this question means

Future opportunities or emerging research needs

Recent bio-engineering advances in interventions such as image-guided surgery have become very mainstream and are now taken for granted in diseases of the spine and gut. The development of nano- and micro-robots and their integration with medical imaging is an exciting opportunity for reducing the morbidity of therapies, and should also be included. The integration of neurosciences with imaging, and in general efforts towards the body-computer and mind-computer interface are de facto becoming key elements of medical technology, and should be included in the grand plan.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

As identified the framework of the strategic plan takes advantage of the giant steps in technology and application to health research. Another strategic effort is to take advantage of crossing over health

research silos for funding and information. My main worry of ask in the plan is for there to be some effort to address the length of time from research to implementation or practice on the street. The current timeframe is unacceptable as is the payer systems and how they accept research interventions.

Compatibility of the framework with the broad scope of the NIH mission

I agree with the direction and the level of effort demonstrated by NIH in exercising the mission.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Pubmed needs an overhaul. Not a facelift. Not some new bells & whistles. The interface is busy & confusing; it's hard to use, to support, to teach. The underlying MeSH infrastructure is creaky, difficult, odd, and not properly integrated into the search experience. There should be a more nuanced & modern implementation of "basic" vs. "advanced" searching. There must be a modernized use of color, help, set-usage, post-search analysis, data-visualization, and more. Important work in the controlled-vocabulary (indexing, "MeSH") side of things is largely ignored or badly utilized in the interface. Work with MLA, Google, Ovid, Web of Science, Apple, futurists, etc. to give the world an all-new Pubmed, one which is suitable for lay-person discovery and one which is suitable for busy clinicians and one which supports truly advanced & innovative literature-searching manipulations.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Excellent framework, but implementation leaves a major gap. Focus is on innovation, and to some extent commercialization capability. Many drugs and supplements have been proposed, patented and tested for specific pathologies (prevention and treatments), but have not been seriously tested in humans. If the drugs have significant patentability, they often will be studied with commercial funding via start-ups or other large entities. The result is that many, many people take untested, and poorly characterized supplements or over the counter remedies or preventatives. Good human clinical study data can limit the wasted money spent on non-functional agents, and hopefully increase use of ones that have proven efficacy. These proposed uses are often not novel, but are just untested in a careful study protocol. By requiring good analytical data on an agent for a required IND, that agent will be the one called out for efficacy if it works. This would limit similar agents with no good analytical data from being used. It is a way to require supplement quality control for the best materials, and by allowing claims for that one (or at least reference to the study results), it would limit alternatives similar in name only, from being used.

Compatibility of the framework with the broad scope of the NIH mission

If adequate funds were provided for such studies, not only efficacy but also mechanism understanding could be obtained. For instance: genomic, proteomic and metabolomics screening and bio-repository use. Markers of inflammation and oxidative damage would provide clues to a host of related diseases that have similar biochemistry, but different targets for damage: like IPF and Parkinson's. The cost for such studies would actually be less than traditional drug development since less toxicology needs to be done for over the counter supplements like coconut oil, i.v. ascorbic acid, or quinine. The most expensive part would be the research coordinator and the biochemical/genetic testing or MRI. PK/PD studies could provide basic science that would be useful for modified drug delivery formulations later. One example of growing need is Alzheimer's disease where mild cognitive impairment converts at a significant rate. A modest delay in that rate would have very large consequences. Care givers are desperate for clinical studies that are manageable, so good will from that group would be large. If successful, the agents would be more accessible to underserved communities than the currently overpriced hep-C drugs for instance.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Many diseases have common local pathologies such as fibrosis, inflammation and oxidative damage. However, they target different organs and at different rates as well as interact to a significant extent (e.g., persistent inflammation causes fibrosis). Many logical treatment, such as antioxidants, do not seem to work well for various reasons. The type of research proposed here could lead to occasional success, and certainly to better science that can be used later if good PK/PD studies which include micro-dialysis, for instance, are done.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Economic impact of improved health care innovations that might be imagined. For instance, a kidney repair or disease modifying therapy to prevent dialysis.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

Communication of best practice to impact use of best practice is needed since smaller sites tend to not provide the best care available. How to promote better prevention (such a more walking) for both healthy and diseased people.

Future opportunities or emerging research needs

Non-invasive diagnostic methods: using breath, saliva, urine and skin.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

I applaud NIH's efforts to Enhance Stewardship, which is described as "stewardship of the research enterprise by recruiting and retaining an outstanding biomedical research workforce, enhancing workforce diversity, , encouraging innovation, optimizing approaches to guide how decisions are made, enhancing partnerships, promoting scientific rigor and reproducibility, reducing administrative burden, and employing risk management strategies in decision-making." However, I belong to a generation of early stage investigators who remain unfunded. I was scored on 9th percentile during sequestration not awarded an R03 grant; and an R01 is clearly out of reach. I am also a Black female, membership in two groups that experience lower funding rates than non-Hispanic white males. In my experience NIH has allowed a generation of young researchers to struggle in their academic careers, forcing them to leave academic positions, failing to reward them for years of pre-doctoral and post-doctoral training. The only consolation has been the NIH Loan Repayment Program. There also appears to be no accountability required of Academic Institutions and Centers that receive T32s funding; a requirement should be to monitor the proportion of minority and female trainees who are mentored to receive K-awards, then move onto independent research careers. If these issues are not addressed then NIH will be unable to enhance stewardship of the research enterprise with an outstanding and diverse biomedical workforce. Instead, what will remain are well funded senior researchers who are better positioned to secure the majority of grant awards, and who receive accolades because they had diverse T32 trainees, yet lose track of these trainees who leave academia due to their inability to develop independent research careers. Challenges remain for junior minority investigators, and I would like to see a proposed plan on how these issues might be addressed by NIH. Respectfully Submitted.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an

NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

There is fundamental mis-orientation when moving from NIH's mission of "extending healthy life and reducing illness and disability" to the NIH-wide Strategic Plan framework, which requires activities to be exclusively framed in terms of biomedicine. In the more than 150 years since its conceptualization, the biomedical model of health and disease has been replaced by more comprehensive and complex understandings of the modes of production of disease and health and their relative patterns in our society. With regards to improving population health, the exclusive biomedical frame employed in this strategic planning is not supported by the sum of empirical evidence (Woolf and Aaron 2013)(House 2015)(Bradley and Taylor 2013), but seems rather a derivative of organizational self-preservation. Given the Institutes' influence in policy and on the scientific community, I encourage its leaders to use this strategic process to undertake an authentic reevaluation of the health-production model(s) they choose to structure the NIH's activities. At the very least, this upcoming strategic plan should incorporate a process to make explicit the evidence for and tradeoffs of using this narrowed model, and encourage review of this information by critical stakeholders.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

I'm extremely concerned about the focus of research on relatively healthy individuals, which comes at the expense of those who are seriously mentally ill and who are the most overlooked segment of the population, most difficult to treat, and least able to seek or accept services on account of being SMI. Those with SMI often live torturous lives that no one should have to endure, especially when evidence

based interventions have been shown to improve lives of the SMI. Many organizations and agencies whose purpose is or should be to make the SMI their priority, instead brush these severely ill people aside in lieu of dealing with easier to treat clients. They focus their spending and efforts on general mental wellness for mild and/or temporary mental ailments. This is not to say those are not worthy issues. But the emphasis should be on research for the SMI who are: filling our jails and prisons, living homeless and in the streets, committing suicide at high rates, committing tragic acts of violence everyday against family members or in mass shootings, all as a result of being left untreated or treated with ineffective methods. It is imperative that research focuses on the most seriously ill.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

(Submitter left answer blank)

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

To date the human microbiome project has focussed on the bacteriome in spite of the fact that recent research has shown that the fungal community can also contribute to health and disease. In certain cases the mycobiome and not the bacteriome has been shown to influence diseases (e.g. IBD including Crohn's). Study of the mycobiome and bacteriome and how they influence each other and impact disease apply across biomedicine and should be investigated.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Benefits - Define good structure to carry forward best research and practice. Challenges - "Nothing without us" is the newer version of a request from millions of able Americans with "disabilities" and the challenge is to include the wide diversity in meaningful ways to advance the NIH mission and goals. Added areas of consideration - as above and only to add "for adults of all ages) so that older adults can also be seen as potential valuable researchers and contributors

Compatibility of the framework with the broad scope of the NIH mission

We assume the NIH broad scope includes encouraging more compatible collaborations and partnerships to enhance all endeavors.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Please see above and also - Our focused interest is provision of "equal communication access" using quality captioning - high quality speech-to-text systems (still in development for increased accuracy) and professionals who have training, skills, and experience to serve so many citizens who must "listen" with their eyes. Of almost 50 million Americans with hearing loss or deafness, 95% or more do not use sign language. Quality captioning for all media (including all Internet media) is a public health concern since if there is no quality captioning, millions are excluded or get only partial messages. We suggest many more public events use "live captioning" also - vital for inclusion. Government needs to attend to these concerns and in terms of the NIH mission, we suggest there are ways to recognize and validate hearing loss as a public health concern also, as it is. One small example is the isolation and illness that too many incur due to hearing loss and not enough education or public support for resources needed. Thank you for giving us the opportunity to reply. We are not funded by NIH and wish the programs well. We would be happy to confer with others using emails to the CCACaptioning@gmail.com or on our web communications (CCACaptioning.org)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

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Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

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Future opportunities or emerging research needs

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Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Continued focus on addressing the unmet needs of individuals with severe and serious mental illness and substance abuse is critical. Future historians will say, "For shame, America. For shame. One of the richest nations in the world put individuals with severe mental illness in jails and prisons while shutting down psychiatric hospitals. For shame." NIH and SAMHSA looked the other way for decades and ignored the shameful incarceration of individuals with the most severe mental illness, indeed, supporting the closure of state psychiatric hospitals. Due to my years of intense involvement, I believe this: Initially, the motivation was in response to the horrible conditions of state hospitals; the shift was needed and welcome. However, it has been replaced by two thriving industries: community programs that train far too many compliant individuals to "malingering" for life; the other is the departments of corrections. They cry Public Safety! And legislatures respond with funds. Yes, two financially robust systems thriving on the backs of persons with mental illness and substance. Neither will give up these good customers voluntarily. THIS IS YOUR JOB. A RESPONSIBILITY YOU, TOO, HAVE SHUNNED I would love to say this "sudden awareness" of the plight of individuals with mental illness and their families is the result of advocates such as myself. Tragically, it is not the family advocates, not the voice of those with less devastating illness, not ACLU. It is the voice of the media that has shamed NIH and SAMHSA into recognizing the need for change. You, too, like people with schizophrenia or those with dual disorders must confront the challenges of Reality. You must make the choice. Good luck. I am certain you have the skill and knowledge to succeed. Just Do It. . . .

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Unsolicited proposals for the research areas that scientists find important and are skilled in are likely to result in the most efficiently spent research dollars for innovation. Multiple modest sized grants to not-so-famous researchers and institutions are also a good bet. The recent trend in trying to direct what fields of research will be funded has the tendency to cause established labs to scramble to sell themselves as competent in fields in which they are mediocre. We will also be a leaner operation without large numbers of priority setters and direction pushers. I think recent trends have caused a

bigger gap between the "haves" and the "have nots" and resulted in huge sums being spent on what people think will sell as opposed to what is innovative, fascinating, outside-the-box, etc.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Any study of the brain could potentially lead to advanced diagnostic and treatment methods for diseases of the brain like the schizophrenias and other psychotic illnesses. As a parent of a young adult with severe and persistent psychosis, we need advances in effective treatment with minimal side effects.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

There has been success in other countries with the efficacy of using CBD from cannabis to treat schizophrenia. Our research needs to include this type of study. CBD has been proven to help ameliorate symptoms of other brain illnesses, like epilepsy. There are minimal side effects from CBD. We are missing an important opportunity to help those who suffer without effective treatment if we don't study CBD.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

A curious gap is the absence of a bullet on Translation Research in clinical, prevention, and programmatic sciences. Given our poor track record on Translation, and the recent efforts by NIH to address this issue, I am concerned that Translation research does not have a greater weight in the listings (or any weight?). As a truly nascent field, substantial work is needed to move beyond “line and box models” to more sophisticated work that will be able to empirically evaluate the probability of success, costs, and value to society of translation at multiple levels of the health sciences continuum. These and other key questions await major commitment to the field of Translation sciences.

Compatibility of the framework with the broad scope of the NIH mission

Generally very good

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Translational Sciences

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

A curious gap is the absence of a bullet on Translation Research in clinical, prevention, and programmatic sciences. Given our poor track record on Translation, and the recent efforts by NIH to address this issue, I am concerned that Translation research does not have a greater weight in the listings (or any weight?). As a truly nascent field, substantial work is needed to move beyond “line and box models” to more sophisticated work that will be able to empirically evaluate the probability of success, costs, and value to society of translation at multiple levels of the health sciences continuum. These and other key questions await major commitment to the field of Translation sciences.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

no comment

Future opportunities or emerging research needs

A curious gap is the absence of a bullet on Translation Research in clinical, prevention, and programmatic sciences. Given our poor track record on Translation, and the recent efforts by NIH to address this issue, I am concerned that Translation research does not have a greater weight in the listings (or any weight?). As a truly nascent field, substantial work is needed to move beyond “line and box models” to more sophisticated work that will be able to empirically evaluate the probability of success, costs, and value to society of translation at multiple levels of the health sciences continuum. These and other key questions await major commitment to the field of Translation sciences.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

I think that this framework does a nice job of clearly articulating the key areas of focus. Considering

mental health, however, I see a problem with emphasis. As has been the subject of intensive discussion in recent years, there is a problem with an imbalance of resource allocation in the areas of basic and medical science (psychopharmacology). This has for decades not been delivering tangible results to the public. Of course it is important, but while we explore those areas there is a desperate need for an improved understanding of clinical interventions and associated implementation science. In this framework, there is minimal emphasis upon direct clinical research.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

The piece around equity is needed and relevant. Implementation science could be better referenced.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Where does this framework concentrate on the seriously and persistently mentally ill? Why is the focus on studying "healthy individual"? I'm concerned because as a parent of a son who at 23 succumbed to mental illness, I think the health crisis is with this population. I'm curious as to the "prevention" of ebftsl disease you mention: when the cause for schizophrenia and other psychotic illnesses is unknown, how are we focusing on prevention?

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

The cause of serious and persistent mental disease.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

I have difficulty with the term biomedicine which is defined as "a conceptual model of illness that excludes psychological and social factors and includes only biologic factors in an attempt to understand a person's medical illness or disorder." Is there a reason psychosocial factors are to be excluded? I think public health has shown us that Social Determinants of Health (SDOH) should NOT be excluded from our research. how about Apply Across Clinical Translational Research

Compatibility of the framework with the broad scope of the NIH mission

needs compatibility with CTSA which is focused beyond biomedicine

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

SDOH

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

genetics/genomics/individualized healthcare/medicine

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

the plan includes many areas that do not fit the definition of the term biomedicine - I think they are appropriate and would keep them - just change title.

Future opportunities or emerging research needs

genetics/genomics

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

1. NIH should not only foster science, it should serve a role in evaluating and serving as a check on pseudo-science adopted by other agencies. Ex. SAMHSA and CMS 2. For NIMH, the important thing is to focus on the most seriously ill. Am concerned about reference in framework to "Importance of studying healthy individuals"

Compatibility of the framework with the broad scope of the NIH mission

I am worried about political correctness at IOM. Ex. latest report on psychotherapy robustly endorses Peer Support but is absent evidence that peer support improves meaningful outcomes in people with serious mental illness (as their own report on veterans did). NIH has to serve as a check on pseudo-science.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

It is not enough for NIMH to support 'evidence-based' interventions, the Institute should focus on those most likely to improve meaningful outcomes like reductions in homelessness, arrest, incarceration, violence, and hospitalization rather than soft measures like "feelings of empowerment", "sense of wellness" etc.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Prioritization should be given, especially within NIMH, to improving meaningful metrics in the most seriously ill.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

NIH should require NIMH to independently opine on "programs and practices" certified by SAMHSA in the National Registry of Evidence Based Programs and Practices (NREPP). SAMHSA encourages states to spend Mental Health Block Grants (MHBGs) on these interventions in spite of the fact a) few have independent evidence; 2) few improve meaningful outcomes; 3) few are for seriously mentally ill. NIH Institutes should serve as a check on non-science proclaimed by other agencies. Ex. CMS is allowing reimbursement for "peer support" in spite of massive evidence peer support does not improve meaningful outcomes in people with serious mental illness.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The plan does not focus on improvements in the basics of patient care especially in the areas of dealing with chronic diseases on a daily basis. This should be mentioned as a primary strategic goal of the NIH along with its interest in prevention and basic medical research.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

The plan does not focus on improvements in the basics of patient care especially in the areas of dealing with chronic diseases on a daily basis. These diseases use up a large proportion of the nation's healthcare dollars and patients often require ongoing interaction with caregivers in homes, rehab clinics, and nursing homes. Improving these continuous kinds of interaction by creating safer and more usable Durable Medical Equipment devices and methods is simply "not on the NIH's radar". Some mention of addressing the basic needs of patients with chronic diseases which limit mobility and access to health care, recreation, and a better quality of life is needed in the plan.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an

NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

The NIH is very weak in looking for devices and methods of improving basic everyday patient care. Much medical care involves basic nursing practices that help patients with chronic diseases in daily living. Safe patient handling in the form of patient transfer, transport, showering, toileting, feeding, and mobility to access remote care in doctors offices, clinics, and hospitals is central to the basic health of the patient as well delivery of basic healthcare. This should be a primary strategic goal of the NIH but has been largely ignored by the NIH. The mobility aspect of patient care is labor intensive and dangerous to patients and caregivers while using up vast sums of Medicare and Medicaid dollars in hospitals, nursing facilities, and home care. The lack of NIH-supported research in improved mobility and patient care devices is a mystery given the cost of workers comp., nursing musculoskeletal, and law suits resulting from injuries as a result of patient falls and immobility (such as decubitus ulcers).

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Promote Fundamental Science, basic science is the foundation for progress. European culture gave birth to and developed modern science as a means to investigate and explain the natural world. The biomedical disciplines that have since emerged presuppose a web of basic presuppositions, background assumptions and implicit cultural values that are often overlooked and escape peer review. These “hidden subjectivities” are widely taken-for-granted while exerting a powerful hold on the scope, direction and patterns of disciplinary thought. Cognitive attachments to materialism, reductionism, mechanistic thought, naïve realism, pervasive subject-object dichotomies between mind and matter, scientist and nature, experience and reality, and values such as control over nature among many others remains largely unattended within biomedical disciplines. Most biomedical disciplines have no accepted means of collectively attending to hidden subjectivities embedded within their fundamental methods and practice. A process of critical reflection that acknowledges the cultural nature of these hidden subjectivities can allow biomedical disciplines a means for surfacing and critically examining these cognitive attachments, stimulating discourse around the extent to which they constrain and/or support the evolution of thought that complex problems call for.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

See attached article

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

It is my opinion that some one needs to look at the Thyroid numbers once again these test are not quite accurate and the symptoms of millions of Americans over ride the test results, the test results are a joke if you look on the internet at All of the people having trouble with the Thyroid, just to hear the same answer over and over again from reg M.D's People have resulted in going to Natural Pathic doctors just to find that thier symptoms were correct, doctors are not looking at the symptoms they are relying on the test you provide them with and the numbers you provide them with, can you please look into this for the Americans who suffer every day. Thank You . . .

