

Summary of Responses

Request for Information: NICHD Strategic Plan for Fiscal Years 2020-2024

(NOT-HD-18-031)

March 5, 2019

The purpose of the Request for Information (RFI) was to solicit feedback on the scientific themes, goals, and opportunities under consideration for a new strategic plan for the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD). It was published on January 2, 2019, to obtain input on six draft research-related themes and was open for public comment through February 15, 2019. The themes laid out in the RFI were based on input received through several previous engagements in the second half of 2018, including multiple interactions with NICHD staff, a mailbox available to the public on the NICHD website, a two-day research retreat involving 200 scientists from within and outside of government, a public webinar hosted by the NICHD Director that drew nearly 300 attendees, and a meeting of key stakeholder organizations.

In the RFI, NICHD expressed interest in receiving input on its strategic research directions over the next five fiscal years. In the preamble, NICHD stated that it had engaged in a collaborative process to allow multiple stakeholders to weigh in on the Institute's research priorities that would allow it to, among other goals, address health disparities and improve its prevention efforts. The text of the RFI follows:

Request for Information (RFI): NICHD Strategic Plan Fiscal Years 2020-2024

Notice Number

NOT-HD-18-031

Key Dates

Release Date: January 2, 2019

Response Date: February 15, 2019

Related Announcements

None

Issued by

Eunice Kennedy Shriver National Institute of Child Health and Human Development ([NICHD](#))

Purpose

The *Eunice Kennedy Shriver* National Institute of Child Health and Human Development ([NICHD](#)) is updating its strategic plan to help guide the research it supports over the next five years. The purpose of this Request for Information (RFI) is to solicit feedback on the scientific themes, goals, and opportunities under consideration for the new NICHD strategic plan.

Background

For more than five decades, NICHD has provided both national and international leadership for research involving children, pregnant women, and people with disabilities. In the fields of developmental biology, reproductive health, child development, pediatrics, population health, and medical rehabilitation, the institute's broad research portfolio has advanced the biomedical and behavioral health of our nation.

Today, the United States and the global community face an array of challenges, such as the opioid crisis and high rates of maternal mortality, that threaten to erode gains in public health. At the same time, technology breakthroughs, whether in genome sequencing, artificial intelligence, mobile devices or other fields, offer new opportunities for scientific discovery and advancements in health and wellbeing. NICHD must remain well-positioned to accelerate the basic, translational, and clinical science needed to address these challenges and opportunities. There is a great need for innovative and transformative work to harness new technologies and methods that address health disparities and improve prevention efforts among the populations we serve. Therefore, in January 2018, NICHD launched a collaborative process involving external and internal stakeholders to propose overarching scientific themes for its updated strategic plan. Six themes have emerged from this process for public consideration.

Information Requested

NICHD seeks input from researchers in academia and industry, health care professionals, patient and family advocates, scientific or professional organizations, federal partners, internal NIH stakeholders, and other interested members of the public. Organizations are strongly encouraged to submit a single response that reflects the views of their organization and membership as a whole.

Specifically, NICHD seeks comments and suggestions on the following research themes, goals, and opportunities:

Research Theme #1: Understanding Early Human Development

Goal: Enhance knowledge of genes and regulatory networks at the single- and multi-cell levels during preconception, conception, and gestation to understand human development, improve fertility, and reduce pregnancy loss.

Opportunities: This goal includes the development of novel platforms, tools, and techniques to characterize the early stages of development. By categorizing and profiling single cells, as well as integrating these data, we will better understand novel cell types in humans and model

organisms, signaling pathways in vertebrate development, the role of 'omics in controlling development, and gene regulatory elements that potentially cause disease. This work will be enhanced by research on the influence of environmental exposures on early development, which may help to identify potential targets for prevention. Additionally, this work will capitalize on newly available technology to identify and describe the full range and function of cell types present during development. This research area provides opportunities to understand at a cellular level what developmental factors contribute not only to typical development but also to infertility, miscarriage, stillbirth, birth defects, and other congenital conditions.