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

What appears to be missing is any focus on health services research (HSR), which is vital to measuring changes in health care delivery that will be necessary in the future. Additionally, HSR has been instrumental in measuring health disparities and benefits/risks of the Affordable Care Act.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

(Submitter left answer blank)

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Setting Priorities Section: Setting the priorities should be based on multiple factors such as disease burden, disability factor, morbidity associated productivity loss, lack of productive research & investment currently, lack of understanding of pathophysiology of certain conditions leading to having no treatment options. Include accountability as one criteria if not the money spent on research is national waste.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Looking at the MECFS research scenario where there is no meaningful progress in decades and millions are debilitated causing a tax loss of atleast \$5Bn annually apart from economic burden due to the disease to nation, it is so imperative to evaluate any condition using the above parameters to prioritize research spend & to ensure accountability.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

I think the following areas require attention 1.- Novel ideas, clearly the old mechanisms are over explored. We need new mechanisms and approaches 2.- Then, the main challenge is bring into different areas expertise that are different. For example in HIV, the field is mostly controlled by population, clinical and applied science, but basic (basic-two times) science is poorly accepted in the area 3.- A better review process. The system do not allow to answer wrong concepts. A two way conversation is necessary. This will be constructive in the long run 4.- Identify novel (no always the same people) ideas

and approaches and support them. Look for reviewers that think outside of the box

Compatibility of the framework with the broad scope of the NIH mission

I think the framework is there, but identification of novel areas require new people and expertise

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Like journals identify the experts in DIFFERENT areas to enrich the development of novel ideas and approaches to several diseases. I really think the current efforts to provide funding to novel ideas has fail. Because the same people that is in the regular study section are in these innovative grants. We have to look for new people that see further that the ongoing efforts. The PO, SRO and other officials have this expertise

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Several new areas of research that really do not fit in any institute require additional funding. We are in the work that research in cancer can provide excellent treatment for other diseases or basic science can provide new targets for several diseases. But most of these applications are evaluated in cancer or basic science study sections. We need a group that take the risk of combining several areas of research

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

due to the interest of companies in clinical trials. we can use this interest to reduce the participation of the NIH in big and expensive testing. Companies are getting money for this. Only surveillance

Future opportunities or emerging research needs

As indicated above we need new areas of research that combined the expertise of several institutes as well as take risks on new ideas. R21 are not enough.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Population health research promises to have the broadest impact on the health of the nation. What is missing in our nation's health research portfolio is a body of science on interventions that can impact populations rather than targeting individuals. Our nation has an "illness care system". One might say that it lacks a "health promotion system." There is a unique opportunity for the NIH to provide leadership through research in informing the nature of population-based interventions that have promise for broad scale, cost-efficient health impact. Compared to other developed countries we spend more per person than any other nation, yet the nation's investment in health has not translated into better health for our people; at least not consistent with the level of our expenditures. Research must lead the way in providing the knowledge required to transform the nation's considerable investment in health, approximately 18% of our GDP, to an investment that will have a broad impact on health. Nowhere does an investment in research have the possibility of effecting better health that in research on health disparities. Epidemiological research has demonstrated that social determinants are critical contributors to health disparities. Research on interventions that can either impact these social determinants at a population level, or moderate the impact of the social determinants on health outcomes is urgently needed. Further, once such evidence-based interventions are available, we will need implementation research to inform how such interventions can be scaled-up.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Research on population based interventions that can improve the health of communities and the nations in a cost-effective fashion.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

All research is the study of differences. One special area of differences is same racial and ethnic health disparities. We must move beyond the study of the causes of health disparities to the biological, behavioral and social mechanisms by which social determinants impact the health of racial and ethnic disparities, with a focus on mechanism that are amenable to interventions.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

One area for consideration regards the current emphasis of the cellular, molecular and atomic scale, with less emphasis on the whole organism. At one level, this is reduced to a massive emphasis on cells and their contents and processes (such as signaling pathways). However, their intervening extracellular matrix (ECM), which is known to regulate cell behavior and provide structural properties on which organs depend for optimal function, is crosscutting, affecting all aspects of biology, all systems, and all disorders, yet has been relatively neglected. This is the next frontier. It is surprising that ECM molecules and assemblies, comprising as they do such a crucial quantitative and specialized component of the human organism are so poorly emphasized in training, research and translation. The current structure of NIH study sections and cross-NIH initiatives does not promote the science of extracellular matrix. As a result, there is an emerging dearth of young scientists trained in the area and thus prepared to address the needs of this next frontier.

Compatibility of the framework with the broad scope of the NIH mission

The equal emphasis on fundamental knowledge (as related to development of therapies) is laudable, because it recognizes that there is still very much to discover about how biological systems work. This seems to have been overlooked in recent years in the headlong pursuit of "translation" and intellectual property. Science and institutions have lost their way to a certain degree, by rewarding tangibles (intellectual property, impact factors, indirect costs), rather than valuing pure new knowledge. The stated framework above promotes a balanced research enterprise. It should also be pointed out that the private sector does not usually pursue fundamental knowledge, because its stakeholders (investors and employees) require and reward a marketable product. The NIH mission is unique and has distinct stakeholders from private enterprise - the taxpaying public of course, but more directly, the academic

sector (scientists, students, teacher, universities), which is a large part of our present and future workforce. Therefore, a pointed NIH emphasis on fundamental knowledge will produce a more effective public-private partnership for promotion of public health and economic enterprise, because it will complement the private sector.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Biology of Extracellular Matrix and Cell-Matrix interactions is an area I wish to see emphasized. I provide two examples where its biomedical relevance has been neglected: Developmental biology, which is typically not seen as translational, actually provides many of the most exciting advances in biomedicine, applicable to many adult disorders and tissue regeneration. Although developmental processes rely enormously on the matrix and how cells interact with it, this area has been relatively neglected by developmental biologists. The new NIH Brain initiative does not mention matrix even once. Yet, neural development, connectivity and plasticity are highly regulated by its extracellular matrix. There is quite a lot of matrix in the brain, and it is highly specialized. These are just two examples of how improved NIH funding for matrix biology to bring it on par with cell biology, would redirect many of our groups to using their exceptional skills to pursue matrix. NIH, through its funding priorities has the power to redirect science in a big way and it should use it.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

There is much justified concern that the funding paucity will dissuade young people from a career in science. Since graduate students and fellows provide the basis for our workforce, present and future, it is imperative that the NIH focus on support for and promotion of research at academic institutions.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Just from reviewing the above documentation it appears as though tails are being chased as past mediators and specialists have completed this same exact research. Duplicating their efforts will never get us anywhere at this rate.

Compatibility of the framework with the broad scope of the NIH mission

It's good if you want to waste five years of your time to try and reinvent what has already been invented. There's nothing to it but to do it. No more research needs to be completed - get to work and let's start changing things. The data and research is there, BRING IT TOGETHER and EXECUTE.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

None.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Not applicable.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

Moving from the foundation, now on to the framework of level #1. Biomedicine should not be a factor and should be null and void in all future research/projects as a whole.

Future opportunities or emerging research needs

Where is the collective data/analysis of past research and needs that were met? From there we can determine and apply opportunities for all across the board.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

Although brief, I very much like the proposed framework. In my view, NIH should be funding research to improve research methodologies as described 'clinical research methodologies stimulate scientific progress'. These advances have the potential to positively impact all research. I also strongly agree with the concept that "Leaps in Technology often catalyze major scientific advances". This is an area that, in the past, NIH has not taken full advantage. Technologies are changing very rapidly. Basing research on old technology results in studies that may be obsolete by the time that they are complete, mechanisms should be created to upgrade technologies in studies after funding has been approved. In this way, the research might be slightly riskier, but the likelihood of its meaningfulness will greatly increase. It is clearly true that: 'Data science increases the impact and efficiency of research'. NIH has done a great job in establishing data sets for use by researchers, but I believe that NIH should go further. As a condition of receiving funding for care, all major EHR systems should be required to provide de-identified data for use in research. These huge databases should prove to be a gold mine for naturalistic studies that can be validated with prospective clinical trials.

Compatibility of the framework with the broad scope of the NIH mission

(Continued from above question) I believe that 'Advances in early diagnosis/detection Evidence-Based interventions to eliminate health disparities Advance Treatments and Cures is essential. Although I am a behavioral health researcher, studying prodromal schizophrenia, I believe that across health care early intervention, before symptoms of a disease are manifest, is likely to be most effective. In oncology, we should not be performing barbaric surgeries aimed at removing massive amounts of diseased tissue. We should be eliminating pea sized lesions before they bear significant risk of destroying adjacent tissues. particularly in mental health, but in all medical disorders more broadly a "Breakdown of traditional disease boundaries" is essential. No basic nosology of mental illness, based on scientific evidence exists. It is essential that we develop detailed quantitative nosologies based on pathways and that we then aggregate the illnesses to look more holistically at the person. I don't believe that this represents a contradiction, it simply means looking at the puzzle from both perspectives. Only through this approach can we both better understand disease and its impact on people.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

(Submitter left answer blank)

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

(Submitter left answer blank)

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

I am very pleased that NIMH is focusing clinical research on 'impact'. I believe that taking on a larger portfolio of projects that have uncertain outcomes, but which have the potential to lead to a 'breakthrough' would be desirable. I believe that one of the most productive areas for cutting edge research lies at the boundary between information technology and clinical research. Using software to improve research methodologies has the potential to decrease cost and greatly expand the nature of findings that will improve quality of life. Sincerely, . . .

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

In the section entitled Promote Fundamental Science, I think it is important to mention the need for greater understanding of the newly evolved, primate association cortical circuits that are the focus of many mental disorders. The reason that this is so important is that data are showing that these circuits are often regulated at the molecular level in a manner that is very different, and sometimes even opposite, to classic synapses in sensory cortex, hippocampus, and rodent prefrontal cortex. The unique molecular regulation of these newly evolved circuits appears to confer vulnerability to dysfunction and degeneration, and thus should be a focus for both understanding the etiology of mental disorders, and identifying strategies for treatments that will be successful in human patients.

Compatibility of the framework with the broad scope of the NIH mission

(Submitter left answer blank)

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

These newly evolved circuits are afflicted in many other important cognitive disorders (e.g Alzheimer's Disease, Frontal Temporal Dementia) that are the purview of other NIH Institutes, and are now known to be fundamental to disorders of addiction as well.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Greater understanding of the primate association cortices would be relevant to disorders covered by the NIA, NINDS, NIDA and NIAA in addition to the NIMH

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

(Submitter left answer blank)

Future opportunities or emerging research needs

Viral/genetic manipulations of primate brain are beginning to see fruition, and could be a great help in

understanding how genetic insults produce higher cognitive dysfunction.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The development of a sound theoretical framework is the essence of scientific pursuit. NIH should strongly advocate the potential benefits of employing transdisciplinary approaches to the investigation. Health promotion or disease prevention has to consider both personal and societal factors that may facilitate or impede the achievement of better performance and sustainable outcomes. We need to encourage collaborative and team science to foster the R&D activities. We can't no longer ignore the need for interdisciplinary or integrated scientific research. I think that the challenge is related to the disciplinary or boundary spinning that will go beyond a disciplinary focus.

Compatibility of the framework with the broad scope of the NIH mission

The overall mission is still very disease-specific focused investigations. I believe that the next breakthrough in science is going to be evolved from a transdisciplinary perspective.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Both short- and long-term strategic plans should be well-coordinated at both academic and practicing fields. The strategic goals should target on high priority areas as noted in the recent report on County Health Rankings, prepared by the University of Wisconsin Population Health Institute. If we are going to improving the health status ranking of the US population, we have to pay great attention to behavioral and social factors that account for 60% of the total variance in health improvement at the population level.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

One potential area is to develop predictive analytics, using the Big Data-to-Knowledge approach. More specifically, we need to develop better and effective decision support systems, applicable to individual and societal changes. Simulated learning should be encouraged if we can rely on scientific evidence or models generated from researchers.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

Healthcare informatics research is a new area that will go beyond the exploration of bioinformatics or epi-genetics.

Future opportunities or emerging research needs

Mechanisms should be available to assist in the use of high-speed computers to process massive clinical and administrative data. In most of the universities, the application is very restricted to engineering and physical sciences. I think that it is a timely strategy to help universities develop and use high-speed computers for conducting a variety of team-based research in health and healthcare.

The following RFI responses were submitted as attachments through the web-based portal.²

Dear Dr. Rockey,

. . . appreciates the importance of the NIH-wide Strategic Plan and welcomes the opportunity to provide comments. . . . has been engaged in funding and advancing research methodologies since it was established in 1993, in order to provide support for the cross-cutting field of 'Alternatives' to the traditional uses of animals in research, testing and education. Our foundation has awarded a total of \$3 million to individual researchers at universities in the U.S. and has also generously supported scientific conferences.

. . . experience in the field of Alternatives is particularly relevant to this Request for Information, because it evaluates and prioritizes issues that apply across biomedicine. In particular, . . . would like to call your attention to three areas referenced in the NIH draft documents:

Leaps in Technology often catalyze major scientific advances

We agree wholeheartedly. We underscore the potential of break-through technology such as ultra high-throughput testing systems (uHTS) and organ-on-a-chip technology. uHTS are currently being used to revolutionize toxicity testing through the National Center for Advancing Translational Sciences (NCATS)-driven "Tox21" Consortium, a partnership with the Environmental Protection Agency and the Food and Drug Administration. NCATS is similarly deploying this technology to screen huge numbers of small molecules for activity against disease targets, which echoes the Strategic Plan's theme of "unprecedented opportunities on the basis of molecular knowledge." The organ-on-a-chip technology is also poised to catalyze major scientific advances, providing a much-needed model of organ-level function. This technology shows promise in dramatically advancing safety and efficacy testing.

Promoting scientific rigor and reproducibility

The widespread concern about the reproducibility of animal experiments should be targeted in the Strategic Plan. How much of this irreproducibility can be addressed by enhancements in the methodological quality and reporting quality of animal studies and how much is practically irreducible owing to the bewildering array of variables in animal experimentation (species, strain, age, animal supplier, type of caging, familiarity of animal handler, etc.)? Because of that, we would suggest that alternative (non-animal) models should be pursued. Indeed, a focus on reproducibility should be matched by a vigorous probe of the relevance of animal disease models to the human situation. Reproducibility alone is only half the issue. The five-year horizon of the NIH Strategic Plan is well timed to build on the scientific community's demonstration in recent years of a greater willingness to take a critical look at individual animal models of disease.

Encouraging innovation

We applaud the work of the NTP (National Toxicology Program) Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) in encouraging innovative methods in toxicity

² Identifying information has been removed

testing. Innovative methods of safety assessment will help reduce the unacceptably high attrition rate of promising pharmaceuticals, which will aid NIH in its efforts to advance treatments and cures.

Dear Dr. Tabak,

I write you today on behalf of the community of individuals impacted by pulmonary hypertension (PH) to thank you for the opportunity to provide comments and suggestions on developing the framework for the upcoming NIH-wide strategic plan (NOT-OD-15-118).

The . . . is a 501(c)(3) nonprofit organization, serving more than 16,000 members and suppliers. We continue to work every day to end isolation, provide education, involve our constituents in everything we do, and find a cure for pulmonary hypertension. Our mission is to find ways to prevent and cure PH, and to provide hope for the PH community through support, education, research, advocacy and awareness.

. . . has been working with NHLBI through the Institute's Strategic Vision process to promote condition-specific research opportunities. In a more general sense, I have three recommendations for the overarching NIH plan framework at this time. Specifically:

- That the ongoing process be transparent, open, and continue to include the voice of the patient community in a meaningful way.
- PH can occur as a result of numerous medical conditions and could benefit from better coordination given the rapid medical advances in the field. Attention should be given to improving cross-cutting research activities in areas that are studied by multiple NIH Institutes and Centers.
- Due in part to the successes of NIH-supported research, PH now has nearly a dozen FDA-approved therapies. NIH should expand programs to better translate breakthroughs in basic science to innovative therapies and treatment options.

Dear Dr. Tabak,

I write you today on behalf of the community of individuals impacted by . . . to thank you for the opportunity to provide comments and suggestions on developing the framework for the upcoming NIH-wide strategic plan (NOT-OD-15-118).

The . . . is the national non-profit organization for Our mission is to provide support, facilitate education, and advance research to improve the lives of affected individuals.

The . . . has been working with NIAMS through the Institute's Strategic Planning process to promote condition-specific research opportunities. In a more general sense, I have two recommendations for the overarching NIH plan framework at this time. Specifically:

- That the ongoing process be transparent, open, and continue to include the voice of the patient community in a meaningful way.
- That attention be given to breaking down barriers between Institutes and Centers when working on research of a cross-cutting nature. For example, scleroderma is a prototypical disease for studying fibrotic illness due to the fact that scleroderma can cause fibrosis in multiple organs systems. The Senate recently acknowledge such an opportunity in the Committee Report accompanying the FY 2016 Labor-Health and Human Service-Education Appropriations Bill with the following language;

- Fibrotic Diseases.—The Committee encourages NIH to continue to support research into fibrotic diseases affecting different organs, including the lung, liver, kidney, heart, and skin, and to ensure appropriation coordination between its Institutes as they conduct single organ or cross-organ fibrotic disease research.

Dear Dr. Tabak,

I write you today on behalf of the community of individuals impacted by heritable connective tissue disorders to thank you for the opportunity to provide comments and suggestions on developing the framework for the upcoming NIH-wide strategic plan (NOT-OD-15-118).

Before our founding in 1981, Marfan syndrome was largely unknown or misunderstood, but our efforts have led to many life-changing advances in our fight for victory over Marfan syndrome and related disorders. We tirelessly advance research for treatments that save lives and dramatically enhance quality of life for affected people. We provide a supportive community for everyone affected by Marfan syndrome and related disorders. We always have the latest and most accurate information, and we educate everyone—from patients and families to medical professionals and the general public—about Marfan syndrome and related disorders.

The Foundation has been working with NIAMS through the Institute's Strategic Planning process to promote condition-specific research opportunities. In a more general sense, I have three recommendations for the overarching NIH plan framework at this time. Specifically:

- That the ongoing process be transparent, open, and continue to include the voice of the patient community in a meaningful way.
- That NIH consider opportunities to ensure that data and information from supported studies and registries continue to be made available so that researchers can build off of these important efforts to further advance science as opportunities continue to emerge that improve healthcare costs, quality, and outcomes.
- That NIH provide innovative support so that breakthroughs in basic science can ultimately, become innovative therapies and treatment options.

Thank you for your time and your consideration of this request.

Dear Dr. Tabak,

I write you today on behalf of the community of individuals impacted by peripheral autoimmune neuropathies to thank you for the opportunity to provide comments and suggestions on developing the framework for the upcoming NIH-wide strategic plan (NOT-OD-15-118).

The . . . is the preeminent global non-profit organization supporting individuals and their families affected by Guillain-Barre syndrome (GBS), chronic inflammatory demyelinating polyneuropathy (CIDP), and related syndromes such as multifocal motor neuropathy (MMN) through a commitment to support, education, research, and advocacy. We work to ensure every person affected by GBS, CIDP, or related syndromes such as MMN, will have access to early and accurate diagnosis, appropriate and affordable treatment, and knowledgeable support services. In this regard, the organization advances research, promotes education, and supports the community.

The Foundation has been working with NINDS to promote condition-specific research opportunities. In a more general sense, I have two recommendations for the overarching NIH plan framework at this time. Specifically:

- That the ongoing process be transparent, open, and continue to include the voice of the patient community in a meaningful way.
- That attention be given to adequately supporting conditions with cross-cutting research value, particularly autoimmune diseases. NIAID and other Institutes and Centers at NIH have a tremendous opportunity to improve our understanding of the mechanisms of a number of diseases through coordinated, sustained, and reinvigorated efforts in this area.

Thank you for your time and your consideration of this request.

Dear Dr. Tabak,

I write you today on behalf of the community of individuals impacted by . . . to thank you for the opportunity to provide comments and suggestions on developing the framework for the upcoming NIH-wide strategic plan (NOT-OD-15-118).

The . . . is a 501(c)(3) non-profit organization with an ever increasing worldwide membership. . . . is dedicated to serving patient, parents, professionals, and others impacted by The organization's mission is to improve the quality of life and care for affected individuals and families through collaborative education, advocacy, research, and support.

The Foundation has been working with NIAMS through the Institute's Strategic Planning process to promote condition-specific research opportunities. In a more general sense, I have two recommendations for the overarching NIH plan framework at this time. Specifically:

- That the ongoing process be transparent, open, and continue to include the voice of the patient community in a meaningful way.
- That an acknowledgement is given to healthcare costs, quality, and outcomes so breakthroughs in basic science have the necessary support to be translated into innovative therapies and treatment options that improve and extend human life.

Thank you for your time and your consideration of this request.

Dear Dr. Collins:

On behalf of the 7.5 million Americans living with . . . , the . . . appreciates the opportunity to offer comments on the National Institutes of Health (NIH) Five-Year Strategic Plan. . . . is deeply committed to the work of the National Institutes of Health (NIH). As the agency gathers input from stakeholders, we hope that the NIH will continue to incorporate the patient perspective in its mission to support and pursue biomedical research.

. . . is a member of the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) Coalition and works closely with the Director and staff to drive discovery and development of medical treatments and cures. It is clear that a significant amount of work has gone into this effort during the last strategic plan period. Overall, we applaud the NIH and the 27 Institutes, Centers and Offices (ICOs) for providing guidance and direction of the context of the plan that will both include patients in the biomedical research process and address unmet medical needs.

. . .

As the NIH continues to build upon the framework, the . . . urges you to strongly consider the following specific recommendations in ***Areas of Opportunity that Apply Across Biomedicine:***

Fundamental Science: Compatibility of the Framework with the Broad Scope of the NIH mission

We applaud this section, as the primary funder of scientific research in this country, it is important that the NIH is transparent in how it decides what to fund, effective in funding the most important research, and flexible enough to adapt to the rapidly changing research environment. We are aware that NIH's 27 Institutes and Centers have already developed their own strategic plans. We believe that high-risk, high-reward science can yield major breakthroughs and recognize that the most effective therapies for psoriasis, psoriatic arthritis, and many other diseases result from targeted disruption of fundamental biological pathways. Yet, the current federal research structure often does not incentivize this type of research.

Access to breakthrough therapies and devices is important to people with psoriasis and psoriatic arthritis. Building, maintaining, and effectively analyzing large datasets for the sake of scientific exploration and evidence-based treatment is of great value to patients. Patients and physicians need better ways of becoming informed of clinical trials, and researchers and health care providers need access to data that will help direct them towards the most pressing research needs and ultimately improving quality of care. A data sharing framework could help achieve this goal so capitalization on the recent trend of registry development should form a key component of the strategic plan. Further, the needs of children with chronic disease are sorely unmet in this country; building a dataset across

multiple institutions sharing the common goal of helping children will help meet this need. We recommend that you include patient advocacy groups in the consultation with clinical experts section, as organizations like the . . . are heavily involved in registries. Such partnerships would help the agency determine the unmet needs in various disease communities and having access to NIH data would benefit private foundations like the . . . best direct their resources to support their community through education and research.

Improve Health Promotion/Disease Prevention: Potential benefits, and Areas of Consideration for the Current Framework

. . . believes that patient aspirations and goals should guide all decisions related to the care of patients with chronic health needs. Chronic disease management with the patient's aspirations and goals in mind ensures that care provided is appropriate both to their needs and their wants. Experiential knowledge informs the patient's journey in treatment and care for their chronic health needs. There must be a balance to ensure that patient-centered care is achieved. The goal of this approach is not only to improve outcomes, but also to ensure that medical decisions are made in consultation with the patient and support the patient's immediate and longer-term aspirations. Aforementioned, there are several public health aspects of psoriasis which are not formally captured in clinical trials. These aspects include monitoring and addressing the health related quality of life effects as well as the comorbidities associated with psoriasis. The disparities that exist among women and minority participation in clinical trials isn't enough for clinical significance. The strategic plan is an opportunity to change the way clinical trials in drugs and devices are conducted.

Additionally, we know the next generation of researchers is critical to maintaining America's status as a leader in biomedical research. The framework that encourages efforts to cultivate young and future scientists in pursuing careers in research is critical to the long-term health of our nation's scientific efforts.

Advance Treatments/Cures: Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

The patient experience plays a significant role in how, and if, a patient engages in disease management. Trends that have pushed payment and delivery models away from traditional fee-for-service systems toward value-based care can improve the patient experience, which we believe is deeply linked to improved health outcomes. Technologies incorporating telehealth capabilities and remote monitoring help patients remain proactive in their health management without burdening providers who are already spread thin. These innovative models and tools are the future of an evolving system and can be used more effectively if the patient is targeted in their design and implementation. While improving chronic disease care will take time and require effective partnerships between health plans, drug manufacturers, providers, and patients, these investments will both improve outcomes and lower overall costs associated with chronic conditions.

Conclusion

The . . . thanks the NIH again, for this opportunity to comment on the strategic plan framework. We believe that our recommendations and comments can make a tremendous difference in the lives of 7.5 million Americans living with psoriatic disease. We are optimistic about the direction and guidance of the NIH and look forward to our continued relationship. If you have any questions about these comments, please contact Thank you in advance for your consideration.

Dear Dr. Collins:

. . . , appreciates the opportunity to submit comments in response to the draft framework that has been disseminated for an NIH---wide Strategic Plan.

As the leading sponsor of research in the US and worldwide, the NIH has long recognized the central importance of human subjects protections, the ethical conduct of science, and scientific integrity in its stewardship of the research enterprise. With its encouragement, ethics has become an integral component of scientific design, the training of scientists, grant and contract review, and the sharing and dissemination of research results. We respectfully suggest that the NIH build on this history by ensuring that its new strategic plan emphasizes the centrality that ethics plays in the research enterprise. Specifically, . . . urges the NIH to carefully consider elevating ethics to a unifying element within its framework.

In addition to the two unifying principles already identified in the framework—Set NIH Priorities and Enhance Stewardship—. . . encourages the NIH to incorporate the following unifying principle:

Integrate Ethics—NIH integrates ethics, including principles for the ethical conduct of science, robust human and animal subject protections, and scientific integrity, by ensuring that ethics is an integral component of scientific design, the training of scientists, grant and contract review, the sharing, dissemination, and assimilation of research results, and public education.

Without question, the success of the three crosscutting objectives that the NIH identifies in its framework—promoting fundamental science, improving health promotion and disease prevention, and advancing treatments and cures—rests on a scientific enterprise that is and *appears to be* based on ethical principles, including transparency and independence from financial and other outside interests. A new NIH---wide Strategic Plan provides an opportunity for the NIH to communicate its commitment to these ideals.

In response to the National Institute of Health’s (NIH) request for comments on the strategic plan framework, we would like to offer our feedback. The NIH has been pivotal in supporting organizations dedicated to biomedical research and improving health outcomes in our country. Echoing the mission and values of the NIH, we recommend the current framework be amended to include *Diversity* as a unique pillar of focus, rather than a subsection. The importance of diversity in biomedical research has been well established among scientist, and given the increasingly changing demographics of the U.S, diversity will become more important in overall health outcomes. With this trend in mind, we recommend implementing a diversity pillar into the strategic plan as its own, distinct component. This overarching, trans-NIH theme could include subcategory plans that improve health disparities and increase diversity over a 5-year term, and could build on the current divisions dedicated to diversity. The areas of opportunity, and unifying principles outlined in the current NIH strategic framework are seamless, however we would encourage the NIH to implement a *diversity* pillar, with several subcategories that can be implemented over the term. An example of the diversity strategy bullet is outlined below:

Diversity:

1. Improve Diversity in Biomedical Research

- Increase funding & support for research in therapeutic areas that particularly overburden minority communities, including: Heart Disease, diabetes, HIV/ AIDS, and breast cancer.
- Increase research on reasons for barriers to minority participation in clinical research.
- Make efforts to support small organizations or individual researchers that have strong presence in minority communities.

2. Expand National Institute on Minority Health & Health Disparities:

In efforts to improve minority health we recommend that the NIH implement a short and long-term plan to expand the NIMHD by a) increasing research on health disparities, b) expand funding for health disparities and minority organizations, and c) increase training and research opportunities to minority and underrepresented groups.

- Create a long-term strategy to increase staff in the NIMHD.
- Implement a short and long-term strategy to increase funding for research in therapeutic areas that overburden minority communities.
- Assure that clinical trials adequately represent the incidence rates of diseases or conditions being researched.
- Increase support for studies researching social determinants of health, and overcoming social barriers to healthcare.

3. Increase Training Opportunities:

Minority researchers are often leading in ethnic minority research, thus, improving access to training opportunities for minority individuals interested in research will increase clinical research in minority health topics. Increasing training opportunities will also improve diversity in the biomedical field.

- Implement action plan to expand Diversity Program Consortium over the next three years.
- Increase number of training and educational opportunities for minority and disadvantaged individuals interested in biomedical research.
- Create a strategy to increase interest in health disparities research, and ethnic minority health by hosting seminars, training sessions, and cultural competency

Dear Dr. Collins

The . . . appreciates the opportunity to comment on the framework for the overarching five year NIH strategic plan. The focus in the framework on improving health promotion and disease prevention and advancing treatments and cures are very important areas for cross-cutting research. For kidney disease there are many opportunities within these two areas. Improving diagnosis and detection of kidney disease is an important public health and patient safety issue that staff at NIDDK has been working to address, in addition to its work to improve outcomes for those with the advanced disease including kidney failure. However, greater resources and collaboration are needed to support these efforts. Over 26 million people have Chronic Kidney Disease (CKD), yet only 10% are aware they have it¹ and another 73 million are at risk. Over 636,000 Americans have End-Stage Renal Disease (ESRD). A recent study published by researchers leading the CDC's CKD surveillance program shows that the burden of CKD is increasing and that over half of U.S. adults age 30-64 are likely to develop CKD.² Yet last year, only \$551million was allocated to NIDDK for kidney disease research. With this in mind, . . . offers the

following considerations to assist NIH in the development of a five year strategic plan that will be submitted to Congress in December 2015.

Within the advancing treatments and cures priority there are two critical concepts identified: 1) breakdown of traditional disease boundaries and 2) breakthroughs need partnerships and often come from unexpected directions. These two concepts should also apply to the health promotion and disease prevention priority. In fact the breakdown of traditional disease boundaries could be a stand-alone “main area of opportunity” or a “unifying principle” as breaking down disease boundaries and building partnerships are important across biomedicine research priorities. For example, both are critical aspects in advancing early diagnosis and detection of kidney disease – which is often caused by other underlying conditions most notably diabetes and hypertension. In addition, kidney disease is a risk factor for cardiovascular disease, bone disease and other comorbidities. Collaborative research efforts across NIH Institutes and on kidney disease could lead to improvements in outcomes in other disease states just as a focus of kidney disease as an outcome in other disease states could lead to greater insight on how to prevent kidney disease or delay its progression.

External partnership is also important to creating efficiencies in research and in turning research findings into new treatments, prevention strategies, and cures. A great example of interagency and external collaborations is the diabetes prevention program, which used NIH research findings to create evidence-based programs, operated by external organizations in cooperation with the CDC. A similar approach could also work in kidney disease.

Great research is being conducted on kidney disease at the CDC to study the burden of kidney disease and the impact of early diagnosis and detection. CDC’s findings, on the disease burden and cost-effectiveness of testing at risk populations, provide not only a case for a much needed investment in preventing progression of kidney disease but also provides a foundation for further research into evidence based strategies and programs that can address kidney disease early on. Further partnering externally with organizations that are working on evidence-based practical solutions to address kidney disease and assess outcomes can further national disease prevention goals. For these reasons it is also important that NIH focus on pragmatic trials.

. . . appreciates recognition in the NIH framework that data science increases the impact and efficiency of research. The United States Renal Data System has provided for over two decades of data on outcomes, treatment patterns, and costs associated with end-stage renal disease and for the past eight years expanded its scope to provide data on CKD. There is no doubt that this data has facilitated greater research, interventions, and understanding in kidney disease. However, there remain gaps in collecting data on people with CKD, particularly those under age 65. A CKD registry could help bridge that gap. Therefore, . . . encourages NIH to continue its focus on supporting and funding data collection and registries.

Within the area of opportunity for health promotion and disease prevention, addressing evidence based interventions to eliminate health disparities is an important topic and yet another example of where external partnership is important given the multitude of agencies and organizations focused on this area. In addition to practical interventions, there remains a need for research into the causes of health disparities including potential genetic causes. For example, kidney disease has a disproportionate impact it has on minority populations – most notably faster progression of disease among African Americans that is unexplained by other risk factors such as age, sex, diabetes, blood pressure, albuminuria,³ and socioeconomic status. However, new research suggests two APOL1 gene variants (G1 and G2) found in

some African Americans is an independent contributor of faster progression to ESRD regardless of cause of CKD. Approximately 16% of all African Americans carry two risk variants and thus have a genetic predisposition to developing non-diabetic end-stage kidney diseases.⁴ Genetic variants in APOL1 are thus common and confer strong risk for ESRD and may be one of the most important common genetic variants ever discovered for a chronic disease. The researchers of these two studies conclude that while APOL1 variants are a significant contributor to faster progression to ESRD in African Americans, more research in this area is needed.⁵ Lack of research in this area precludes further studies to determine whether screening and interventions for persons carrying both APOL1 risk variants can prevent or delay CKD. Research in this area also transcends another priority of NIH, that of personalized medicine.

Also not explicit in the strategic plan is the need for research into new and existing biomarkers and surrogate endpoints for diseases. This issue was raised by multiple stakeholders during the formation of the 21st Century Cures Act, which has passed the House of Representatives. This issue also transcends biomedicine, and greater research on markers of disease and disease progression would likely facilitate investment and development into new cures and treatments.

Nutrition is another topic area that transcends biomedicine and is tied to health promotion and chronic disease prevention. Individuals with kidney disease, particularly those receiving dialysis, are advised to reduce their phosphorus intake, yet the widespread use of phosphorus additives and lack of labeling information about the amount of phosphorus in foods makes it difficult for patients to make proper decisions about their intake. Recent studies indicate that higher levels of phosphorus can also increase mortality in the general population.⁶ For individuals with obesity, reducing phosphorus intake has also been associated with less urine albumin excretion (UAE). UAE is one of the first signs of kidney disease.⁷ While phosphorus intake is just one example where high intake levels show increased mortality in a specific disease population and later were also associated with higher mortality in the general population, further research into various nutritional links to health and specific diseases could produce results that allow people to better tailor their diets to improve health outcomes as well as facilitate changes in the food industry.

In conclusion, . . . believes that an NIH strategic plan that focuses on cross-cutting health issues, health promotion and disease prevention and advances in treatments and cures for those with chronic conditions is important. The plan should guide the development of each Institute's strategic plan for how to better partner across Institutes and externally on these common areas, but should not supersede the need of each Institute to advance treatments and cures for the specific disease areas in its purview.

1 Tuot DS, Plantinga LC, Hsu CY, et al. Chronic kidney disease awareness among individuals with clinical markers of kidney dysfunction. *Clin J Am Soc Nephrol*. Aug 2011;6(8):1838-1844.

2 Hoeger, Thomas, et al. The Future Burden of CKD in the United States: A Simulation Model for the CDC CKD Initiative, *Am J Kidney Dis*. 2015;65(3):403-411.

3 Hoerger, Thomas J., et al., Cost-Effectiveness of Screening for Microalbuminuria among African Americans, *J Am Soc Nephrol*. 2012 Dec; 23(12): 2035-2041.

4 Friedman, David J., et al., Population-Based Risk Assessment of APOL1 on Renal Disease, 2011; *J Am Soc Nephrol* 22: 2098–2105.

5 Parsa, Afshin et.al., APOL1 Risk Variants, Race, and Progression of Chronic Kidney Disease, *NEJM*, 2013 Dec 5; 369 (23): 2183-2196

6 Nadkarni GN and Uribarri J. Phosphorus and the kidney: what is known and what is needed. *Advances in nutrition* 2014;5:98-103.

7 Chang, Alex, et al. Association of a Reduction in Central Obesity and Phosphorus Intake With Changes in Urinary Albumin Excretion: The PREMIER Study. *American journal of kidney diseases: the official journal of the National Kidney Foundation* 2013; 62:5: 900-907.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

On behalf of the imaging science community, the . . . greatly appreciates the NIH's open and collaborative process in developing a Strategic Plan. The imaging community supports the initial framework and approach from NIH. The benefits of the proposal are a clear delineation of overarching themes, underpinning the strong societal value of a leading national medical research program. In our research of seven other established and emerging public research agencies from around the globe, three do not have Strategic Plans (China, Singapore and Japan) while four nations do (UK, Canada, Australia, and the EU). In comparing the NIH's draft framework with other nations that have produced strategic plans, the NIH approach thus far is similar in that it does not try to steer specific research aims (leaving that to the ICOs). However, one aspect that is missing so far is strong language and goals surrounding the NIH's historical role as a pillar of the nation's innovation economy. We would suggest that NIH leaders consider flushing out this section, possibly with examples and metrics (see question 4), in order to reinforce the idea that a strong commitment to NIH not only improves human health, but provides a strong economic return on investment as well.

Compatibility of the framework with the broad scope of the NIH mission

The draft framework seems fully compatible with the NIH mission, as well as with the general themes that are most prevalent in other national strategic plans for medical research. Two areas, however, that are prominent in the Mission but are absent from the draft Strategic Plan are: a focus on building national research infrastructure (second bullet of the NIH Mission) and the economic value of NIH research (third bullet of the NIH mission). As in question #1, we would suggest including strong language in the Strategic Plan surrounding both of these goals and strategies, since they are well-accepted to be uniquely within the role of a public research agency and beyond the reach of the private sector alone. Such a commitment to innovative research and shared/high-end instrumentation adoption has also been shown many times to provide a strong national return on investment, as well as provide the technological and human capital required to make bold and highly-impactful discoveries that catalyze additional downstream development.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

As the structure of the NIH has evolved in recent decades, the newest ICOs (NGHRI, NIBIB, NCATS) have all followed a similar trend of focusing on multidisciplinary and technologically-focused thematic areas, rather than traditional disease-based or specialty based research paradigms. While we would certainly suggest that the NIH leadership consider compelling areas of the Strategic Plans of all of the ICOs, the NIH may want to perhaps look at the themes and approaches outlined by these three ICOs in particular, as these reflect new models of collaborative research and the "breakdown" of traditional disease/body based approaches that NIH emphasizes in the current draft Strategic Plan. In looking at the imaging space and NIBIB as an example, there are rising expectations among researchers that use inspired basic research (Pasteur's Quadrant research, a blend of basic and applied science) will realize new and improved medical technologies and health care delivery models to enhance patient experiences and health outcomes. This approach is built on the key ideas of new knowledge development, clear application, technological advancement, systemic cost reduction, diagnostic

certainty, multidisciplinary collaboration, and high risk/high reward projects – often through the creation of ‘solution shops’ that can combine diagnostic information across traditional disciplines. Given the success of the NIBIB in delivering a significant number of novel innovations since its inception, many of the Pasteur’s Quadrant-type themes and methodologies prominent in the NIBIB strategic plan (as well as NHGRI and NCATS) – particularly those focusing on the speed of discovery, convergence of disparate technological fields, and evolving health needs (i.e., point of care delivery) – might serve as strong principles under a wider NIH Strategic Plan as well.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

Quantum leaps in technology are creating a number of significant, mutually reinforcing trends that are appreciably changing the way medical research and knowledge translation is conducted. As such, we were pleased to see “technology” broadly recognized in the draft Strategic Plan as a catalyzing force to “Promote Fundamental Science”. Given the increasing alacrity in technological advancements and their revolutionary potential across many disciplines and disease states, we recommend elevating a re-named theme of “Advancing Technology Development” to a featured Area of Opportunity, rather than a sub-bullet of Scientific Advances. We would also recommend that the NIH provide sub-strategies for how to implement strategies for accelerating technological leaps at the ICO level. The reasons for this are twofold: there is enough scientific and economic rationale for ensuring a dedicated strategic focus on technological development, and the shift in the NIH review structure from a “biology-centric approach” to one that can adequately review advances in multidisciplinary technologies will require broad NIH support and guidance. We also appreciate the NIH’s recognition of the need for advances in clinical research methodologies to stimulate scientific progress. In particular, the advancement of biomarkers and molecular endpoints, and more specifically the standardization of imaging methodologies (in support of pooling data across studies), could be worthy of dedicated strategies under this sub-bullet. These data-driven and increasingly quantitative approaches may even deserve elevated focus within the Strategic Plan, as the strategies to achieve success are complex while the potential to greatly speed the delivery to patients is compelling. We would also recommend that the NIH strategic plan include innovation-based performance measures (e.g., number of patents, licenses, startups, etc) to monitor economic output in way that quantifies the public’s return on investment. Keeping such would also enable science policy researchers to study the data to better understand the economic impact of federally-supported medical research.

Components of the Areas of Opportunity that Apply Across Biomedicine that are not applicable to an NIH-wide Strategic Plan

One area that will be a challenge in our view is the “Setting Priorities” section. The “value” of eradicating a pandemic or disease is hard to define and compare against other diseases, even if NIH were to provide further guidance under this bullet. It may also pit disease groups against each other in an unanticipated way, and could be in conflict with the language above about supporting interdisciplinary research that “breaks down traditional disease borders”. Perhaps the NIH should consider de-emphasizing “Setting Priorities” by having language about disease burden simply be one of the other Unifying Principles listed in that section.

Future opportunities or emerging research needs

Imaging science is truly crosscutting in terms of its team structures, involving radiologists, neurologists, oncologists, medical physicists, computational scientists, bioengineers, and numerous other disciplines. Its blend of STEM and biological sciences results in its use in over 84% of NIH RCDC codes, and its innovations serve as a foundation for one of our country’s strongest domestic sectors. While we

understand that an agency-wide strategic plan is not the place for disease- or discipline-specific themes, we believe that imaging's strong multidisciplinary make-up, technology-forward approach, and data intensive outputs – much like genomics, therapeutic development, molecular science – is achieving a valuable dual aim of publicly-funded science: powering novel bench-to-bench interdisciplinary research solutions and bench-to-bedside clinical interventions for the betterment of human health. As such, we would recommend that specific strategies for facilitating imaging science be included under most of the targets under the Areas of Opportunity, most notably:

“Basic science is the foundation for progress”: strategies for use-inspired basic imaging science, quantitative imaging, disease processes;

“Advances in clinical research methodologies stimulate scientific progress”: strategies for imaging biomarkers, molecular endpoints;

“Leaps in technology often catalyze major scientific advances”: strategies for enabling technology development at the ICO level and study sections;

“Data science increases the impact and efficiency of research”: standardization of molecular imaging data as a pooled resource;

“Importance of studying healthy individuals”: biobanks capable of housing imaging datasets;

“Advances in early diagnosis/detection”: commitment to technology development;

“Evidence-based interventions to eliminate health disparities”: low cost point of care technologies;

“Unprecedented opportunities on the basis of molecular knowledge”: molecular imaging data as precision medicine;

“Breakthroughs need partnerships and often come from unexpected directions”: strategies for partnering with private sector researchers to ensure domestic development in technology-facing fields like imaging

As an international organization comprised of over 1,000 . . . experts representing scientists, physicians, patient advocates, academia, industry and government, the . . . strives to be a unifying voice for the field of . . . Thus, we value the opportunity to provide feedback regarding the NIH 5-year strategic plan during this seminal period in biomedical research. Progress in the last few years has clearly demonstrated the potential impact of tumor immunotherapy in prolonging, and possibly, curing patients with cancer. Breakthroughs in our understanding of how the immune system can mediate tumor regression as well as the development of agents that support immunity and block immunosuppression have led to novel therapies associated with durable clinical responses in cancer patients. An investment in both basic and translational tumor immunology can now take advantage of progress in precision medicine to validate genomic profiles and predictive biomarkers that define clinical response and drug resistance. Another understudied area is the impact of tumor immunotherapy on patient outcomes and cost-effectiveness analyses, which need to be thoughtfully addressed as immunotherapy becomes a major treatment modality for most types of cancer. These advances were the culmination of creative insights in basic tumor immunology and a more intense effort at immunotherapy development in the clinic. The results of these proposed areas of research are anticipated to not only have a major impact in cancer, but also in other areas of medicine, such as infectious disease, autoimmunity, transplantation, metabolism and others. Therefore, increased funding for basic and translational immunology research should be a high trans-NIH priority with the potential for immediate and far-reaching clinical impact. Overall, greater NIH-wide investment in basic and clinical immunology research is expected to translate into well-tolerated, more effective therapies that will improve the lives of patients with cancer and other diseases.