Research Theme #2: Setting the Foundation for a Healthy Pregnancy and Lifelong Wellness

Goal: Improve pregnancy outcomes to maximize the lifelong health of the woman and her child(ren).

Opportunities: This goal is focused on the developmental origins of health, including the development of early indicators of risk for threats to maternal health during pregnancy, such as preeclampsia, gestational diabetes, post-partum hemorrhage, and placental anomalies. It also includes understanding how these pregnancy-related conditions contribute to maternal mortality and influence health and wellbeing later in life. Research in this area aims to determine the biological underpinnings of these conditions and potential targets for intervention by studying genotypic, phenotypic, exposure, and other biomarkers. This work includes efforts to incorporate new and/or existing datasets to better understand the course and complications of pregnancy that contribute to health outcomes for woman and child through adulthood. Continued study of the placenta, including non-invasive methods to determine placental health, will play a key role in this opportunity. This work will inform new prevention strategies by considering lifestyle factors (e.g., maternal weight, substance misuse, etc.), exposure to infectious diseases, nutrition, and other influences during pregnancy that promote health or lead to disease at the very earliest stages of life. Understanding the contributors to morbidity and mortality will help to identify and validate targets for preventing preterm birth and related adverse events. Testing of early interventions, both domestically and globally, will be a vital component of this research opportunity.

Research Theme #3: Promoting Gynecological, Andrological, and Reproductive Health

Goal: Enable men and women to manage fertility and minimize the impact of gynecological and andrological conditions.

Opportunities: There is an opportunity to improve basic biological understanding of the male and female reproductive organs; knowledge that may lead to treatments for conditions that affect them. NICHD is interested in the use of integrated genetic and phenotypic exposure data to understand the underlying mechanisms of conditions such as endometriosis, fibroids, pelvic pain, vulvodynia, pelvic organ dysfunction, undescended testes, cryptorchidism, varicocele, and other factors that affect urogenital health. We will maintain a focus on the science of pediatric gynecology, especially as it relates to congenital conditions or complex pediatric gynecologic conditions. Understanding the basic biology of healthy reproductive development, especially the

role of menstruation and endometrial biology in health processes, will lead to new avenues for addressing gynecologic conditions. Ensuring options to allow women and men to manage their fertility, as well as developing solutions for infertility, will continue to be an area of focus for NICHD. The institute will seek to identify modifiable factors to solve infertility both through basic science, as well as through an examination of clinical and epidemiologic data on treatments used prior to assisted reproductive technologies.

Research Theme #4: Identifying Sensitive Time Periods to Optimize Health Interventions

Goal: Understand sensitive time periods during development and rehabilitation when prevention and treatment strategies may have the greatest impact.

Opportunities: This opportunity focuses on change brought on by normal development or by injury or disease. For our efforts to be successful, there is a need to understand sensitive time periods in which an exposure to a disease or event—or the use of a particular intervention—will have the greatest impact. NICHD aims to identify the timing and mechanisms of plasticity in early developmental stages. Investigations of the mechanisms that determine the initiation and termination of these sensitive time periods, including different periods during gestation, will be a novel and transformative area of science. In addition, identification of sensitive time periods after disease or injury when plasticity is high will inform the timing of prevention and management, including early interventions for intellectual, developmental, and learning disabilities and therapeutic approaches in critical care and rehabilitation settings. Exploring factors that can promote health during these sensitive time periods, such as nutrition, sleep, or behavioral interventions, will be a key component of this effort. Including very early exposures, whether to infectious disease, to early language interventions, or to technologies or digital media will help us to understand the impact of the environment on the health of the developing child. The plasticity of systems, whether motor, cognitive, or behavioral, will be a key component of this work. Finally, looking at social determinants, in conjunction with biological factors, that influence these sensitive time periods will enhance our ability to target interventions.