. . . appreciates the opportunity to comment on the framework for the NIH-wide Strategic Plan. . . .

The . . . fully supports the NIH's proposed framework and suggests several points of consideration as the NIH continues development of the Strategic Plan. We agree that an agency-wide plan cannot provide an exhaustive overview of the myriad scientific directions and questions supported by NIH funding. We also agree that opportunities for specific disease applications are best addressed in the strategic plans from the NIH's Institutes, Centers, and Offices, which are able to focus on research strategy for these issues at the appropriate level of detail.

The . . . believes that the current framework of the plan outlining the three Areas of Opportunity—fundamental science, health promotion/disease prevention, and treatments/cures—captures the most pressing and emerging opportunities in biomedical research for the NIH. The . . . recognizes the unique role of the NIH in supporting the nation's biomedical research enterprise, particularly in its funding of basic science—the foundation for translation into treatments and cures. We appreciate that the proposed plan accommodates the rapidly changing scientific landscape: expansion in both “-omics” and systems-level biology; an exponential increase in amounts of data produced from research itself, including medical records and many other sources; and a progression of challenges beyond traditional categories of organ- or disease-based research. These changes are also accompanied by the recognition that studying healthy individuals is necessary to achieve a more complete understanding of the biological basis of disease.

The . . . has also long supported building an evidence base to eliminate health disparities and would like to stress that such development involves a systems approach across the Areas of Opportunity to understand the causes of inequity at individual, community, and societal levels, and the interactions between those causes. Additional opportunities to narrow health inequities will come from incorporating the social determinants of health into all aspects of medical research. We encourage the NIH to ensure the further development of evaluation, implementation, and dissemination science so that successful, evidence-based interventions can be scaled and spread.

The . . . supports a Strategic Plan that can be updated or revised as needed to fit the goals and unpredictable nature of scientific research, particularly when attempting to bring together diverse disciplines in the biomedical, social, behavioral or other sciences. As a fundamental matter, public health needs and disease burden should factor into setting funding priorities to adequately address issues including the emergence of new health threats and the ongoing burden of chronic disease. However, the plan should also retain enough flexibility to take advantage of rapidly changing tools and techniques; new opportunities that arise during the course of investigation; and other shifts in the research ecosystem.

The . . . also encourages the NIH to develop a Strategic Plan that complements the plans and research goals of other agencies in the Department of Health and Human Services and to explore opportunities for collaboration where possible, with the shared goal of improving the health of the nation. The Association strongly favors the inclusion of goals to enhance the stewardship of the research enterprise and believes the conduct of research and development of the biomedical workforce are critical factors to the NIH successfully carrying out its mission. Specifically:

- The . . . recommends that the Strategic Plan support efforts to broaden the scope of research training programs and encourage the continued development of initiatives that support a diverse workforce.
- In the interest of reducing administrative burden associated with research regulations, the . . . encourages the NIH whenever possible to engage in efforts at harmonization and retrospective review of regulations to determine if they are leading to the desired outcome.
- The . . . strongly supports the ongoing NIH efforts to improve research rigor and reproducibility through new guidelines, updated grant policies, and training for researchers at all levels. These concepts are vital for the creation of a learning research system, which benefits researchers and is essential for scientific progress.
- The . . . urges that the Strategic Plan emphasize the value of research partnerships, which are essential to advance our understanding of biomedical science and translation of basic research into clinical care.

The . . . is again grateful for this opportunity to comment and appreciates the efforts of the NIH to gather input from the research community and general public as it develops a Strategic Plan. We would be happy to provide any further assistance to the NIH as it moves forward in this process. Please feel free to contact me, or my colleagues . . . with any questions about these comments.

Dear Director Collins:

We urge that the National Institutes of Health include in its strategic plan framework:

- Explicit recognition that disease burden includes the number of people with the disease and informal caregivers, symptomatic duration and intensity, economic and budgetary impact, and financial cost to affected families;
- Need to develop more accelerated capacity to uptake congressional funding increases (e.g. proposed 50% to 60%ⁱ FY 16 increase in dementia research funding);
- Prioritization of developing evidence-based interventions that align with population based health care delivery, that improve care of people living with dementia, and that protect the physical and mental health of informal caregivers;ⁱⁱⁱ
- Greater focus on data transparency and data sharing, including for ‘failed’ studies;
- Increased harmonization and, where possible, integration with other countries’ national research programs and with private sector research enterprises including industry, academe, and philanthropic funders;^{iv}
- Prioritization for reimagining the status quo clinical trial recruitment and retention system that is unacceptably slow, uncertain, expensive, and burdensome on participants and their informal caregivers, and lacking in participant diversity, all of which intolerably delays new means of prevention, detection, diagnosis, care, treatment, and cure.

Thank you for considering our views and for your commitment to overcoming all causes of

dementia. Please contact . . . with questions or for additional information. We look forward to continuing to work collaboratively with NIH and our partners throughout the research community.

i <http://appropriations.house.gov/uploadedfiles/hrpt-114-hr-fy2016-laborhhsed.pdf> “The Committee has provided a \$300,000,000 increase for Alzheimer’s disease research initiative in the National Institute on Aging...”

ii <https://www.congress.gov/114/crpt/srpt74/CRPT-114srpt74.pdf> “NIH-funded research is the only way to manage this disease in the future. Therefore, the Committee recommendation includes an increase of approximately \$350,000,000 for the National Institute on Aging, the NIH Institute with the primary responsibility for preventing, treating, and curing Alzheimer’s disease.”

iii http://www.leadcoalition.org/?wpfb_dl=158

iv <http://appropriations.house.gov/uploadedfiles/hrpt-114-hr-fy2016-laborhhsed.pdf> “The Committee requests NIA to convene a working group of stakeholders, including patient advocacy organizations and nonprofit funders of Alzheimer’s and dementia research, within 180 days of enactment of this act to develop possible frameworks and strategies for a direct public-private partnership to fund meritorious research proposals on Alzheimer’s Disease that are not supported directly by NIH. NIH shall provide a report annually in its fiscal year 2017 and out year budget requests identifying the total level of NIH peer-reviewed research supported by qualified third party Alzheimer’s Disease researchers through such a partnership.”

Below are recommendations for translational eye research and address areas of consideration for the current framework and emerging needs.

Capitalize on relative ease of retinal imaging and associations with disease risk. As examples, quantify retinal vessel diameters to predict stroke. Quantify features in optical coherence tomography or adaptive optics to identify metabolic abnormalities or predict neurodevelopment.

Value work beyond an innovative discovery. Expand the concept of innovation or originality to include research relevant to human disease and health. One scientist identifies a novel protein, but another may study the protein in a different tissue under conditions that occur in a particular disease. The subsequent study can be criticized as not being innovative, but the original study may not have translated to a particular disease and the subsequent work adds value in understanding dysregulated signaling and biologic dysfunction. Also, innovation has some value, but not all innovation is carried beyond the first discovery, and it cannot be assumed that a protein or signaling pathway will work the same way in every tissue.

Strong translational research can come from mid-career scientists who have additional training in research and who have accrued sufficient clinical experience to identify problems most important in medicine. Mid-career scientists are often excluded from funding opportunities that focus resources on young investigators. Funding mechanisms can be developed for established investigators, as well as young investigators, to fund investigators to perform high impact research.

Focus on models representative of human disease. Genetic murine models provide information on *in vivo* mechanisms but do not always represent human conditions. Humanized mouse models may not translate well if there is not interaction or homology of the human gene product with pathways in

the mouse. Focus on models representative of human disease and not only on models that identify genetic mechanisms.

Alcohol use and alcohol use disorders (AUDs) represent significant health problems in the US, and the Center for Disease Control and Prevention (CDC) ranks alcohol as the third leading cause of preventable death in the United States. Untreated addiction costs America \$400 billion annually. Fifteen percent of this amount is the cost of medical consequences and alcohol treatment; more than 70 percent is due to reduced, lost and forgone earnings; and the remainder is the cost of lost workforce productivity, accidents, violence, and premature death. Further, heavy drinking contributes to illness in each of the top three causes of death: heart disease, cancer, and stroke. It is estimated that at any one time up to 20 million Americans suffer from an AUD, yet funding for research into the causes, prevention, and treatment of this illness is woefully inadequate. The draft NIH-wide indicates that disease burden is not the “sole” factor in priority setting for NIH, but it is still deemed “important.” We believe it would be a mistake to underweight the importance of public health burden in any Strategic Plan and that the broad influence of alcohol across diverse health conditions warrants considerable attention. In addition, the awareness of the general population regarding the magnitude of the problem caused by excessive alcohol consumption is woefully lacking. Despite the fact that harmful alcohol use affects 40% of American families, there is considerable stigma and a lack of awareness of modern research into the causes and treatments. For example, most Americans do not know how alcohol affects the brain and are unaware of the neuroscience of addiction. Furthermore only 20% of those needing treatment actually receive it and only 10% of those actually receive the most modern and effective interventions which should include both psychosocial interventions and pharmacotherapy. Without this awareness, Americans do not seek care that may help them or their family member and they don’t understand the importance of increasing funding for alcohol research in general. In addition, health care providers do a poor job of identifying those with alcohol related problems and they often also lack the knowledge of appropriate treatments. With this background we offer several suggestions regarding the NIH’s proposed new Strategic Plan:

The **Areas of Opportunity that Apply Across Biomedicine** section of the new NIH Strategic Plan proposal is heavily weighted to basic science initiatives. Consequently the role of applied research related to disease, including alcohol-related conditions is significantly underappreciated. Applied research includes research on human populations and includes studies of diagnosis and nosology, etiology, developmental, psychosocial and behavioral processes. A strong emphasis on the translation of findings from model organisms to the human condition is urged (This might entail working with SAMSHA, the VA, or Defense Department to bring knowledge of diagnosis and treatments to the clinic. This would include biomarkers and pharmacotherapy and psychosocial interventions). Furthermore, the development of non-interventional technologies for improving diagnosis and treatment outcomes should be emphasized in the pursuit of “early detection and diagnosis” as well as monitoring therapeutic process and treatment outcome. These range from use of alcohol sensors and other types of ambulatory assessments (physiological response, geolocation and near-environment assessments, motor activity) to comprehensively assess health and disease processes in the natural environment. Similarly, in the area of alcohol treatment the use of alcohol sensors in automobiles, the use of social media for delivering or enhancing therapies, including medication compliance, are important areas of research that require a multidisciplinary approach. These novel perspectives could produce important new products, reduce risk, and improve public health, not only for AUDs, but initiatives in this area are likely to be beneficial across NIH.

The breadth and depth of existing collaborations across Institutes and Centers are inadequate given alcohol's impact across a spectrum of diseases. The NIAAA in particular and NIH in general would be well-served by establishing/nurturing collaborative funding efforts with diverse NIH Institutes, Centers, and Offices (ICOs). In particular, encourage the use of alcohol screening (verbal and biomarkers) during recruitment for clinical trials in other areas of medicine/investigation including cancer, cardiovascular, gastrointestinal and perhaps even Head and Neck and Dental. Perhaps work more with the Nursing Institute to incorporate heavy alcohol use into screening and other work with patients.

In addition, the NIH (including NIAAA) should pursue joint research and educational funding opportunities with non-profit entities/foundations and industry. In regard to enhancing interaction with non-profits and/or industry, initiatives focusing on the development of technologies or products directed to reducing barriers to effective collaborations might increase opportunities. Continue to work with Pharmaceutical Companies to reduce regulatory risk and establish best practices and methods in clinical trials. Many companies could benefit from "a toolbox" in order to make it easier for them to contemplate investing in this area. Continue to educate and encourage the FDA to clarify and ease the regulatory burden for the approval of new drugs for AUDs.

"Innovation" is typically presumed to provide advantage. However, emphasizing innovation at the expense of other scientific objectives can be costly. While innovation is highly valued, it must occur in the context of replication and reproducibility. Currently, the concept of innovation is poorly defined and applied inconsistently according to members who serve on study sections. Thus, judgment of innovation is difficult and highly variable. Focusing excessively on innovation may be associated with the premature pursuit of new technology and the devaluing of solid/effective approaches/methods to address identical questions.

The parameters of medication development are too narrowly drawn. A greater emphasis on interactive molecular mechanisms might provide an effective means of addressing complex issues such as those existing at the interface of alcohol and HIV. Consideration should also be given to the application of already known medications or molecular targets approved for one application that may have important applications in another disease. Many medications now used to treat alcohol dependence were developed and approved for other neurological diseases.

Historically, there has been an inadequate engagement of the general public in the efforts of the NIH as a whole and in particular NIAAA. There is an immediate need to enhance public awareness of advances in the prevention and treatment excessive alcohol use and AUDs and the public health relevance of alcohol science. Specific, programmatic efforts to promote the NIAAA as a vibrant player in the Nation's commitment to improving health across the lifespan are essential and timely. This would include advances in addiction neuroscience, impact of underage drinking and its prevention, the negative effects of alcohol in the fetus, genetic basis of alcoholism, and specific effects of alcohol on women. As stated above, these NIAAA-specific issues could also relate to NIH-wide initiatives. Related to public engagement, is the need for primary care and third party payers to appreciate the benefits of early treatment and adequate coverage. Effective treatments for diseases that are developed due to NIH research will still require directed outreach, engagement and education.

Try to engage third party payers to educate them about the causes, prevention, and treatment of alcohol use disorders and the cost savings that might result for proactive identification and intervention.

Fund targeted research in this area to acquire data to make this argument from an economic/business perspective.

- Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

The proposed framework calls for balanced support for:

- critical fundamental science that, while not predictable, can lead to paradigm-shifting breakthroughs
- disease prevention, and
- translation of discovery for treatments and cures.

Maintaining balance is crucial for short, intermediate, and long-term progress of for NIH's mission to enhance health, lengthen life, and reduce illness and disability. Loss of focus and support for any one of these areas undermines the effectiveness and impact of the others; likewise additional resources for all, once balance is achieved, will fuel the pace of discovery, prevention, and treatments.

Issues: how to assess current emphasis, determine the desired balance, fund at the levels required?

In the current framework, the "Treatment and Cures" box first mentions opportunities for molecular knowledge, then mentions the breakdown of traditional disease boundaries. It may be important to emphasize that the "breakdown of traditional disease boundaries" may require that research go outside of "molecular knowledge." For instance, we now know that mechanical cues play a key role in a number of diseases and understanding the role of mechanics in disease may precede uncovering molecular knowledge.

Given there will always be resource limitations, there could be a focus on supporting efficiency in diagnosis, intervention, etc. in addition to effectiveness for helping human health.

- Compatibility of the framework with the broad scope of the NIH mission

The proposed framework provides the mechanism for achieving the mission and implementing the goals, and is thus in harmony with the broad mission. The mention of understudied diseases/rare disease as an opportunity is valuable.

- Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

Beyond touting the crucial need for support of fundamental science, the framework misses the impact of engineering that should be recognized as co-existing with fundamental science. An environment that builds engineering expertise can develop new tools for quantitative measurement and analysis, predictive modeling, and design that are crucial for support of science breakthroughs and for practical manifestation of the discoveries. While receiving some NIH support, the growth and potential of the field of biomedical engineering has far outstripped its current resources. The block of "Fundamental Science" should be re-labeled "Fundamental Science and Engineering" to bring the needed recognition to this emerging realization.

- Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

The bi-directional arrows depicted in the framework diagram to link the 3 main components is a key portion of the framework. It emphasizes their contribution to a *bi-directional cycle* of discovery, prevention and treatment, and also the ability to short-circuit the cycle by *direct* relationships between any of the two.

There is an increased need to train students and postdocs to be prepared for both careers in academic and industrial research. The pipeline of training is getting increasingly long, which is steering some scientists away from science. This increasingly long training period may also affect workplace diversity.

The current framework captures many opportunities for the future of the NIH. Several points are worth emphasizing: 1. Strong investment in fundamental (basic) science produces unexpected rewards and benefits over long time periods. Basic science must include research across all species, from unicellular organisms, non-human primates and of course humans. This long-view has been essential to the current strength of the NIH and is critical to maintain future strengths. 2. Congress needs to be aware of the value and essential need to invest in young investigators and physician scientists. The stewardship of the future of biomedical research requires a strong, diverse, deeply trained workforce. Just as long-term benefits to NIH research come from studies of diverse species, so do long-term benefits to the NIH mission come from a broadly trained workforce and serendipitous encounters between broadly trained investigators. 3. Groundbreaking multidisciplinary discoveries in brain research are occurring at an unprecedented pace, partly because of trans-NIH initiatives and innovative collaborative efforts leveraging NIH support with other funding sources. Future opportunities in brain research are consistent with key elements of NIH strategic plan to strengthen basic science, study healthy individuals, and reduce illness and disability. 4. The Common Fund and the Blueprint are valuable strategic mechanisms that promote high-impact trans-NIH initiatives and rapid responses to new ideas at the NIH. They should be maintained and strengthened, ensuring that they have support from individual ICOs. 5. A final issue is for the NIH to enhance communication with Congress. They can accomplish this goal by partnering with professional research organizations, such as FASEB, Research!America, and the Society for Neuroscience.

On behalf of the . . . , we urge you to consider the benefits of psychological science in general, and of cognitive science in particular: The nation's health goals cannot be met without basic and applied research on cognition. Psychological science is a critical component of basic biomedical science and its applications. Cognitive psychology and cognitive neuroscience provide foundational knowledge for assessment and diagnosis of cognitive dysfunction and brain disease, and for the development of treatment regimens to combat those diseases. Cognitive impairment accompanies many diseases that are central to the mission of NIH, and is especially prevalent within the growing population of older adults. The techniques and measures used to characterize these impairments, to identify behavioral and lifestyle interventions to prevent them, and to assess treatment effectiveness are informed by basic research in cognitive psychology on perception, attention, memory, language, and decision-making. Psychological science utilizes a large range of measures, ranging from behavior to activity in individual neurons. These models provide testbeds for assessing theories of cognitive dysfunction, and are essential to understanding and improving brain function. Because psychological science places great weight on the rigorous measurement of behavior, its relation to neural mechanisms, and theories that bridge this divide, it is in an especially strong position to coordinate findings from across a wide range of

related disciplines—molecular neuroscience, systems neuroscience, neuropsychology, cognitive psychology, and clinical psychology—leading to health applications beyond the laboratory. Despite its demonstrated and continuing importance to health and well-being, funding for basic cognitive research has declined dramatically. Few fields offer such breadth of theoretical, computational, and statistical expertise at such a low cost of investment. We strongly endorse the strategic plan, especially its emphasis on basic science and healthy functioning, and plan for cognitive psychological science to be a major contributor to its goals.

Areas of Consideration:

Social Determinants of Health and the Importance of Representativeness

Research on social determinants of health points to the disproportionate distributions of diseases and mortality rates across social groups. This strongly suggests that the evaluation of representativeness should be an explicit priority in the NIH Strategic Plan across institutes. This may require important innovations in data collection and data integration from multiple sources. Survey data, the use of alternative administrative data sources (such as electronic health records, Medicare records) or other innovative but possibly resource-intensive approaches (mobile devices to capture real-time behaviors, etc.) may be required. NIH has been paying more attention to this issue in recent years, but we don't see much in the strategic plan outline indicating that representativeness is a priority. Failure to account for unobserved differences between those successfully recruited and retained in any panel or cohort and those who are not could have unfortunate consequences for the use of the any cohort to improve population health. The experience of the National Children's Study is especially troubling here; representativeness doesn't come easy.

Temporally Distal Factors for the Onset of Diseases (Life Span Approaches)

Retrospective and prospective designs supported by NIH must make longer biographies of health extending back as far as possible and including family histories, repeated measures of biomarkers, and genomic data a priority. Biopsychosocial factors interact over time in latent and manifest ways, not readily captured by proximate data alone, to affect health.

Geographical Contexts of Health

Exposure to adverse health conditions and the accessibility of health resources are not readily captured in national surveys, except at levels that do not necessarily represent the day-to-day conditions of living. The collection of demographic, administrative, visual information (e.g. Google Street View) along with direct observational data from multiple, diverse geographic contexts should be a priority.

Strategic Objectives:

Recognize that basic science research is the foundation for progress leading to curing human diseases.

Integrate translational and clinical research in the study of disease with allocation of adequate resources.

Perform studies that are inclusive of multiple methodologies, experimental designs and disciplines.

Perform inter-professional research across the spectrum of care environments (from 'homes' to clinical and community and public health settings).

Understand the full spectrum of human disease through the lifespan.

Include racially and economically diverse sections of the population in research.

Advance diagnostic, treatment and delivery methods to eliminate disparity in healthcare services.

Dear Dr. Collins:

On behalf of the . . . , thank you for the opportunity to provide comments on the proposed National Institutes of Health (NIH) framework for developing an agency-wide five-year strategic plan. ASN is pleased to offer the following comments for your consideration.

Kidney diseases affect more than 20 million Americans, are the 9th leading cause of death in the United States, and are potent risk factors that independently associate with many of the leading additional causes of mortality, including heart disease, diabetes, hypertension, and stroke. Kidney diseases are also one of the most economically costly conditions in the United States. As NIH considers its strategic planning for the next few years, ASN suggests that the agency emphasize developing budget requests for Congress that distribute research funding based on 1) the federal cost of care, 2) disease burden, including disproportionate burden on underrepresented minorities, and 3) opportunities to improve overall public health and the federal cost of care.