Research Theme #5: Improving Health During the Transition From Adolescence to Adulthood

Goal: Improve the transition from adolescence to adulthood by identifying behavioral, social, environmental, and biological factors that enhance health, especially for adolescents with disabilities or other chronic conditions.

Opportunities: The period of adolescence is poorly understood, but encompasses rapid and transformative development of cognitive, behavioral, social, and health behaviors that continue throughout life. Hormonal changes in the adolescent, and their impact on the development and maturation of the reproductive organs, contribute to the significance of this period. NICHD aims to identify the behavioral, cognitive, social, environmental, hormonal, endocrine, and genetic factors that contribute to adolescent development and may give rise to specific health behaviors that place the adolescent at higher risk for specific disorders in adulthood. Lifestyle factors, such as diet, sleep, and exposure to social media and other technologies, will be a focus of the environmental and behavioral aspects of this opportunity. Finally, the impact of the medical

transition from pediatric to adult care, especially for children with disabilities or other chronic diseases, has been understudied and will be an area of interest for NICHD.

Research Theme #6: Ensuring Safe and Effective Therapeutics and Devices

Goal: Develop, test, and validate safe and effective therapeutics and devices specifically for pregnant and lactating women, children, and individuals with disabilities.

Opportunities: Pregnant and lactating women, children, and individuals with disabilities have specific needs that can only be addressed through their inclusion in the development, testing, and validation of therapeutics and devices. Evaluating medications, including safe and effective dosing, in these specific populations will allow for better management and treatment of common conditions. This opportunity includes the potential to use real-world data—such as electronic health records, existing datasets available through research networks or registries, or other big data approaches—to discover potential adverse events, positive outcomes, or common comorbidities in these populations. Finally, acceptability and adherence research to ensure that these interventions can be meaningfully used in these populations will enable implementation efforts in health systems.

How to Submit a Response

To ensure consideration, responses should be submitted via email to NICHDStrategicPlan@nih.gov no later than Friday, February 15, 2019.

Please indicate “RFI Response” in the subject line of the email.

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 U.S. Government will use the information submitted in response to this RFI at its discretion. The U.S. 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 U.S. 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.

Inquiries

Please direct all inquiries to:

NICHD Strategic Planning Group

Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD)
National Institutes of Health

Email: NICHDStrategicPlan@nih.gov

Responses

As of February 15, 2019, NICHD received a total of 924 responses. Comments were submitted by individuals and families, policymakers, researchers and academic institutions, nonprofit organizations, and professional societies. About ten percent (94) of the comments were submitted on behalf of organizations and their members. Of the total, 428 were from families who had experienced a loss due to Sudden Infant Death Syndrome (SIDS). Many respondents commented on more than one theme.

Key points raised in the comments are summarized below by theme.

Theme 1

The majority of the 129 responses commenting on Theme 1 called for greater emphasis in the final strategic plan on the role of animal model systems in developmental biology (including early embryo development), invertebrate systems as well as vertebrate. Specific models such as zebrafish, drosophila, xenopus, and *C. elegans* were all mentioned. Such models should also be used for studies into the bases of behavior, and one comment suggested doing cross-species comparisons for a more complete picture of development.

Several commenters found the theme itself too narrow, reading it to focus on single cell sequencing, and suggesting instead that the theme be expanded to focus on developmental biology, e.g. to enhance knowledge of genes and gene regulatory networks at the single- and multi-cell levels during preconception, conception, and gestation to understand human development (including intellectual and developmental disabilities and mitochondrial effects), the etiology of birth defects, to improve fertility, and to reduce pregnancy loss. Respondents also called for more explicit emphasis on research looking at gene-environment interactions and epigenetics including epigenetic changes that occur during gametogenesis, the effects of manipulating the germline, and the influence of the father's genome on germline DNA. Single comments called for expansion of human embryonic stem cell and regenerative medicine research.