Currently, NIH investments in kidney research (\$585 million) are less than 1% of total Medicare costs for patients with kidney diseases (\$80 billion). In fact, costs of care for patients with kidney failure alone—the only health condition for which Medicare automatically provides coverage regardless of age or disability—are more than NIH's entire budget (\$35 billion vs. \$30 billion annually). Despite the medical and economic burden of kidney diseases, NIH invests less per patient in kidney research than many other diseases (see Table 1). . . . recommends that NIH take into account the cost of care to the federal government as it considers disease funding allocation in the new strategic plan. Besides examining the cost of various diseases as a percent of the Medicare budget versus population affected, NIH may also consider examining the most costly chronic disease dyads and triads as identified in the "Chronic Conditions among Medicare Beneficiaries Chartbook" online at <https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Chronic-Conditions/Chartbook.html>.

Clinical advances in kidney care in the past 25 years have been sporadic, paling in comparison to the consistent advances made in other diseases such as HIV and cancer therapies that have improved treatment and patient outcomes. It is not an exaggeration to note that patients with kidney failure are treated much the same way today as they were when Medicare began universal coverage of dialysis treatment in 1972. Most patients still require multiple dialysis sessions a week—three treatments for three to four hours at a time—which are often both emotionally draining and physically exhausting and, while life sustaining, fail to optimize quality of life for our patients.

Patients on dialysis have other doctor visits in between treatments for their comorbidities and are frequently admitted to the hospital. As a result, only 1 in 5 dialysis patients work, and many receive Social Security Disability Insurance benefits. On top of that, outcomes for patients with ESRD are grim. Fifty percent of patients with kidney failure die within three years of initiating dialysis, and most people who are wait-listed for a kidney transplant, the optimal therapy for most of patients, die before receiving a donor organ.

Furthermore, kidney diseases disproportionately affects African Americans, Hispanics, and other under-represented minority populations compared to Caucasians. For example, African Americans make up approximately 13% of the United States population but account for 32% of Americans with kidney failure. Hispanics and Native Americans are twice as likely as Caucasians to develop kidney failure.

The above facts underscore . . . recommendation that the disease burden is an important element that should influence how NIH allocates funding in its new strategic plan. Moreover, . . . suggests that NIH also consider prioritizing funding to study diseases with a disproportionate burden on racial/ethnic minority populations; investing in science to explain the causes of these disparities, and to develop targeted therapies to treat and prevent them, should be a national research priority.

Better and more cost-efficient treatments and therapies are desperately needed to slow or prevent progression of kidney diseases and improve care for all patients with kidney diseases. The good news is that in recent years there have been a number of exciting scientific discoveries in the kidney field that present opportunities to improve overall public health and have the potential to lead to a new generation of effective therapeutics.

One such example is the discovery of risk alleles in the APOL1 gene that are strongly associated with non-diabetic kidney diseases among African-Americans, a racial group at much greater risk for progressive kidney failure than Caucasians and other minorities. Improved understanding of the genetic origins of diseases opens the door to broadly-applicable, revolutionary therapies that provide hope at a population level. . . . encourages NIH to prioritize funding in a way that enables investigators to capitalize on scientific discoveries to produce new therapies in these and other areas that are likely to advance overall public health.

In summary, . . . believes NIH should allocate funding based on disease burden, opportunities for improving overall public health, and the federal cost of care. These guiding principles and goals should be incorporated within the framework and subsequent strategic plan.

Increases in the NIH budget have not kept pace with inflation and the agency has lost nearly 25% of its purchasing power since 2003. Moreover, there is no reason to believe the current trend is likely to change anytime soon given the federal government's long-term fiscal outlook. The consequences are well-known: grant application success rates are near record lows and the average age a first-time investigator is awarded her or his first research project grant is at a record high.

Cuts to NIH salary caps and efforts by NIH to spread funding further have forced universities

and hospitals to absorb research costs, which many are not in a position to bear given current fiscal challenges. As a consequence, a number of universities and hospitals are restricting research grant applications and/or are shutting down research labs forcing promising young researchers (including those receiving NIH training awards) and highly productive senior investigators to leave research altogether. Researchers are ending their careers as a result, moving to industry where research may become proprietary, or moving overseas to pursue their work in countries where the research funding outlook is brighter.

Perhaps the greatest tragedy is the discouraging effect the funding crisis has had on young scientists who see their mentors and other leaders in their fields being forced to end productive research programs. These young scientists may not even try to open the door to a research career. This reluctance to plunge into research will compromise America's position as the global leader in research and the development of innovative treatments and cures for patients. . . . encourages NIH to ensure future funding strategies both support young investigators and create sustainable research career path opportunities in the long-term.

The current budget and funding challenges compel NIH to take a broad and systematic approach to evaluate how to improve the current funding structure. There is no better time to do this than at the start of the strategic planning process which will guide NIH into a future that all of us hope will be brighter and more promising for young scientists, patients with kidney diseases, and the health of all Americans.

Thank you very much for your consideration of . . . recommendations. For questions about this letter, the burden of kidney diseases, or . . . , please feel free to contact me at . . .

I write as an individual but note my multiple hats that have given me points of view and experiences with NIH and the biomedical community: . . . and current and former NIH research grantee. Overwhelmingly, I agree with the Plan in terms of emphasis on technology, interdisciplinary research, and workforce development. I organize my thoughts according to my affiliations.

. . . The NIH Strategic Plan strongly recognizes the role of technology in basic research and the importance of research and development for the creation of new technologies in support of research as well as medical practice. We note especially . . . and NIH involvement in neural engineering, biomedical imaging, and biomedical and health informatics as critical areas receiving excellent support. Hence NIH priorities align significantly with our priorities.

. . . strongly emphasizes the role of industry and the medical community, not just the academic community, in medical technology research and development; conversely, it is active in promoting interdisciplinary, inter-institutional collaboration for the betterment of medical practice and for the careers of . . . members. An example is the Hence . . . is pleased to see the emphasis on interdisciplinary work evident in the NIH Strategic Plan and the commitment to engaging a broad set of researchers.

We also strongly support the emphasis on workforce development and retention. We represent a very large class of scientists and engineers whose fundamental education is significantly outside of the normal biomedical science training; we believe (and the discussion of the NIH Strategic Plan confirms)

that cross-training these individuals is of great importance to the mission of the NIH. Simply stated, the great projects of the coming years require not only teams of people from different disciplines but also individuals with cross-training in order to lead and make the projects work.

Finally, we encourage the NIH in its Strategic Plan to explicitly recognize that the nation's medical future, both research and practice, is inextricably wound up with its technological community, represented by . . . and other organizations. Our involvement with enhancing the promotion of health care gives us perspective, recognizing that significant contributions come from very different disciplines and populations. Hence we strongly encourage the NIH to continue to listen to its multiple constituencies.

My Role as an Educator

I rose through the ranks in Electrical Engineering at the At . . . I am particularly involved in undergraduate education emphasizing engineering systems as an intellectual base for biomedical engineering. I have been privileged to contribute to institutions among the world's best in their contributions to NIH and medical progress and in their education of students.

Concern for Workforce

I am very concerned about placement of BME graduates at all levels. Much of my concern stems from the fact that many BME graduates emphasize the life sciences to the point where they face the same shortage of appropriate positions as do life scientists. The NIH has recognized the problem at the PhD and Post-doc level, while BS level underemployment is much older. I would like to see more active concern for the biomedical workforce, not just by tilting the scales a modest amount for new investigators, but by career guidance for alternative careers or, at the extreme, reducing the number of new trainees so these talented individuals may early on make other societal contributions. The recognition of the importance of appropriately developing and protecting the scientific workforce is a real strength of the NIH Strategic Plan. I advise a broader view where this workforce is directed not only to NIH objectives but also to broader societal biomedical objectives.

I do applaud the NIBIB DEBUT (DEsign By Undergraduate Teams) program as a novel and effective way to encourage much more creativity by undergraduates towards solving biomedical problems. I believe we have to engage an ever expanding group of bright young people who want to solve biomedical problems; we are counting on them for our future.

Comments a Research Investigator

I am grateful for my federal funding as it has enabled me to make scientific contributions and to have had the career opportunities with which I have been blessed. I absolutely maintain that, despite the criticisms, the NIH review and grant process is the most rigorous and fair process that exists, and remains a model for the entire world. Its basic problem is lack of money proportional to the number of good ideas. I appreciate the efforts to make the process more time efficient. I think the Strategic Plan should have a plank wherein explicit recognition is made that the NIH review processes need to improve in their respect for the time commitments investigators make in reviewing and in compliance.

As a Citizen

I am biased that the investment in healthcare via the NIH is of extraordinary return for my tax dollar. Still, it is heartening to see that this very high level framework is proposed and being discussed. It is deceptive in that what is proposed seems obvious, but it surely establishes both intellectual and pragmatic guidelines that define what is within the NIH mission. I applaud the effort and result and I sincerely hope and believe that it will guide the next level of implementation planning that must take

place. I also believe that it will be helpful in explaining mission and priorities to the Congress and Administration, i.e. to the people we entrust with making national decisions as to priority of effort and expenditure.

Consciousness is now at the forefront of the most advanced research in neuroscience. Experimental and clinical studies have become powerful in their methodologies and sophisticated in their interpretation, and steady progress is being made in understanding the neural substrate of consciousness and its disorders. However, consciousness is currently not on the list of the NIH RDoC Domains and Constructs, unlike related topics such as attention, perception, and cognitive control. Especially in the US, funding specifically provided for research on consciousness is scarce or absent. We think situation needs to be rectified, especially in the light of the remarkable scientific progress made in the past decade:

- There are novel experimental paradigms such as masking and binocular rivalry to manipulate consciousness; quantitative measures for assessing the level and types of consciousness; and demonstrated applications for detecting preserved consciousness in vegetative state patients
- Cognitive neuroscience research on consciousness has matured significantly, with studies now routinely appearing in the highest profile academic journals such as Science, Nature, Lancet, New England Journal of Medicine, etc. The amount of funding provided is disproportionately low given the impact of the research.
- European funding agencies such as the European Research Council and Wellcome Trust now routinely fund such research which creates a glaring disadvantage for researchers based in the US.
- There has been a spate of young researchers taking up independent positions within the field, many of them in prominent places. The field is going through a stage of rapid expansion. And yet, perhaps because of the last point, most of these researchers are based in Europe or have recently relocated there. The US runs the risk of losing its status as a world leader in this important field.

Consciousness is no doubt a topic of tremendous relevance to many different institutes within the NIH, such as the NINDS, NEI, NIHM, NIA. Many core topics of neuro science cannot be discussed in isolation from consciousness. Aside from patients who suffer complete or partial loss of consciousness as a result from major brain trauma, many other diseases such as Alzheimer's, autism, Parkinson's, schizophrenia, etc., involve significant disturbances in conscious experience and metacognition. Understanding these issues are critical for etiology as well as treatment development.

NIH has, in the past, tended to focus on the diseases and conditions affecting the largest number of people in the nation, but I believe NIH has not effectively taken into account the impact of diseases on the nation or the amount of support and research provided for these diseases by the private sector. I would like to see this tax-payer funded institution do what private drug companies cannot. I believe the focus of the NIH should be on the less common, and less profitable to the private sector, diseases. I also believe the focus should lie where these diseases tend to make the largest long-term impact on our nation, the diseases affecting children and young adults. The impact of these "rare" diseases is huge, even if the numbers stricken are relatively small. Childhood cancers continue to have the largest impact among these "orphan" diseases, and should receive a much greater portion of the NIH's funding and focus. The positive economic impact of curing and finding safer cures for conditions affecting the young

would be enormous! Children battling disease have their educations interrupted, and often need assistance overcoming the emotional impact of the battle. Many face lifetime disabilities due to an incurable condition or the harsh nature of available treatments. The parents of minor children and young adults are often forced to leave the workforce to care for their child. Many of these parents battle the effects of PTSD after facing scary odds and the reality of helping their children endure harsh treatments. Children and young adults who die leave behind grieving parents and siblings that often struggle with the emotional impact of such an unnatural loss. For these reasons, I believe pediatric diseases should receive priority, followed by diseases affecting those under 50.

The NIH, and frankly every USG funding agency, should introduce a section to their grants that explores the broader implications and possible dual use applications of any proposed project. In a world where technology is advancing at an unprecedented pace, it is our responsibility as scientists to take the time to scenario map where our research may lead, for good or for ill. While this analysis will not necessarily be complete or correct, it represents the kind of responsible conduct our nation deserves from us. Just such a review process has been implemented for synthetic biology projects conducted at the DOE. This model can quite easily be adapted to fit the NIH grant review protocol. Their process and some early results were published this year. The abstract and reference are included below.

Abstract:

Serious concerns have been raised over the possible intentional use of synthetic biology approaches to engineer pathogenic organisms as well as the possible accidental environmental release of genetically engineered organisms. Scientists pursuing synthetic biology research must diligently consider issues such as these. As such, the U.S. Department of Energy (DOE) Joint Genome Institute (JGI) has developed a Synthetic Biology Internal Review process to assess, beyond technical and scientific merit, certain broader aspects (e.g. environmental, biocontainment, biosafety, or biosecurity) of the research proposals associated with the JGI's DNA synthesis program.

Simirenko, Lisa, Miranda Harmon-Smith, Axel Visel, Edward M. Rubin and Nathan J. Hillson (2015) The Joint Genome Institute's synthetic biology internal review process. *Journal of Responsible Innovation* 2(1):133-136.

The . . . is a national non---profit organization with the mission to save and improve the lives of people living with neuromuscular disease. . . . is dedicated to finding therapies for the muscular dystrophies, ALS and other neuromuscular diseases, and to that aim has funded over \$1 billion in research grants since its inception. However, regardless of how much funding . . . and other organizations are able to contribute to research, robust support from the National Institutes of Health (NIH) is absolutely critical to achieving our shared goals.

. . . appreciates the forward---looking approach set forth in the framework for the NIH---wide Strategic Plan. . . . is pleased to see that advancing research opportunities related to rare diseases is included as a priority and welcomes the commitment to identifying areas for research where there is scientific opportunity---thus permitting funding to follow the science. . . . also appreciates the consideration of the breakdown of traditional disease boundaries and the importance of partnerships.

. . . appreciates the opportunity to be part of the strategic planning process and extends our gratitude to the NIH, and to the Directors and staff in each of its Institutes, Centers and Offices for their ongoing dedication and commitment to biomedical research and achieving the NIH mission.

Dear Sir or Madam:

. . .

We would first like to congratulate and thank the NIH for the inclusion of “advancing research opportunities presented by rare diseases” as one of the NIH’s priorities within its strategic plan. The rare disease patient community relies on the NIH to conduct or fund much of the essential basic and translational research on rare diseases. This research lays the groundwork for therapeutic development for neglected diseases with inadequate or no treatment. The following comments outline several ways to accelerate rare disease research.

Advancing rare disease research starts with adequately funding the NIH, a goal that has been sorely missed over the past ten years. . . . has long advocated that Congress allow NIH funding to keep pace with inflation, and recognize the critical importance of the NIH to the nation’s health and economy by prioritizing NIH funding in each budget cycle.

Second, the Office of Rare Diseases Research (ORDR) plays an integral role in championing and coordinating rare disease research within the NIH. It also stimulates rare disease research outside of the NIH by providing logistical expertise. The ORDR coordinates the Rare Diseases Clinical Research Network (RDCRN) and serves as the central locus of rare disease data and research expertise for rare disease researchers around the world. The ORDR also houses the Genetic and Rare Diseases Information Center (GARD), the central hub for rare disease information. We request that any further development of the NIH strategic plan recognizes the importance of the ORDR to the rare disease patient community.

We also request that the National Center for Advancing Translational Sciences (NCATS) continues to play a key role throughout the NIH. NCATS works to translate the findings of basic research into treatments or cures for diseases. This is important for the rare disease community because developing novel therapies can cost upwards of \$1 billion, and 95 percent of therapies fail in the lab or in clinical trials without ever reaching the patient. NCATS works to improve and accelerate this process by filling the gaps that exist in the current framework, and by researching innovative research and drug development techniques. This includes clinical trial design as well as efficacious biomarker and endpoint identification.

Through its Therapeutics for Rare and Neglected Diseases (TRND) program, NCATS encourages collaborations aimed at stimulating drug discovery and development research among NIH and academic scientists, nonprofit organizations, and pharmaceutical and biotechnology companies working on rare and neglected diseases. NCATS is already achieving many of the goals set forth in the strategic plan framework, such as enhancing impact through partnerships, ensuring rigor and reproducibility, and more. For this reason, NCATS should be prominently featured throughout the NIH’s Strategic Plan

Finally, the Undiagnosed Diseases Program (UDP) also plays a critical role in advancing rare diseases research as it is solving the medical mysteries that plague millions of undiagnosed patients. We request the strategic plan recognize the importance of the UDP in finding treatments and cures for the rare disease community.

We thank NIH for the opportunity to comment, and we look forward to working with the NIH as the strategic planning process moves forward. For questions regarding . . .

Thank you in advance for your consideration.

. . . Given the tremendous human and economic toll of more than 1,000 brain diseases and disorders that affect millions of Americans — including autism, depression, schizophrenia, traumatic brain injury, and Parkinson's and Alzheimer's diseases — continued progress in neuroscience research is powerfully needed. The field has already made great progress, and . . . encourages substantial additional investment in neuroscience, including the creation of new tools and technologies being prioritized in the BRAIN Initiative. The broad basic and translational efforts funded through more than 15 NIH institutes will then leverage those and other tools to make progress toward better understanding and better treatments. To realize this progress, the NIH strategic plan should prioritize:

- Promoting fundamental science. Basic research is central to the quest for knowledge, a foundational element to addressing our greatest health challenges, and the driver of other science - driven industries. Federally - supported fundamental research is foundational to private industry capacity to translate these findings into life - saving products and treatments.
 - Investigator - initiated science, which is a proven pathway to breakthroughs. Since 2003, the percentage of investigator - initiated grants relative to total spending has decreased. These grants should be balanced with important NIH - led research.
 - Peer - review, ensuring scientific promise drives decision - making. This NIH system — which is emulated around the world — ensures leading, working scientists evaluate grants and determine those that have greatest potential.
 - The future scientific workforce. America's future health and economic growth will depend on researchers who are well - trained to advance science and contribute to society in an array of diverse careers. That future workforce will be most effective if it is diverse, ensuring science benefits from broad perspectives and experiences.
-

Dear Dr. Collins,

On behalf of . . ., I am writing in response to the draft Strategic Framework put forth by the National Institutes of Health (NIH). . . appreciates the opportunity to provide feedback on this draft NIH - wide 5 - year plan and commends NIH for focusing attention on areas such as disease prevention and early detection, identification of novel treatments, diversifying workforce, and fostering greater scientific opportunities to ensure the sustainability and stability of the biomedical field. Our specific comments are below.

Comprehensive trans-NIH research themes that have not been captured in the Areas of Opportunity that Apply Across Biomedicine

. . . has concerns that NIH has not been able to capture the need to genuinely invest in younger investigators who do not have previous funding experience from bodies such as the National Science

Foundation, Department of Defense, and Department of Education. Ronald Daniels, J.D., L.L.M., President of Johns Hopkins University, recently pointed out in the Proceedings of the National Academy of Sciences (2015 Jan 13; 112: 313 – 318) that there has been a steady decline in grant funding awarded to younger investigators and an increase in the age at which investigators are receiving not just R01 grants, but all NIH research grants. Due to this trend, early researchers are leaving the workforce, which carries serious implications for the health and future of biomedical research. . . . believes that NIH investment in young and early career researchers will allay these concerns and will go a long way towards rebuilding the pool of scientific researchers in the United States.

Relatedly, providing guidance for new investigators through structured mentorship programs is vital. The establishment of an independent research career is often long and fraught with challenges, including securing funding; publishing and presenting findings; obtaining necessary training in biomedical and behavioral research; and learning how to balance research with clinical and other professional demands. Physician - scientists who can serve as mentors and role models can help young investigators navigate these obstacles and increase their chances of successfully maintaining careers in psychiatric research. Mentorship is particularly important for minority researchers, who face unique hurdles in securing and maintaining research funding and whose participation in psychiatric science is vital to the diversity of the workforce. NIH - supported mentoring programs can be extremely effective in addressing these needs and should be a prominent area of focus moving forward.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

. . . believes there needs to be more emphasis on funding genuine high - risk, high - reward ventures. Although the draft Strategic Framework includes comments about “stewardship”, which include workforce development, it lacks any statement reflecting a key strategic direction for NIH. . . . believes that NIH should shift its focus away from purely conservative studies, and doing this correctly will require a strategy - level commitment.

Relatedly, it would be beneficial for the Framework to reflect the importance of ensuring the availability of adequate data systems and procedures to capture metrics on all strategic initiatives. NIH does not appear to do this currently. For example, how many awards under a high - risk program actually fund projects with limited preliminary data? Is there a difference, ultimately, in the scientific productivity of those grants? Which initiatives targeting young investigators actually end up yielding R01s awarded under the median age?