Several organizations recommended using a broader definition of child health and human development that includes social, emotional, and cognitive aspects, and one strongly urged incorporation of sex as a biological variable in all research efforts. They asked for research to determine the behavioral indices for healthy development, and recognition of the role of diversity of experiences in development or social determinants in adverse health outcomes and disorders of development, such as intellectual and developmental disabilities. Respondents also called for basic research to elucidate specific conditions and outcomes, including the genetic determinants of reproductive success, preeclampsia, miscarriage and stillbirth, and the causes of Sudden Infant Death Syndrome (SIDS).

Various approaches were recommended that would allow these avenues of research to proceed. Cataloguing cell types would foster better understanding of the steps in cell differentiation. Several respondents suggested testing candidate disease genes generated via ‘omics approaches (starting with the genome and extending to transcriptomics, metabolomics, and the microbiome). Other approaches included the use of high-resolution imaging techniques, the development of artificial intelligence methodology, and use of mobile devices to gather information. The creation and use of large databases, such as the Human Cell Atlas and Model Organisms databases, would allow research to progress more quickly.

One professional society strongly urged that NICHD use different terminology going forward, replacing “preconception, conception, and gestation” in Theme 1 with “prepregnancy, early pregnancy, and pregnancy,” and that “pregnancy” be explicitly defined as the “physiologic state of a woman that follows implantation of a blastocyst(s).”

Theme 2

Using the overarching theme of “pregnancy as a window to future health,” 144 respondents provided comments on Theme 2.

Several comments described the period prior to pregnancy as important. To reduce the maternal mortality and morbidity that may result from unintended pregnancies, expanded contraceptive options for both women and men contributes to the ability to plan a pregnancy. In addition, other commenters pointed out that further research into *in vitro* and other methods of improving chances of pregnancy allows for better planning, including improved preconception care for both women and men. Many respondents urged more research into factors that may affect pregnancy positively or negatively. Chief among these were factors involving social and behavioral determinants, such as research on healthy intimate relationships, or conversely, on the impact of trauma, toxic stress, adverse events, and social and health disparities. A few respondents noted that more work is needed on the intergenerational and epigenetic origins of disease.

Respondents called for expanded research throughout pregnancy, with many urging the use of animal models for studies on how maternal health may affect fetal brain development, early embryonic development, and the molecular and cellular bases for birth defects, implantation disorders, miscarriage, and postnatal development. Placental research, specifically including research conducted under the auspices of the Human Placenta Project, was suggested by a number of respondents as a possible avenue for examining interactions between the immune system (immunological effects of pregnancy), the placenta, and vasculature, and the pathophysiology of development of the hypothalamic-pituitary-gonadal axis. Several comments called for specific studies on the causes of abnormal fetal growth/IUGR, and the impacts of nutrition and physical activity on a healthy pregnancy; inflammation during pregnancy; toxic environmental exposures; intimate partner violence; drug, alcohol, tobacco use; and maternal periodontal disease. Some additional concerns were also expressed by individual respondents, including the need for research on the care and prevention of risk factors for mental and behavioral health disorders during pregnancy, predictors of preeclampsia, *in utero*

transplantation of fetuses with thalassemia, and addressing the unique needs of pregnant women with disabilities.

Many comments were submitted related to the neonatal period and beyond. The majority of these urged NICHD to continue to fund its research related to SIDS and other infant mortality and morbidity. SIDS research should include the reasons for the health disparities and risk reduction efforts, such as continuation of the Safe to Sleep® public education campaign, and research on grieving after loss of a child. Respondents recommended further research on screening for adverse pregnancy outcomes, standard health histories for women giving birth to gather data regarding maternal mortality and morbidity, and improved interventions for labor and delivery. In addition, commenters suggested research on the postpartum health of women, particularly to manage and treat pregnancy complications. Several respondents commented that “early human development” extend beyond the neonatal period to allow researchers to look more carefully at the long-term impact of early life experiences, such as mother-infant interactions, and the longer-term effects of preterm birth; one suggested expanding the definition to include individual and group levels. Another respondent suggested expanding the newborn screening public health system to allow collection of data for longitudinal studies (in collaboration with population scientists) and increasing the number of rare conditions screened through the system. Increased clinical research focused on rare conditions and preterm birth was recommended, as well as research on health outcomes for infants with intellectual and developmental disabilities to allow for earlier intervention.