. . . agrees with NIH that fostering opportunities for scientific advances is a vital priority. To that end, greater funding of program grants could increase opportunities in translational research. Similarly, development of a new K2 award could provide greater prospects for researchers at the later stage of their career. . . . also would favor increasing funding for education and training in neuroscience to recruit more M.D./Ph.D. students into psychiatry research and increasing diversity (e.g., ethnic/racial minorities, women , members of the LGBT community) among psychiatry researchers through community outreach programs. We would welcome the opportunity to work with NIH in recruiting researchers to these types of programs and research funding.

Future opportunities or emerging research needs

There are numerous emerging areas in neuroscience and psychiatry that can significantly improve our understanding and treatment of neuropsychiatric disorders. For example, large - scale patient registries

of clinical, demographic, and health outcome data, including blood, saliva, and biomarkers, could be useful for drug effectiveness testing and development of personalized therapies. It also could serve as a robust resource for data mining to inform research efforts. A strong national network of “brain banks” is lacking and could help advance research on structural and molecular pathologies of psychiatric and neurological disorders. Lastly, progress in neurogenetics and neuroscience technology is facilitating the translation of psychiatric genomics into brain biology, which could stimulate the discovery of mechanisms associated with disease susceptibility, inform development of novel drug therapeutics, and improve treatment response.

Finally, we would like to emphasize the importance of NIH increasing its focus on translational studies, which will help us move from the preclinical and clinical research stage into a better understanding of how the latest scientific discoveries can meaningfully impact patients’ lives. Recent collaborations, such as the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative and the National Center for Advancing Translational Sciences (NCATS), are anticipated to significantly enhance the detection and treatment of neuropsychiatric illnesses by combining expertise from basic scientists and clinicians all working toward a shared goal: improving our understanding and practice of psychiatry. The identification of therapeutic targets and discovery of novel drugs can be extremely lengthy processes. But through multidisciplinary efforts, such as those demonstrated by BRAIN and NCATS, advances in genetics, neuroimaging, psychopharmacology, and neurophysiology can accelerate the speed at which patients receive the diagnoses and treatments they need to lead more fulfilling lives.

Thank you for the opportunity to provide feedback. The development of a trans-NIH framework is an important endeavor and . . . appreciates the opportunity to provide comment. We look forward to release of the 5 - year strategic plan to the Congress in December. If you have any further questions, please contact . . .

Dear Dr. Collins:

The . . . appreciates the opportunity to comment on the proposed NIH strategic plan framework. The framework identifies many important cross-cutting areas of focus that will help the NIH in pursuing its mission.

The emphasis on promoting fundamental science, including basic research, is an important principle that applies across all fields of biomedicine. A critical step in the integration of basic research findings is applying that knowledge in the context of a whole organism. Years of research into the molecular components of biological systems have amassed an enormous storehouse of information that can help us understand the functions of cells, tissues, organ systems, whole organisms and even populations. To translate this knowledge into therapeutic advances we must integrate these findings in the context of how they apply to organisms in all of their physiological complexity. Doing so will lead to a better understanding of human health and disease, and facilitate the development of new treatments and prevention strategies. We recommend that the strategic plan emphasize this important point. One way to do so would be to alter the data science bullet point to read: “Data science and integrative understanding of complex physiologic systems increase the impact and efficiency of research.” In the full version of the strategic plan, additional detail is also needed in this bullet point to provide a brief definition of data science and an explanation of how it can contribute to increased impact and efficiency of research.

The . . . agrees that advances in clinical research methodologies can help stimulate scientific progress. However, the bullet point as written is currently restrictive in focusing only on the benefits of clinical methodology. We suggest that the bullet point might be more impactful if it read: “Advances in research methodologies stimulate scientific progress and clinical success.”

We also suggest that under the heading “Advancing Treatments and Cures” the first bullet point be broadened by changing the wording to read: “Unprecedented opportunities on the basis of all advances in Fundamental Science.”

Finally, the . . . endorses NIH’s efforts to recruit, train, retain, and promote a talented and diverse research workforce. This remains a significant challenge for the research community that should be emphasized in the agency’s strategic plan.

...

We are pleased to submit this response on behalf of the . . . , a professional scientific society with

The . . . believes that any NIH-wide strategic plan should have a central focus on promoting foundational knowledge and the development of cross-cutting technologies that will span all 27 Institutes and Centers. Indeed, everything else that NIH does depends on the knowledge base generated through investments in basic research. As such, . . . strongly endorses the first opportunity highlighted in the proposed framework: “Promote Fundamental Science.”

Many transformative discoveries in the history of biomedical research came about not because of a singular focus on developing a treatment or cure for a specific disease, but because of NIH’s history of empowering the research community to think creatively, to initiate and pursue diverse research opportunities, and to seek novel approaches to long-standing challenges. We therefore agree that NIH must retain the freedom to enhance its support for basic science as the most important priority for the agency.

Because humans share much of their basic biology with all living systems, we also believe that robust and expanded support for model organisms—from microbes to plants to mammals—is an essential part of this pursuit of foundational knowledge. One of the most effective ways to advance progress in biomedical research is to understand the fundamental biology of model systems. We therefore urge NIH to balance those parts of its strategic plan focused on human disease with complementary work on a diverse array of model organisms. There is a rich history of the benefits of this dual approach and the opportunity for a future rich in discovery.

Dear Dr. Tabak,

The . . . is pleased to offer comments to the National Institutes of Health (NIH)’s request for information on its NIH-wide Strategic Plan. As biomedical research has become more interdisciplinary, the need for

an objective set of NIH-wide principles to guide cross-cutting research topics has become clear. . . . firmly believes this strategic plan will enable the NIH to guide and prioritize its resources to more effectively deliver lifesaving medical advances urgently needed by many patients. Below, we offer specific comments within the topics listed in the announcement.

Potential benefits, drawbacks/challenges, and areas of consideration for the current framework

. . . supports the framework’s statement that measures of disease burden should be a factor, but “not the only factor” when setting research priorities. The NIH’s investments must be cognizant of which research opportunities have the highest impact on the many diseases facing patients. For example, while threats from some infectious diseases, such as antimicrobial resistance, may currently incur a moderate disease burden in the U.S., without sustained investment into improved treatments, they can escalate into major public health crises.

Infectious diseases also know no boundaries. While antimicrobial resistance is already a well-documented problem in the U.S., new and even more highly resistant bacteria, such as those containing the New Delhi metallo-beta-lactamase (NDM) enzyme, continue to be imported into the U.S., significantly worsening the impact of resistance on patients. As the recent outbreaks of Ebola virus disease, MERS-coronavirus, and Chikungunya fever have illustrated, new and emerging infectious diseases may have low incidence in the U.S. but nevertheless pose high public health risks. Strong research investment is essential to address these global threats before they can incur a heavy disease burden to the American public, and . . . urges the NIH to ensure they remain high priority for research investment.

Co-morbidities are another important cross-disciplinary consideration. For example, patients who have undergone transplantation, are being treated for cancer, or are suffering from heart disease, are more prone to other diseases, including infection. Improved treatments for infections can decrease the disease burden for these patients who are most at risk. In addition to prioritizing research that aims to directly address diseases with a heavy public burden, we urge the NIH to consider the value of research that may lead to treatments that indirectly improve other diseases.

. . . also strongly supports the strategic plan’s statement that the value of eradicating a pandemic should be considered when prioritizing research. The robust investment by the NIH into developing therapeutics to HIV has saved millions of lives, and . . . urges the NIH to continue its strong support of efforts to eradicate the HIV/AIDS pandemic. . . . also recommends prioritizing vaccine research programs, all of which hold great potential to eradicate or significantly reduce the risks of pandemics. For example, in addition to ongoing seasonal influenza vaccine research, the development of a universal influenza vaccine that can generate multi-season protection should remain a NIH priority. . . . also recommends that the NIH considers the value of research that improves existing vaccines, such as to pertussis, where outbreaks in recent years highlight the need for improved vaccines.

Finally, . . . strongly agrees with the NIH inclusion of early diagnosis and detection within its area of opportunity for “Health Promotion and Disease Prevention.” Improved diagnostics are essential to improving other areas of the healthcare spectrum, such as antimicrobial stewardship. Since common diagnostic technologies can improve testing for multiple disease burdens, . . . urges the NIH to prioritize cross-cutting diagnostic research so these new tests can improve patient care.

Additional concepts in ICO strategic plans that are cross-cutting and should be included in this trans-NIH strategic plan

. . . is pleased to see the NIH lists the need for partnerships for breakthroughs in its areas of opportunity. . . . has strongly supported NIH public private partnerships (PPP) such as the Accelerating Medicines Partnership (AMP), and believes that AMP should be expanded to better take advantages of untapped partnership opportunities such as antimicrobial drug development and rapid diagnostic technologies. . . . urges that the NIH consider similar PPP models for prioritization, such as the biopharmaceutical incubator called for by the National Action Plan for Combating Antibacterial Resistant Bacteria (CARB) to promote antimicrobial development.

Our society also supports the NIH's inclusion of reducing administrative burden in its "enhancing stewardship" focus area. As this strategic plan focuses on cross-cutting efforts, . . . believes this is an excellent opportunity for the NIH to consider a systematic plan to develop, in collaboration with its institutes and centers as well as funded academic institutions, standard metrics or best practices that focus on the most efficient policies to ensure regulatory compliance without creating undue burden.

Future opportunities or emerging research needs

. . . is pleased to see the NIH include recruiting and retaining an outstanding biomedical research workforce in its focus areas to sustain the biomedical research enterprise. As the NIH moves to more cross-disciplinary research, the unique perspectives of physician-scientists, who sit at the intersection between basic and translational/clinical research, will only become more valuable to biomedical research. . . . urges that the NIH prioritize the strengthening of the physician-scientist workforce to enable the cross-cutting research the strategic plan endorses.

. . . appreciates the opportunity to provide its recommendations to the NIH as it further develops its NIH-wide strategic plan to strengthen the biomedical research enterprise. Should you have any questions or concerns about these comments, please feel free to contact . . .

The . . . appreciates the opportunity to submit comments on the National Institutes of Health (NIH) RFI on the Framework for the NIH-wide Strategic Plan.

NIH support of microbiological research has led to major advances in diagnosis, treatment, and prevention of infectious diseases. Less appreciated is the NIH support of fundamental microbial research that has revolutionized biology, enabled the NIH translational research vision, and led to formation and growth of many companies. Examples include discovery of restriction enzymes or plasmids that are core elements of molecular biology and biotechnology; identification of microbes and nucleic acid enzymes that enabled development of PCR, high-throughput DNA sequencing, genomics, and completion of the human genome project. NIH funded studies of microbial pathways identified the source of reactive oxygen species and linked them to aging and debilitating diseases. Over the years, NIH has funded phage biology which led to identification of CRISPR, which is emerging as a key approach to genome editing from microbes to human cells.

. . . wants to ensure that microbiology continues to provide the knowledge and innovations needed to solve future grand challenges. However, we are concerned that these future transformative microbial discoveries and the resultant intellectual, translational, and economic benefits will either not occur or will occur outside the U. S. unless NIH strategically invests more in fundamental microbiology research. As an example, NIH may not be strategically positioned to make future microbiology discoveries. At a minimum, NIH should have a Center for Scientific Review study section devoted to microbiome

research, to promote study both of systems level issues and to unravel the basic genetics and physiology of its largely unexplored microbial constituents. The vast and beneficial microbial communities that live in our guts and on our skin have profound effects on metabolism, immunity, and behavior. Understanding the role of our microbial partners is crucial to treatment of allergies, asthma, obesity, and auto-immune disorders. Thus, in-depth investigation of the central role microbes play in these and other conditions is vital to the development of novel therapeutics.

NIH has provided support for the, microbiome initiative. However, we believe that much more funding of this area is needed if we are to continue to link microbial activities to human health and disease. In addition, cross institute initiatives in experimental or computational analyses of living systems should be expanded to include studies of microbial function and the interactions of microbes with each other and the host. Although we cannot predict specific discoveries of these initiatives, in keeping with the long tradition of NIH funded research, we are certain they will transform future biomedical research. We would also argue that it is important that NIH ensure that its individual fellowships and institutional training programs include a sufficient number of individuals being trained in these specific areas, including microbiome research.

The . . . recognizes the value of the National Center for Advancing Translational Sciences and the Clinical and Translational Science Awards (CTSA) as an important contribution to clinical innovation and application of the discoveries made through basic research. We further encourage greater coordination between the NIH and other government agencies (e.g. BARDA) and the commercial sector in the translation of promising discoveries to actual products, especially for those diseases and conditions where an obvious commercial market is lacking. For example, much has been written recently about the fact that the development of promising Ebola countermeasures languished until the current West Africa Ebola epidemic drew global attention. Recent outbreaks of Ebola, Chikungunya, MERS CoV and high pathogenicity avian influenza have highlighted the importance of support for studies in basic virology and the development of diagnostic reagents, vaccines and antivirals.

We cannot over emphasize the importance of not only rigorous peer review of research grants but ongoing funded programs, especially given the extraordinary sums of monies going to single individual investigators but also to complex consortia of investigators at multiple institutions. Regarding peer review of grant submissions, the quality of the feedback given to investigators, must be based upon sound scientific data with meaningful guidance to enhance the proposed research in the event of the resubmission to NIH or another funding source.

Enhancing workforce diversity is an important goal of NIH which . . . supports. In order to ensure that the needs of the future scientific workforce are met it is important for NIH to actively pursue this goal on many different levels. NIH should have mechanisms to ensure that underrepresented scientists are being trained and mentored in the best possible fashion. One possible mechanisms would be to make the inclusion and training of underrepresented scientists a significant part of the grant review and renewal process.

NIH currently supports training of a diverse scientific workforce by mechanisms which expose underrepresented scientists at various levels to research and innovation at NIH supported labs. An example of this is the MBRS/MARC U-STAR programs. Broadening the impact of these programs is important to ensure that the future needs of the scientific workforce are met. This can be accomplished by incorporating teaching innovation into the MARC programs which will help to engage students who may not be directly involved in MBRS research labs. Strategies such as including funds for faculty

development training and travel to conferences which specifically encourage teaching innovation in the sciences would help to accomplish this. This may be especially helpful at minority serving institutions as a fair number of these are already involved in the MARC program. The effect of the inclusion of these funds should be measured by proof of curricular redesign and enhancement of teaching in the sciences.

Concerning the training of graduate students, NIH should make it a goal to diversify the outcome of scientific training. As the workforce for scientists has diversified away from academic research positions these grants should encourage education initiatives which expose students to a diversified workplace. Specifically trainees should be actively exposed to and encouraged to participate in areas outside of academia at the R01 level. This should involve the inclusion/enhancement of funding for programs which promote training of graduate students in teaching at the undergraduate level as well as education on alternative career paths.

Finally, . . . believes that the efficiency resulting from coordination and communication across the federal government has the potential to multiply the value of all research funded by different agencies. In other words, NIH could and should enhance its stewardship in this way. Discoveries made by microbiologists working on optimizing biofuel production could propel the research of microbiologists studying human health, and the fundamental research on microbial physiology and ecology supported by the NSF could be translated into revolutions in applied research in multiple areas, especially in the area of antimicrobial resistance. However, it is difficult at present for these communities to benefit from each other's advances, form productive collaborations, or identify common infrastructural needs and transformative technologies. As a result, the US is not reaping the full value of federal investment in research. From highly transparent, searchable databanks, to new imaging and high throughput spectroscopy technologies, to long term environmental data collection efforts, many investments exceed the scope and resources of any one federal agency, but collectively funding them would improve the productivity of all scientists and leverage the value of their combined research.

Dear Dr. Tabak,

We write on behalf of the . . . and thank you for the opportunity to provide comments and suggestions on developing the framework for the upcoming NIH-wide strategic plan (NOT-OD-15-118).

. . . We act as a nationwide, grassroots network of scientists and academic and healthcare leaders who work together to educate Congress and the Administration about the value and importance of federal clinical and translational research and of research training and career development activities. . . . goals are to ensure that the full spectrum of medical research is adequately funded, translating from the bench, to the bedside, to practice, to public benefit and policy, with real impact on health. We join the nation in believing that the ultimate goal of the "H" in "NIH" is that there should be a focus on *health*. To serve that, we believe that the NIH must support the full spectrum of such research and must ensure that the next generation of researchers is well-prepared. We also support a regulatory and public policy environment facilitates ongoing expansion and advancement of the field of clinical and translational science.

In keeping with these core objectives, we have two recommendations for comprehensive trans-NIH research themes that have not been captured in the proposed Areas of Opportunity that Apply Across Biomedicine. Specifically:

- Supporting the *full spectrum* of medical research at NIH and more-formally integrating clinical and translational research programs and activities across all NIH Institutes and Centers.
- Advancing research training and career development activities at NIH to ensure that we are adequately preparing the next generation of clinical and translational researchers

Thank you for your consideration of this request.

The . . . appreciates this opportunity to provide feedback on the draft NIH-wide Strategic Plan framework. As a non-medical school with significant NIH funding - . . . in Fiscal Year 2015 - we applaud NIH's explicit support for fundamental science in the proposed framework. Basic research is often undervalued because it seems to have no immediate practical applications and yet it often contributes to the biggest economic and biomedical payoffs. We would also like to offer several specific suggestions for consideration and inclusion. We urge NIH to prioritize the following in its framework:

Fundamental Science

- Invest in research that cannot be monetized, funding scientific inquiry where industry cannot or will not;
- Increase theory-driven research, which shows where to seek the data needed to solve bioscience problems and increase impact and efficiencies; and
- Expand opportunities for groundbreaking, high-risk fundamental research awards.

Treatments/Cures

- Ensure behavioral and environmental variables are incorporated in developing treatments and cures; and
- Utilize alternative and unconventional animal models, whether vertebrate or invertebrate, to expand scientific understanding of human health.

Enhancing Stewardship

- Provide continuous and predictable grant funding to minimize disruptions that harm the advancement of biomedical knowledge;
- Expand interdisciplinary research and training programs;
- Implement training opportunities for non-citizens to retain an outstanding biomedical workforce;
- Incorporate support for research infrastructure including purchasing, maintaining, and providing training for instrumentation and equipment essential to the biomedical enterprise; and
- Increase uniformity in standards, processes, reviews and terminology across Institutes, Centers and Offices.

. . . greatly values its partnership with the NIH and we thank you for considering our recommendations to the draft framework.

On behalf of the . . . , thank you for the opportunity to comment on the framework for the NIH-wide strategic plan. Our members . . . bring expertise necessary to the success of biomedical research.

The NIH-wide strategic plan must support the need to maintain a diverse and robust workforce. We are pleased to see that the initial framework calls for enhanced stewardship of the research enterprise. As this framework is expanded, we urge NIH to remember that veterinarians and other physician-scientists are critical members of biomedical research teams. However, they are often overlooked when collaborative research teams form.

There must be support for the exploration of different mechanisms to train veterinarians to serve as research team members and then to connect them with projects being run at the various I/Cs that would benefit from their expertise. Also, veterinarians are uniquely trained to understand biomedical problems, and this expertise should be included on grant review panels that involve animals. This strategic review process should include ways to improve the grant review process.

In 2014, the Physician-Scientist Workforce (PSW) Report examined what steps NIH should take to sustain and strengthen the PSW. The report called for NIH to increase its efforts to diversify the PSW and to take other concrete steps, like expanding the Loan Repayment Program to more realistically address the debt burden of current trainees. . . . recommends that NIH examine these recommendations and integrate them into the strategic plan that will guide NIH's work.

Dear Director Collins,

. . . We believe advances in the science of aging hold great promise for moderating health costs while improving the lives of millions of older Americans. We urge the National Institutes of Health (NIH) to consider the inclusion of the cost to public healthcare programs into its priority setting for research and funding opportunities. Further, we feel that the NIH's Common Fund should be utilized for age-related initiatives to more rapidly identify and validate cross-cutting disease pathways for improved targeting of interventions for multiple diseases of aging.

The United States population is aging at an unprecedented rate. The 2010 Census projected the United States will undergo a doubling of the population 65 years and older, a tripling of 80 and older, and quadrupling of nonagenarians and centenarians by 2050. As the population of America ages, the number of American's living with costly chronic conditions is expected to rise. According to the Congressional Budget Office, between 2014 and 2050, the Medicare population is projected to grow from 54 to 93 million beneficiaries, and during this time period, net Medicare spending is expected to rise from 3.0% of GDP to 5.5% in 2050. Much of this increase in cost will be attributed to chronic and degenerative diseases for which age is the greatest risk factor. To see a greater return on public investment in research, the NIH should amend its priority setting to include the impact a disease has on costs to Medicare and Medicaid in addition to scientific needs and opportunities, gaps in funded research, the burden of disease in a population, and public health need. When considering the shared effects of America's aging population and increasing life expectancy on the cost to public healthcare programs, the necessity for aging-related research becomes almost incontrovertible.

The NIH needs to address aging head on by increasing funding for cutting edge translational and basic research. The research required to further scientific understanding of the aging process and to develop healthy aging interventions will need to be multidisciplinary, involve multiple investigators, and be flexible enough to adapt to new research and discoveries. The Common Fund program was created to support this type of broad research. We strongly urge the NIH to apply Common Fund resources to fulfill one or more of the published consensus recommendations that came out of the October 2013 Trans-NIH Geroscience Interest Group Summit.

Thank you for releasing this Request for Information and for your commitment to engaging the advocacy community as you develop the 5-year Strategic Plan. Please contact . . . if you have any questions or would like to follow up on our recommendations.