A few comments offered specific suggestions to facilitate NICHD’s research related to pregnancy and pregnancy outcomes. One recommended creating a new theme on newborns and infant care. Another raised the need for further research on infant caregiver behavior. Potential collaborations include between the NICHD-funded Maternal Fetal Medicine Units Network and the Neonatal Research Network, and among the member NIH Institutes, Centers, and Offices of the NIH Pediatric Research Consortium (N-PeRC) to focus NIH’s work on pediatric development.

Theme 3

Many of the 67 respondents who commented on Theme 3 applauded the specific inclusion of andrological health as a research focus for NICHD, in addition to studying gynecological and reproductive health. Carrying further the “window to future health” construct, comments included looking at reproductive health as it contributes to later health, and the impact of RH into overall wellbeing.

Several respondents described the ongoing needs in basic biological research in these areas, including the use of developmental animal model systems in addition to research on single cells, germ cell exposures, mammalian gametogenesis, hormone regulation, and basic research on chromosome abnormalities and the biology of reproductive disorders. Other comments focused on basic science related to andrological health, such as cellular and molecular controls of male reproduction, the biology of gonads, biomarkers to assess sperm quality, spermatogenesis and the contributions of motility, morphology, and DNA fragmentation.

Many of the comments regarding Theme 3 related to the need for research on specific gynecological conditions, with polycystic ovary syndrome (PCOS) representing the majority of these. Others included pelvic floor disorders (one respondent recommended that the terminology be changed to “pelvic organ and pelvic floor dysfunction”), endometriosis, uterine fibroids, and modifying factors to allow better management of related conditions such as pelvic organ prolapse and incontinence. Underpinning research on clinical conditions were recommendations for more basic and translational research on disorders of sexual development, the mechanisms of gynecological pain conditions and research on the cervix and other reproductive organs; this work would be aimed at development of potential therapeutics. A few respondents reminded NICHD not to focus only on adults for this area of research, but to include adolescents in the studies.

Numerous respondents commented on the continued need for NICHD’s support of most aspects of research on fertility and infertility, some pointing out that NICHD is one of the few funders of such research. One suggested that fertility status could be a predictor of later health in both males and females, and another pointed to a possible connection between hormonal regulation, sleep, and lifelong health of pregnant women and children. Several comments recommended research on the impact of chronic health conditions and infectious diseases (including sexually transmitted infections), and their treatment, on preservation of fertility. Additional research should focus on behavioral, environmental, and social conditions that may affect fertility, including reproductive and contraceptive decision-making. Improved methods to monitor ovulation, additional diagnostic tools, and the development of alternatives to ICSI also were proposed. Since unintended pregnancy rates are still high, several respondents urged NICHD to explore modifiable factors to control fertility, including non-hormonal targets and male contraceptives. Overall, studies should take a patient-centered approach, and the particular needs of people with disabilities should be factored in.

Related to these research needs, other comments included recommendations to support longitudinal research, including a long-term study on pregnancy cohorts, and research on perioperative care. Calls for reproductive health education and access to health care were also made.

Theme 4

Theme 4 garnered by far the most comments, with 274 respondents weighing in on aspects of development and rehabilitation during sensitive periods. One respondent suggested that the theme be broadened further to include “identifying interventions to optimize health,” but another commented that the theme was already too broad and costly. Other comments suggested that NICHD should focus on the unique developmental processes that underlie adolescent plasticity, and that “sensitive periods” be defined by illness, not age groups.

Many respondents expressed concern that the RFI seemed to indicate that NICHD would be supporting research only on what developmental changes occur during sensitive periods, not on developmental processes throughout childhood and adolescence. They pointed out that research on how early life exposures may affect development will inform health later in life, consequently

recommending that research should be conducted pre- and post-delivery, and across the life course, including transition to menopause. Instead, NICHD should look at health and behavior indices of typical development, from infancy through different childhood stages (early, middle, pubertal, and adolescent), using validated measures of nutrition, physical activity, obesity, sleep, stress, trauma, and substance use. From these, risk factors for morbidity and mortality may be established, allowing researchers to look more closely at the effects of age and exposures in early development on diseases arising in childhood, such as asthma. Comments included consideration of a wide range of exposures, such as migration/immigration, language acquisition, natural disasters, health disparities, parenting and attachment, resilience, and sociocultural elements such as religion and ethnicity. Multiple respondents called for research on the effects of media on children's health. To accomplish the goals of following development over time, respondents suggested use of population science, longitudinal studies (possibly including data from the newborn screening public health system), and large datasets; another commented that model organisms, such as zebrafish, could provide insights into critical periods of development.

Continued research on intellectual and developmental disabilities (IDDs), and physical disabilities, was identified as a priority for NICHD by several respondents but recommending that research be conducted not only early in life (or at the time that the disability is identified), but across the lifespan and including life stage transitions, to improve the health of these populations. For example, one comment suggested that research is needed on nutrition and exercise for people with disabilities to help individuals keep pace with typical developmental stages. Another urged NICHD to increase its research on the most common IDDs, autism spectrum disorder, and attention deficit hyperactivity disorder.

The bulk of comments on Theme 4 focused specifically on pediatric injury and trauma, child abuse, neglect, and the effects of violence. Some respondents stated that the progress made by NICHD's Pediatric Trauma and Critical Illness Branch should be allowed to continue, and a few suggested breaking this area of research out into a separate theme for the strategic plan. Most of the comments provided examples of the types of research needed in this area, recommending that studies be conducted to look at the impact of injury and maltreatment to explore the effects at different developmental stages, including brain development, and on later health outcomes. Among the research recommendations: the social antecedents and aftermath of childhood injury and abuse, research on violence (both pregnant women and children), shaken baby trauma, head trauma and concussion, sexual abuse, family dysfunction, child suicide, mental health and bullying, the effects of foster care, and homicide. Such research would inform parenting and family-based interventions, and school programs to address mental health issues.

In addition, other respondents addressed research gaps in treatment for acute injury and illness in children, recommending disease-specific research across the pediatric age spectrum, including population level health research. Research was recommended to prevent injury in the first place, beginning with studies on the acceptability and adaptability of prevention strategies in various subgroups, including children with special health care needs. Specific calls for research following injury included burns, hemorrhage, and brain trauma. Further, a few comments stated the need for treatments aimed for various pediatric populations, including to improve the

mobility and rehabilitation of children with life-threatening injuries. NICHD was also called upon to assist in providing the tools needed for an integrated approach to pediatric care for injuries and trauma, including emergency care, pre-hospital and critical care, and studies on the epidemiology of acute care. Several respondents pointed out the value of using a network approach to these issues, such as NICHD's Collaborative Pediatric Critical Care Research Network.

Theme 5

Overall, of the 68 respondents to Theme 5, many applauded NICHD for specifically including adolescent development and transition to adulthood, although some recommended that it be merged with Theme 4 to produce a continuum of research on children.

Many comments reflected on the need for expanded knowledge about adolescent development, beginning with the use of model organisms such as zebrafish and *C. elegans*. One respondent stated that NICHD should resist prioritizing neuroscience and genetics research that is dominating other ICs' work. Some suggested further research on the unique developmental processes that underlie adolescent plasticity, including taking a whole-child approach and looking at positive development as measured by physical and psychological safety, supportive relationships, skill-building. Physical developmental changes, such as transition into and out of puberty and variable fertility cycles, need further exploration. Several others suggested focusing on social and environmental determinants of health in adolescents and following them to determine long-term health outcomes. Using behaviors beginning in childhood as potential predictors, several commenters recommended research studies on violent behavior, injury and suicide prevention, the impact of stress and trauma on adolescent health, and the role of family and physical activity. One respondent requested that the period of "late adolescence" be included (18-25 years), and another asked that adolescents who were born preterm be part of these research studies.