Thank you for the opportunity to comment on the proposed NIH-wide strategic plan framework. The senior leadership at . . . appreciates greatly the NIH efforts in developing this comprehensive plan, and the engagement of internal and external stakeholders in sculpting it. Overall, we are optimistic about what the plan might achieve and we appreciate the focus on collaborative research, cross-cutting opportunities, and the attention to young investigators.

On behalf of the . . . research community, I'd like to mention a few things we thought needed clarification in the document. We were very concerned about the wording regarding "incorporate(ing) disease burden as important, but not sole factor." Although the document does stress the power of fundamental discovery, the idea that disease burden might be one of the most important filters to allocate support may result in many lost opportunities to improve human health, since the quantum discoveries that change the face of health may not come from high disease burden processes. For a component of the overall portfolio, disease burden is certainly one of many filters to guide funding decisions.

Second, we felt the plan would benefit from additional specificity with regard to ensuring that the goals stated are actionable, measurable, and realistic. For instance, what does it mean to "optimize approaches to inform funding decisions?" We strongly believe that the document should specifically highlight the importance of the peer review process, and mention a focus to sustain and strengthen this critical foundation of the system. Finally, we believe that the document should stress a commitment to pilot on a small scale any changes that are to be implemented, with attention to the development of metrics to measure positive or negative effects of these changes.

Dear Dr. Collins:

On behalf of . . . would like to thank you for the opportunity to provide comments on the NIH-wide Strategic Plan framework. The . . . believes that evidence-based medicine is the integration of best research with clinical expertise and patient values. The . . . supports the vital collaboration between clinicians and scientists and encourages training of young researchers. The . . . commends the NIH for presenting a framework that reflects these important principles.

Musculoskeletal conditions represent a significant burden on individuals, the healthcare system, and the American economy. In the United States, 1 of every 2 adults (126.6 million) is affected by a musculoskeletal condition. . . . is committed to keeping the world in motion through the prevention and treatment of musculoskeletal conditions. To this regard, we offer the following recommendations:

General Recommendations

We propose the addition of a comprehensive research theme to the Areas of Opportunity that applies across all of Biomedicine:

Improving Clinical Outcomes

- a. Using research advancements to improve patient safety;
- b. Recognizing and addressing racial, ethnic, sex-based, and socioeconomic disparities in healthcare outcomes;
- c. Implementing sex and gender equality in research and clinical trials.

This theme would act as a unifying principle for all of the Institutes, Centers, and Offices. The specific goals we list under this theme are shared by all Institutes, and reflect the core priorities of the Continued and additional funding of these research priorities is necessary to improve function and mobility and reduce the socioeconomic burden of musculoskeletal disorders. While we understand the NIH Strategic Plan is designed to provide overarching themes applicable to all institutes, the URA is attached as a reference.

Additionally, the . . . supports the NIH's efforts to increase workforce diversity and believes that the Strategic Plan framework should highlight in the "Enhancing Stewardship" section the need to train and expand the pool of the next generation of diverse clinician investigators and basic scientists. Similarly, the Strategic Plan framework should promote the development of interdisciplinary research teams.

Specific Recommendations

- The development and regulation of therapies is increasingly inclusive of patient reported data. Further, variations in risk tolerance among patient populations, particularly those with few or no existing treatment options, are being incorporated into the assessment of safety and effectiveness. We believe it would be beneficial to patients and an efficient use of resources to extend these practices to research that ultimately produces novel therapies. Incorporating evaluations of risk and benefit with patient preference information in the overall study of potential treatments, recognizing that therapies with greater risk may be attractive options to patients who are willing to accept that risk for the potential benefits, is recommended.
- Competitive models, such as the Armed Forces Institute of Regenerative Medicine (AFIRM), offer an innovative approach to resource allocation that may expedite the development of research into new products. Leveraging the expertise of multiple institutions and fostering a collaborative environment means that federal dollars will be more effective in bringing solutions to fruition. We recommend an evaluation of the value of the AFIRM model to determine what aspects might be applicable to various NIH funding mechanisms.
- There is a significant need for more research to describe the short- and long-term effects of biologic therapies, particularly when used in pediatric and adolescent populations. The potential these therapies present is exciting, but important data are lacking regarding how long biologics remain bioactive, their impact on reproduction, and other factors, that make it impossible to assess their safety in humans.

- Cell- and tissue-based therapies also need increased research funding to answer fundamental questions that address long-term safety and effectiveness. Many cell- and tissue-based therapies are currently used without outcomes data due to their categorization as minimally manipulated products. Resources to support safety studies in humans will greatly accelerate the creation of novel therapies to bridge the gap between existing devices and autografts.

Musculoskeletal conditions are pervasive in nearly all areas of medicine and across multiple NIH Institutes. In June 2015, NIH released its "Information on Disease Burden" statement. In the summary, data from the Global Burden of Disease Study matched 69 conditions from the NIH Research, Condition and Disease Categorization to related disease categories and examined funding levels for these diseases. The analysis does not recognize orthopaedic injuries as a major cause of disability. In fact, multiple analyses of burden of disease versus NIH funding demonstrate that orthopaedic injury remains one of the most underfunded areas. Although NIH funding versus US DALYs (disability-adjusted life-years), includes two topics related to orthopaedics, "Arthritis" and "Injuries", whether this is rheumatoid arthritis, osteoarthritis, or posttraumatic osteoarthritis is unclear. Additionally, the injuries section is not classified as orthopaedic or other. The . . . Research Development Committee is interested in providing resources and information to explore and document the true disease burden and the omnipresence of musculoskeletal conditions.

Again, the . . . thanks you for the opportunity to provide comments on the NIH-wide Strategic Plan framework and we look forward to reviewing the finalized Strategic Plan. Please feel free to contact . . . if you have any questions or if the . . . can serve as a resource to you.

Dear Dr. Tabak:

The . . . is pleased to respond to the request for information on the NIH Framework for the NIH-wide Strategic Plan. Below are the comments that we would like to share for your consideration:

Promotion of Fundamental Science

- **Data Science:** Data science is an important topic could benefit from additional development and support from NIH to ensure that there is both access to data and people trained to use the data appropriately. We encourage NIH to support an initiative that surveys and documents data sources and brings the data together in usable forms to provide better access to existing data. We also encourage NIH to support training funds to train data scientists who will focus on oral health issues.
- **Advances in clinical research methodologies stimulate scientific progress.** This is a critical area for NIH as well as public health dentistry, especially in the areas of observational studies, the advancement of epidemiological methods, and clinical research ethics.

Improve Health Promotion and Disease Prevention (HP/DP)

- Health promotion operationalized at levels beyond the individual is needed to influence population level health outcomes. Health disparities cannot be addressed effectively at the individual patient level. For example, significant gains in reducing smoking was not

achieved by counseling patients to quit smoking, but rather was mediated by changing policy, increasing taxes, stigmatizing the behavior, education programs in grade schools, etc. We encourage NIH to support investigations of interventions at higher levels than the individual to better improve health promotion and disease prevention.

- Strong evidence in support of health promotion activities is needed to identify interventions that are shown to be effective. “Traditional” models of health promotion and prevention not shown to be effective need to be abandoned. In particular, understanding how health promotion and prevention activities change in effectiveness across populations is needed, especially in very high disease/high risk populations. Because traditional models of HP/DP often fail in these populations, we encourage NIH to support investigations of HP/DP in high disease/high risk populations as the basis of evidence-based interventions and the path toward disparities reduction.

Advance Treatment and Cures

- Public health scientists make contributions to analytical epidemiology and exposomics. We encourage NIH to include public health scientists as part on an interdisciplinary approach to address advance treatment and cures.

NIDCR 2017 Research Themes.

- **Factors Underlying Differences in Female and Male Incidence Rates for Certain Dental, Oral, and Craniofacial Diseases.** Support of these initiatives should be based on the severity of the sex disparities and the likelihood of this avenue of research leading to insight into cures.
- **Implementation Science.** Implementation Science is an area that is *missing* in the Research Themes for NIDCR. Most new advances in prevention and treatment do not reach patients in a timely manner. Healthcare workers fail to adopt new approaches even when they are clearly superior to existing approaches. We need to better understand why new and better approaches are not adopted. Failing to study this area means that funds spent to support all the other NIH and NIDCR initiatives will not be effectively used to improve patient outcomes. We encourage NIH to make a significant investment to support implementation science.
- **Caries Prevention.** Understanding of dental caries and the safe use of fluoride still needs to be advanced, as there are serious gaps in knowledge in these long-standing areas. Caries research is notably absent from any of the current themes. We encourage NIH and NIDCR to include management and prevention of dental caries in the strategic plan.

Thank you for the opportunity to provide comment in response to the RFI. We hope that this information is useful. Please feel free to contact . . . if you have any questions or would like additional information.

As the NIH looks to the future and develops its 5-year strategic plan, the . . . would like to reassert strong support of the History of Medicine Division (HMD) of the National Library of Medicine. The mission of the NIH to pursue fundamental knowledge depends on its continued commitment to the connection

between scientific knowledge and the history of medicine, a commitment it has demonstrated through support for scholarship and education.

. . . . Research and publication by many of our members and other historians relies on the collections and support of the History of Medicine Division. In addition, many valuable and important historical projects have been made possible by NLM grants for scholarly works.

The National Library of Medicine's unparalleled collection of primary historical sources dating back to the 11th century is of inestimable value to historians for both research and education. The more than 600,000 printed volumes in the History of Medicine Division—including the earliest printed medical works, thousands of books published between the 16th and 18th centuries, and many more up to the present day—make the collection an invaluable research resource. The NLM's historical collections have two very significant functions. First, they are a treasure trove of manuscripts and books that document the human struggle against disease from classical antiquity until today. The riches of the collection were beautifully highlighted in NLM historian Michael Sappol's 2012 book *Hidden Treasures*. They range from unique medieval Islamic texts that provide our best evidence of the foundations of Western medicine in ancient Greece, to the textbooks from which 20th-century American doctors learned their craft, to collections of papers of such key modern figures as Joshua Lederberg, Marshall Nirenberg, Luther Terry, and C. Everett Koop. These print collections are complemented by a growing digital collection, making this library a resource like no other in this hemisphere.

The resources made available by the NLM lay the groundwork for fundamental research with which the NIH may pursue its broader goals of improving health promotion, disease prevention, and advancing treatments and cures. Advances in fundamental science and the technological leaps that promote scientific progress are built on the work of scientific and medical forebears, about whom the collections at the NLM and the expertise of the staff of the HMD provide vital knowledge.

Public education about the history of medicine is vital for promotion of health in modern US society, and the History of Medicine Division is also actively involved in this through its award-winning exhibits and programs. Mary E. Fissell, professor of the history of medicine at The Johns Hopkins University, has provided us with an excellent example of the value of these exhibits:

The HMD has fully embraced the possibilities afforded by the digital age, and has pioneered a series of online exhibits that continue to be one of the most significant resources in our field. I literally cannot tell you how often I direct the students to one of the online resources of the NLM. For example, in my undergraduate survey, one of the assignments is to go to the website Historical Anatomies, and choose images from pre-Vesalian anatomy books to compare with the work of Vesalius himself. Students bring all kinds insights to discussions from their close investigation of such anatomical images. There is simply no way students would access this kind of material in any other setting. But the NLM's prescience in developing this kind of online exhibit enables me to teach undergraduates who will be tomorrow's physicians to understand and appreciate the intellectual processes involved in delving into the mysteries of the human body.

Historians of medicine are also increasingly working with the most innovative digital tools to address research questions. Fields such as historical epidemiology are breaking new ground in understanding contemporary patterns and disease prevention. Historical perspectives on disease, such as that presented in the HMD's blog *Circulating Now*, provide a vital understanding of such diseases as measles and influenza, both of which are of concern to contemporary medicine and public health. Knowledge of

the history of these diseases can improve health promotion and disease prevention. Another example of this work that has benefited greatly from the HMD collections and working with the staff is “An Epidemiology of Information: Data Mining the 1918 Influenza Pandemic.” This project brings together historians, computer scientists, and biomedical scientists to utilize big data understand the spread of knowledge about the 1918 pandemic. As these examples demonstrate, when scientific knowledge and historical inquiry are allied they can reveal new opportunities for innovation.

To sum up, alongside the crucial functions of the NLM in relation to biomedical research, the library has an equally vital role in collecting, curating, and providing access to the rich history of medicine in the United States and across the world. It is a key node in providing crucial links between history of medicine and biomedical science in the United States. As the NIH develops its strategic plan we strongly advise that it continue its 150-year tradition of support for scholarship in the history of medicine through the History of Medicine Division of the National Library of Medicine.

We applaud the inclusion of health promotion and disease prevention research in the NIH strategic plan, and strongly support increased research on developing evidence-based preventive interventions to promote health equity. Prevention research has revealed that the biggest benefits may occur where risk is greatest and opportunity or protection scarcer, including disproportionately low-income and/or youth of color, who frequently demonstrate the largest and broadest benefit.^{1,2,3,4}

We would like to see a broader public health emphasis. Prevention is the best investment we can make in behavioral health⁵. Behavioral health problems cause deep, long-term damage to young people, families, schools, and communities. These problems include: mental health disorders, substance abuse, delinquent and violent behavior, school dropout, and risky sexual activity. Behavioral health is defined broadly because many of these problems share risk factors—and solutions. Preventing one problem often prevents or ameliorates others.⁶

We suggest three additional priorities: 1) prevention-informed basic research to discover and specify the mechanisms of biopsychosocial risk and protection and their developmental interaction; 2) prevention research to develop and test new interventions that extend the comprehensiveness of programs with demonstrated efficacy, develop and test approaches based on emerging findings about biopsychosocial risk, and specify how intervention effects are realized and what works for whom; 3) research to understand how best to “scale up” effective prevention interventions to extend reach and maximize fidelity to achieve population-wide reductions in behavioral health problems, with related economic and health gains. Scaling-up is the ultimate public health goal, transforming extraordinary findings from prevention science into innovative policies and effective programs that are cost effective, promote social justice, and have meaningful impact on population health⁶; and 4) development of innovative methods and technologies to elucidate mechanisms of biopsychosocial risk factors and test prevention strategies and scale up.

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To accomplish the envisioned NIH Framework it would be relevant to foster a multi-disciplinary team approach to gather knowledge on the etiological mechanisms of human diseases, the definition of early biomarkers and the role played by genetic and environmental risk factors.

Animal models can lead to mischaracterization of drug treatment effects on humans and the scientific community generally agrees that alternatives to animal use should be applied whenever possible. In an effort to reduce current translation failure rate, NIH should consider 'return on investment' as a principle to judge traditional research efforts and undertake new research avenues. In this regard, the use of human-based models should be encouraged. Patient-derived cells and, in particular, induced pluripotent stem cell models, have been proven invaluable tools to elucidate disease pathological mechanisms, accounting for patient heterogeneity. Novel microfluidic organ-on-chip devices, while still under development, represent suitable tools to elucidate molecular and cellular mechanisms of disease initiation and progression and test new drugs.

Computational readouts can facilitate the systematic analysis of human-related genes, proteins and signaling pathways in an integrated manner. Knowledge derived from in vitro cellular and computational readouts, should be integrated with data derived from large scale clinical studies.

Considering the role played by environmental and lifestyle-related factors, it would be relevant to increase current NIH research funding in the area of prevention. In this regard, large scale epidemiological and prevention clinical trials focused on nutritional and lifestyle interventions have been proven relevant to unravel the role of risk factors commonly associated with many human diseases, such as diabetes, metabolic syndrome, cardiovascular disease, many forms of cancers and neurodegenerative diseases. These tools will facilitate human-relevant data acquisition, elucidate human pathogenic processes in a human-based setting and the design of treatments and preventive strategies effective in humans.

To the NIH Strategic Plan Committee-

There is a critical need to increase funding for wound care research within in the United States. All areas of wound research, including basic science, clinical science, epidemiology and product testing and development, are underfunded based on the impact this problem has on individuals, the population and the health care system. In 2012, only 0.1% of the NIH's \$30.39 billion dollar budget was allotted to 91 research projects in wound care.¹ More than 6 million Americans suffer from chronic wounds annual and cost the health care system more than \$25 billion per year.¹⁻³ Despite the high impact on individuals and society the NIH provides more funding for rare diseases, such as Lyme disease, Fragile X syndrome and Muscular Dystrophy, than for chronic wounds.

Wounds cause patients considerable pain, depression and often result in social isolation. A chronic wound places an individual at an increased risk for hospitalization, amputations, sepsis and death.⁴ Lower extremity amputation is the outcome of 16-21% of diabetic foot ulcers.³ The 5 year mortality following a lower extremity amputation is 50%.^{2,5} Pancreatic and lung cancers are the only cancers with a higher mortality rate than a chronic wound.⁵ A diabetic foot ulcer places individuals at a high risk of death than does breast or prostate cancer.⁵ The 2 year mortality of individuals with diabetic foot ulcers, pressure ulcers and venous leg ulcers is 28%.² In light of the fact that chronic wounds cause suffering and are more deadly than some cancers, does it not make sense that research in chronic wounds receive similar funding from the NIH?

Research in wound healing is complicated by the large number of comorbid conditions that influence healing including: age, gender, mobility status, diabetes mellitus, renal disease, cardiovascular disease, poor nutrition, medications, infection, tobacco and alcohol abuse and a myriad of socioeconomic factors.⁶ Wound patients have, on average, 8 comorbid conditions.⁷ This complex situation causes difficulties in designing randomized control trials and result in studies that are under powered, have short time periods in which wound healing cannot be captured and have limited clinical applicability.^{8,9} Increased funding for wound studies will allow researchers to expand studies to multiple clinical sites to ensure adequate numbers of patients are enrolled to ensure robust trials.

For the sake of our patients and to improve research in the area of wound care, I strongly urge the NIH to increase research funding in this area.

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Need for research support for Skin Ulcers and Wounds.

Current health research funding priorities focus on mental health, diabetes, obesity, cardiovascular and malignancy disease states. Many of the patients who suffer from these disorders also present with chronic ulcer and it has been reported that the economic burden to the US is of the order of \$25 billion (Sen et al: Wound Care and Regeneration 2009, 17(6) 763-771) . There is also an impact on public health as the quality of life of these individuals is markedly impaired. Current management is mainly palliative. This is in part related to the underlying disease, for example diabetes, where neuropathy can lead to the creation of a foot ulcer. It is unlikely that an effective medication for the primary pathology will treat the comorbid condition of the skin ulcer, which is often chronic and infected. Clinical trials in the area of chronic wound are often unsuccessful because they are fraught with complications of inclusion criteria. This is due to differences in both the underlying pathologies and the nature of the ulcer itself (venous, diabetic foot and pressure). Consequently there is a dearth of available and investigative new drugs in wound management. It is essential that we better understand the cutaneous pathologies to manage the patient ideally prior to the development of a wound and an eventual chronic and infected ulcer, which may lead to amputation as a final outcome. To achieve this effectively, more research funding should be applied to determine underlying dysfunctions in the vascular, neuronal, dermal and epidermal components of the skin in patients prone to such disorders.

Dear Director Collins:

Our nation is experiencing social, medical, and economic challenges due to remarkable increases in life expectancy in recent decades.

Studies in the biology of aging are showing that we can delay aging in animals and there are now potential targets for therapeutic interventions with non-disease specific end-points. By increasing support for the basic biology of aging, we can accelerate the pace of research and implementation so as to achieve delays in the onset of all major age-related diseases, generating large increases in “healthspan”, i.e. the proportion of life lived in a state of good health.

The . . . recommends that the NIH-wide Strategic Plan include:

- An increased focus and funding of research in the Biology of Aging. Currently, less than 5% of the NIA budget is allocated to the Biology of Aging portfolio.
- Increased funding of geroscience research funding across the institutes
- Encourage and increase Trans-NIH geroscience interest group activities and funding.
- More Nathan Shock Centers (or mini centers) of Excellence in the Basic Biology of Aging.
- Building a pipeline of future researchers in the field of aging research.

We believe that increasing investments in these areas will:

- Afford larger health benefits than the usual approach of fighting one disease at a time.
 - Delay the onset of major diseases and disabilities which will improve the quality of life of all seniors, not just the sick and infirm, for current and future generations.
 - Allow us to reap significant economic and social benefits.
-

Data science will become even more vital to the mission of NIH in the next few years. The Strategic Plan should feature a comprehensive vision of support for the advancement of data science, and its integration with both fundamental and translational biomedical research.

Addressing challenges in accessing, analyzing and sharing Big Data requires investment in basic mathematics, computer science, statistics, and subsequent software development. For example, algorithm development for large genomic datasets requires new techniques from multiple disciplines, such as graph theory, statistical estimation, and data mining. Continued advancement in fundamental data science research has the potential to help revolutionize disease prevention, diagnosis, and treatment through predictive modeling, precision medicine, and other innovative health strategies.

Currently, many NIH projects use NSF-funded resources, such as the University of Illinois' Blue Waters supercomputer, to simulate complex biophysical systems and to analyze and share massive datasets. The substantial investment required to create and maintain centralized, large-scale resources is justified by the wealth of research that is enabled, including molecular-level modeling of cellular systems, high-resolution image analysis, *in silico* construction of neural networks, and synthesis of high-dimensional health data.

NIH must also reach beyond conventional wet-lab and dry-lab research, and instead promote a truly integrated research environment in which teams of experimental and computational scientists work not in series, but in parallel to realize the full potential of computing technologies for biomedical research. Hypothesis-generating and hypothesis-driven projects both deserve emphasis, and need better coordination.

Resources, knowledge and infrastructure must be maintained and advanced to keep pace with the exponentially increasing demands of cutting-edge, convergent health research. If they are not, missed opportunities and delayed discovery will result. We encourage NIH to include a roadmap for broad, deeply integrated data science research and sustained investment in world-leading data science resources in the Strategic Plan.

Dear Dr. Collins:

The On behalf of . . . members, we appreciate the opportunity to comment on the National Institutes of Health's (NIH) request for information (RFI) on a framework for the NIH-wide Strategic Plan.

As an advocate of dental and craniofacial, biomedical, clinical and translational research, . . . is committed to supporting and promoting the importance of cutting-edge scientific research that NIH produces and which has the potential of life-saving and life-altering benefits for the country. Research serves as the foundation of dental education, and of the science and practice of dentistry; ultimately, improving the nation's overall and oral health and well-being. The vast majority of dental, oral and craniofacial research in the United States is conducted by dental schools with the support of the National Institute of Dental and Craniofacial Research (NIDCR). NIDCR's research yields new discoveries and effective treatments that prevent disease, provide practical applications of research, and offer quality-training opportunities for faculty and students. As one of the first institutes of the NIH,

the NIDCR serves as the lead agency for scientific discoveries and research on dental, oral and craniofacial health and disease. NIDCR-supported research fosters interdisciplinary research teams, provides evidenced-based practices and interventions to advance oral and overall health and makes significant contributions to the overarching biomedical research portfolio. With the aforementioned in mind, we provide the following comments to the requested topics put forth in the RFI.

- *Effective Dissemination and Application of Research Findings*

Effective translation and dissemination of research is needed to advance any scientific discovery into clinical studies, practice and patient care. Therefore, it is important that the NIH develops, refines, and implements effective methods to disseminate research findings that can be easily understood and applied by individuals, clinicians and public health decision-makers. In the end, implementing comprehensive dissemination strategies is necessary to heighten the visibility and impact of NIH-supported research.

- *Comprehensive Trans-NIH Research Themes Apply Across Biomedicine*

Salivary gland research is a cross-cutting area of opportunity to include in the NIH-wide Strategic Plan that can improve the lives of millions suffering from head and neck cancer and dry mouth. Additionally, saliva can be a non-invasive measure of proteins to indicate disease development in the mouth and the rest of the body. Saliva plays a significant role in preventing infection and tooth decay. The destruction of salivary glands makes it difficult to taste, eat, swallow, and talk. Radiation therapy for head and neck cancer can damage salivary glands and reduce the ability to secrete saliva. Each year, hundreds of Americans are left with severely damaged and destroyed salivary glands after undergoing radiation therapy for head and neck cancer. Salivary gland cancers are rare but they are often fatal and reoccurrence is common, only 66 percent with aggressive treatment have a 10-year survival rate. Also, salivary glands can be destroyed by specific genetic defects in Sjögren's Syndrome, a chronic autoimmune disease affecting as many as four million Americans.

Salivary gland research can involve identifying the quantity, location and function of salivary gland stem cells to learn how salivary glands are destroyed and can be regenerated. There is opportunity to develop more targeted anti-cancer drugs through comprehensive genetic analysis and mapping of salivary gland tumor formation and progression. Research has found functional similarities with salivary gland tumors and endometrial and ovarian cancers, suggesting a promising area of research for more effective therapeutic strategies.

- *Developing the Next Generation of Learned, Diverse Scientific Researchers*

. . . is committed to promoting a robust and diverse scientific workforce capable of *turning research discoveries into health*. The increased demand of research to support evidence-based practice has intensified the need of a diverse, well-prepared workforce. . . believes the upcoming Strategic Plan must include a plan and efforts to develop and maintain a critical mass of investigators from diverse backgrounds and scientific disciplines, especially those dedicated to address the complex and multifaceted nature of chronic diseases, such as dental caries or tooth decay. Eliminating silos and incorporating cross-discipline training will ultimately strengthen the outcomes of the research and improve the health of the public.

- *Investing in Personalized Medicine*

The emerging field of personalized medicine offers an unprecedented opportunity to customize health care decisions, products and therapies to the unique characteristics of an individual. Personalized medicine can foster better-designed clinical trials to yield more targeted therapies with faster results, leverage genetic information and develop a more robust understanding of biomarker treatments; and curtail long-term health care costs by providing the “right treatment for the right patient at the right time.” The possibilities of this kind of research is unlimited.

. . . is excited by the scope and promise of the NIH-wide Strategic Plan. Do not hesitate to let us know if we can be of further assistance in this regard. Please feel free to contact . . .

Dear Dr. Collins:

On behalf of the . . ., thank you for the opportunity to comment on the National Institutes of Health’s (NIH) strategic visioning framework. We are pleased to be a part of this exciting initiative to develop a strategic plan to guide future scientific research across all NIH institutes, offices and centers for the next 5 years. The framework encompasses a wide breath of scientific inquiry into the nature of health and disease and fosters the application of knowledge into real benefit for the individual and society. We support the concept of unifying principles and collaborative effort that transcends disease and organ-specific research and hope that implementation of these principles will lead to improved funding and more importantly, significant understanding and treatment of disease. We have the following recommendations on the strategic visioning framework.

Setting Priorities

1. **Early Origins of Disease.** The . . . believes it is important, if not critical, to include the early origins of disease as a priority. Increasing evidence demonstrates that many adult diseases have their origins in the fetal or early childhood period either due to an underlying genetic or epigenetic mechanism or as the result of fetal or neonatal exposures that affect development. Furthermore, as children with previously lethal diseases, such as cystic fibrosis and extreme prematurity, now survive to adulthood, understanding the long-term consequences and the implications of transitions from pediatric to adult medical care become increasingly important. The . . . recommends the following priority areas for research: a) genetic, epigenetic and environmental influences on development; b) injury, regeneration and repair and; c) prematurity and its lifelong consequences.
2. **Bioengineering.** Collaborations between engineers and medical scientists have fostered rapid advances in the fields of tissue engineering, nanotechnology and computer modeling of the human body. The . . . believes that the interface between engineering and the medical sciences must be fostered to further understanding of disease, and development of novel diagnostic and therapeutic approaches.

Treatment/Cures

1. **Comorbidities.** Almost half of all Medicare beneficiaries have three or more chronic conditions. Effective and efficient treatment of these patients will require a complex array of physician and

non-physician specialists, support staff, infrastructure, sciences, technologies, patient and family skills, and community linkages that must be integrated across multiple venues over time. The . . . believes that research into innovative practice models to treat the multi-morbid patient must be a priority.

Enhancing Stewardship

1. **Recruit/retain research workforce.** Our workforce is in crisis, leading to a significant lack of physician scientists in basic/translational/clinical studies, especially in pediatrics. These scientists have the ability to change the trajectory of diseases with earlier treatment targeted at the primary defect. The . . . believes that there must be a priority to specifically increased funding opportunities for pediatric research training programs. We also recommend that NIH consider creating a mechanism for sustainability throughout the research continuum. This sustainability and continuity effort will insure promising research reaches its full capability, with the goal of ultimately impacting the lives of patients.

Emerging/Evolving Research Needs – The Burden of Lung Disease

Lung diseases are now the third leading cause of death in the U.S., specifically chronic obstructive pulmonary disease (COPD).ⁱ The death rate from COPD has doubled within the last 30 years and is still increasing, while the rates for the other top causes of death (heart disease, cancer, and stroke) have decreased by over 50%.ⁱⁱ Asthma rates in the U.S. have surged over 150% since 1980. Yet, lung disease research is disproportionately underfunded relative to its health burden, representing just 21.2% of the NHLBI's budget in fiscal year 2014. Declines in the death rates from cardiovascular disease and cancer achieved over the last 30 years can be traced to substantial increases in research funding. Thus, the . . . respectfully requests that the NIH leadership consider beginning to shift some resources among the research portfolio to more accurately reflect the rising burden of lung disease and replicate the enormous success of the cardiovascular field in reducing morbidity and mortality.

We thank you for this opportunity to comment and look forward to participation in the next phase of the strategic planning process.

The . . . conducts research to translate data into policy and practice to address critical health and development issues. With support from NIH and other donors, we perform biomedical and social research to develop products to alleviate some of the biggest global health burdens, including unintended pregnancy, infertility and HIV. Our programs increase diversity in the biomedical workforce.

We appreciate the opportunity to provide comments on the framework for the NIH-wide Strategic Plan for shaping decisions on investments in science.

Promotion of human health as well as better understanding of basic mechanisms and treatments for human diseases should remain driving forces behind this Strategic Planning, acknowledging that fundamental mechanisms underpinning health are also dysfunctional elements of disease. For example, basic research in physiology and pathobiology of reproduction has great potential to advance our knowledge of human fertility, infertility, and reproductive tract cancers to inform novel product development.

It is important not to replace the essential role of ICOs in visioning research priorities. The Plan should include support for an Institute's identified gaps-in-knowledge with evolving portfolios of investigator-initiated research. This mechanism provides critical, fundamental research engines which drive progress, addressing life-span improvements in health and discovery research for new therapeutics.

Defined by Institute-specific goals, centers of research excellence should emphasize areas of opportunity that apply across biomedicine. One strategy might be to promote new collaborative partnerships across ICOs. For example, to develop multipurpose technologies within a virtual centers format, ICOs and multi-institutional partners can leverage synergy between basic reproductive and sexual health scientists with bioinformatics experts, clinical, product development and behavioral researchers involved in reproduction, infectious disease and cancer prevention to achieve goals of family planning, safe motherhood and healthy baby outcomes.

We look forward to work closely with NIH to meet its biomedical research priorities.

Dr. Collins,

The . . . appreciates the opportunity to provide comments to the National Institute of Health's (NIH) request for information (NOT-OD-15-118) on the development of a framework for its agency-wide strategic plan. . . . is the unified voice of the Parkinson's community, advocating for treatments and a cure. Parkinson's impacts between 500,000 and 1.5 million Americans.

NIH, through a planning meeting organized by the National Institute of Neurological Disorders and Stroke (NINDS) in January 2014, has taken critical steps to advance Parkinson's research and treatment by identifying priority research recommendations. The success of these recommendations, which are being incorporated into the grant award evaluation process, will depend upon targeted research initiatives and increased capacity that may require NIH to consider innovative support and funding mechanisms. We strongly urge NIH leadership to leverage the momentum of this planning effort to continue to seek and capitalize on the best scientific opportunities to make meaningful advances in understanding Parkinson's disease and other chronic conditions.

NIH has made a commitment to address public health concerns with severe gaps in unmet medical needs. Often, this work is conducted through cross-Institute collaborations. The field of Parkinson's research may benefit greatly from one such effort between NINDS and the National Institute of Environmental Health Sciences to examine the relationship of environmental factors and genetic susceptibilities to the onset of the disease. We encourage NIH in its strategic planning process to make collaborative initiatives among its 27 Institutes and Centers a top priority to maximize a limited pool of resources for transformative gains in knowledge and understanding of diseases like Parkinson's, which translate to more effective treatments, better quality of life, and potentially cures.

Thank you again for this opportunity to comment, and please consider . . . as a resource during the strategic planning process.

The relationship between the federal government and tribes has historically been one of stewardship or

guardianship of Native Americans. This relationship was often used and misused for research that was conducted *on* Native Americans, rather than *with* Native Americans. Today, the disease burden within tribal communities is immense with chronic diseases such as diabetes and cardio-vascular disease at epidemic proportions. The health disparities between Native Americans and the general US population are large. Cancer rates for Native Americans are lower than the general population, but the mortality rates are higher as malignancies are often diagnosed at a later stage. With such large health disparities, it would make sense that NIH would invest heavily in research to help alleviate the disease burden in the communities. However, among the 37,000 NIH grants awarded in 2006, only 24 went to Native Principal Investigators. An online supplement indicated that just 41 Native American PhDs submitted an R01 over a six year period. More federal grant funding invested in the health of Native Americans, and more funding for native researchers working to improve the health of their communities, will help tribes address their health disparities. The NIH needs to be aware of, and open to, the unique relationships that must be formed with native communities prior to initiating research. Utilization of the principles of community-based participatory research will create the ethical, equal partnerships needed to conduct effective research. Making data sharing agreements and biospecimen ownership agreements a part of every project ensures that tribal sovereignty is not violated. In response to a growing need, tribal infrastructure and research capabilities have changed greatly in recent years. Tribes are now ready to assume a role of equal partnership with federal, state, and academic research partners to address the burden of disease that continues to plague native peoples.

As a basic scientist and proud recipient of uninterrupted NIH R01 support for 36 years, I am happy to see your emphasis on fundamental science. The main suggestion that I have is to maintain, even expand, individual R01 or equivalent funding mechanisms. Of course I have been and will be involved in larger grant mechanisms. I recognize that they have some merit, often focusing attention on specific diseases. I recognize the politics of being able to talk about clear health-directed initiatives. But I also recognize that some of these mechanisms do not necessarily promote the best science. Group-think and team-based research, especially where senior PIs dominate junior PIs, do not necessarily foster creativity. Certainly, science has changed since I started. Collaboration, bringing together different areas of expertise, is ever more important but framing this in large program grants does not always achieve the goal in reality even if it does so on paper. On the other hand, I see the Multi-PI grant as an excellent step forward in promoting and sustaining true collaborations.

Please, in this era when every university is trying to squeeze as much out of faculty and the NIH as possible, SAVE THE R01, INCREASE THE PAYLINE, so that good scientists can survive in the University environment and encourage the young to enter scientific research as a career. Recently, I have not known what to tell young scientists contemplating an academic career. I usually end up saying only that you have to start off loving science. Unless we make science more attractive as a career, we will not have a scientific workforce to carry on the great enterprise that has been built up over the past decades.

Dear Dr. Griffin:

Over 29 million Americans have been diagnosed with diabetes, with an additional 8 million undiagnosed cases. The costs associated with this condition now exceeds \$245 billion and ranks in the top five in terms of health resources allocation and lost productivity. Of note, a disproportionate share of the burden is

borne by priority populations in our country. For example, approximately 13.2% of Blacks and 15.7% of American Indians/Alaska Natives have diagnosed diabetes compared with only 7.6% of Whites living in the United States.

Obesity prevention arguably is one of the best measures to confront the growing diabetes epidemic. Both diabetes and obesity have many overlapping antecedent risk factors. Increasingly, it is recognized that a life-course approach is the most effective means of prevention with targeted efforts directed at the prenatal period, infancy, childhood, and continuing onward through adolescence and early adulthood. Important factors to consider include the social/built environment, behavior, physiology, and genetics and their interacting effects over an individual's lifespan. Additionally, targeted efforts must be integrative in nature including the community, educators, clergy, and policy makers.

However, it is important to recognize that prevention alone will not solve the problem. Over 78.6 million Americans are obese and in need of treatment. Unfortunately, effective pharmaceutical treatment options for obesity have been slow to move forward into clinical practice. The National Institute of Health's recent Bench-to-Bedside program is an important step forward, aiming to address key barriers such as traditional silos between basic and clinical researchers. Nonetheless, regulatory approval of emerging compounds has been sluggish over the past two decades and further resources and attention needs to be directed at safely expediting the process. Increased advocacy and communication between the National Institutes of Medicine and the Food and Drug Administration represents an important future direction. The appointment of a special task force with representation from both groups, as well as the . . . , would be an instrumental step forward.

Today obesity is change to world big problem. Briefly, my focus is on obesity and aging which both of them speed up each other. To face with obesity at first we need to recognize it well, then treatment ways which can be surgical and non-surgical therapies. In recognizing, DXA, CT and MRI can correctly illustrate the body tissue distribution but they are expensive and a little harmful for body. Ultrasound among the different instruments can also use and measure e.g. the visceral fat that is one of the cardiovascular risk factor (Pereira AZ 2012). Also, it is reported that obesity especially in core body can hide fetal abnormalities, which not only put its harmful effects on obese person also its footprint can mark the future generation. To combat with obesity we should emphasize that importance of increasing the energy expenditure compare to energy intake, which is physical activity or exercise training. Noteworthy point is to find the prior reason of obesity which is ACTIVELESS LIFE STYLE. To increase the exercise training effects we should walk in new way, HIIT exercise as an example, which one of my colleague work it on obese women and their weight is become under control (under published). Of course obese person should be under control but how could it be possible? Only a little part of obese people go to Dr. to control their weight or take part in studies. GPS is a good and economic way to control people activity level, which can programmed to guide its consumer about activity level needed, calorie burned and so on. Shortly, the most advantaged diagnosis tools, functional treatment and practical ideas are important topics to confront the obesity.

I hope best health future for whole world

For consideration:

Overview

Including challenges as part of the description of the NIH-supported research landscape may lead a reader to think, “Wow, this is important enough that NIH specifically called it out – this must be a top priority for them.” While the challenge may in fact be one of NIH’s top priorities, I believe statements that suggest top priorities in the introductory segment of the plan detract the reader’s attention away from the thought process we are attempting to set out in the framework. However, I do agree that including the very general observation regarding constraints confronting the community in the face of lost purchasing power is a very good way to set the stage for multiple components of the plan that follow. Consider focusing on this fact and not including individual “landscape challenges” in the overview.

Areas of Opportunity that Apply Across Biomedicine

A strategic plan is meant to be forward-looking. As such, it seems strange to include descriptions of recent breakthroughs. These are retrospective in nature. This aspect seems to be geared towards helping Congressional stakeholders understand the strategic plan on a more detailed level. Perhaps this information can be moved to an appendix or supporting document.

A strategic plan should articulate an organization’s highest priorities. As such, I interpret the three Areas of Opportunity to be NIH’s highest priorities. For Congressional stakeholders, it may be prudent to include examples to help them understand what each of the three areas means, but I would caution that the examples themselves are likely to be misinterpreted as the specific NIH top priorities instead of the bullet points within each area of opportunity. HHS may expect subsequent enterprise risks to be associated with the examples. If examples are included, consider ensuring that the examples cited align with leadership’s perception of NIH’s current top enterprise risks. Additionally, consider moving them to an appendix at the end of the plan.

As previously noted, NIH has not yet undergone the effort to identify its top enterprise risks. The following identifies potential enterprise risks associated with the Areas of Opportunity and Unifying Principals. A few of the risks have full risk statements in an attempt to better show how the strategic plan and ERM relate to each other. They are my personal opinion only and do not presume to reflect NIH leadership’s thoughts. I am merely trying to show how it might be helpful to view the strategic plan through the ERM lens.

Promote Fundamental Science:

- Trans-NIH collaboration: *If NIH does not encourage interdisciplinary and team science, bolster support for collaborative and synergistic projects among NIH ICOs, and develop research structures for intramural-extramural collaborations, then essential components for successfully working at the cutting edge of science may be overlooked.*
- BRAIN Initiative
- Management/integration/analysis of large biomedical data sets
- Ensuring stem cell research integrity

Improve Health Promotion and Disease Prevention:

- Precision Medicine Initiative

Advance Treatments and Cures:

- *Alzheimer's: If biomedical research efforts are unable to significantly accelerate progress in developing effective modes of treatment and prevention of Alzheimer's disease and related conditions by FY2025, then the steep physical, emotional and financial toll on our nation will continue to increase.*
- Advancing Translational Science
- Accelerating Medicines Partnerships

Setting NIH Priorities:

- *Strategic Planning: If NIH does not develop, periodically review, and update a NIH Strategic Plan, then the absence of articulated key priorities may result in less than optimal research portfolios and resource allocations thereby delaying fundamental creative discoveries, innovative research strategies, and their applications as a basis for ultimately protecting and improving health.*
- *Common Fund: If NIH does not have an effective mechanism to consider and address the challenges and opportunities that have a high trans-NIH impact, then individual efforts to remove significant bottlenecks may be cost prohibitive or unsuccessful in moving biomedical research forward.*

Enhancing Stewardship:

- *Inadequate or Obsolete Facilities: If NIH is unable to obtain and maintain facilities adequate for effectively supporting all facets of its current and future research needs, then resources spent on interim or emergency stopgap measures may delay progress in achieving NIH strategic objectives and increase the cost basis for NIH mission support.*
- Workforce Diversity
- Future availability of qualified biomedical workforce
- Long-term viability, value and benefits of IRP, Clinical Center and NLM

I note (1) the impact of multidrug-resistant bacteria (~20,000 reported deaths per year), (2) the red queen's race aspect of the typical response, which is to develop more antibiotics, and (3) the similarity of multidrug-resistant metastatic cancer cells and the failed response to managing metastatic cancer. Common sense tells one that a common failure has a common underlying cause. This cause is the use of chemistry, rather than biology, to manage therapeutic-resistant cells. Chemistry is based on complex procedures, is expensive and requires a relatively long time. Biological systems, all microbial, exist to inexpensively respond to the evolution of therapeutic-resistance in days, not decades. A basic procedure for doing this is directed evolution, which also has major applications in basic science. Directed evolution can now be documented via whole genome sequencing. The latter has become practical only within the last couple of years. The microbes of choice are phages, some of which multiply by about 100 in 15 minutes. Phage therapy is one obvious direction, but not as currently practiced. If you want me to formulate a more detailed outline, I will do it. Here, I only mention that, whenever I discuss the details

with either junior or senior investigators, the light bulbs go on very quickly. People are very enthusiastic. But, I think that the peer review system, as now constituted, is not equipped for a transformation of this magnitude. I know of not one NIH or NSF research project that involves making the above transformation.