Several respondents commented specifically on the transition of adolescents to adulthood; many of these focused on the transition to adult health care. The difficulty of certain subpopulations in achieving a successful transition to adult health care and independent living was mentioned for children with IDD (Down syndrome, Fragile X, autism spectrum disorder) or physical disabilities, adolescents who have experienced injury or trauma, those with chronic conditions such as HIV or asthma, gender nonconforming youth, and those in geographic areas with limited care. One respondent suggested looking specifically at the stress that may occur due to a difficult or unsuccessful transition. On the other hand, another respondent suggested that NICHD support research on the opportunities for achieving life-long wellness posed by key adolescent transition periods.

A few respondents pointed to particular health care needs of adolescents, stating that these needs may change across the lifespan (such as autism spectrum disorder). Conditions such as PCOS may be first diagnosed during adolescence, and adolescents may require contraceptive options. Pain management approaches also may change. One comment requested that NICHD consider the use of antiretroviral therapy in youth with HIV.

Commenters also interpreted the theme to include adolescents' transition to the adult health care system, recommending structural changes to improve links between occasionally separate systems of care. One recommended developing the science aimed at improving models of care, including continuity and use of care from adolescence into adulthood, caregiver coordination, and use of electronic health records. Population studies that use long-term data were recommended to examine linkages to care, health status, and psychosocial health, ultimately informing health promotion policies.

Theme 6

Largely focusing on the areas of research already supported by NICHD, 86 comments were submitted related to safe and effective drug and device development. Some urged NICHD not to conduct such research in a vacuum, but to include the context for health outcomes, such as establishing a health equity framework, in its ongoing support for new technologies and methods.

The most specific comments related to research on the development of new drugs. A few reminded NICHD that basic research using animal models (drosophila, zebrafish, and mice) is critical to developing effective treatments and therapies, including understanding embryonic development, tissue physiology, and drug metabolism in infants and children. Another respondent suggested the development of sensory disease models aimed at identifying signaling pathways and novel therapeutic targets. At the other end of the research spectrum, clinical trial and other "real world" data measuring exposures/responses of drugs were called necessary to achieve accurate dosing in pediatric populations, especially in those born preterm, obese, with chronic illnesses, disabilities, pharmacogenomic subtypes, and during different developmental stages. Respondents asked for studies tailored to individuals with IDD (including ADHD, autism spectrum disorder, Fragile X), antiretroviral therapy used by youth and adolescents, critically ill children including those with organ dysfunction, neurotoxicity of anesthetics in infants and toddlers, drugs used in emergency care and optimizing sedation, dose adjustments for pediatric antibiotic use, and therapeutics for gynecological pain. In addition, numerous comments called for expanded research on contraceptives and infertility treatments for women and men, including sperm-targeted contraceptives and multi-purpose prevention technologies.

Most of the comments that addressed device development were supportive, although a few stated that the Food and Drug Administration should lead in this area. Respondents requested that NICHD consider research on disability-related devices, devices tailored to pediatric populations, especially pediatric disabilities and technologies for critically ill children. A few others suggested research on reproductive and gynecological devices, multi-purpose prevention, and emergency care. One commented that device development should be integrated with clinical services and overall care plans.

Respondents offered different approaches and methodologies for research on drugs and devices, urging rigorous testing to ensure optimal and safe use. One suggested using electronic health records to benefit subgroups of children in testing therapies, another suggested leveraging the newborn screening public health system, and a third asked that NICHD's Neonatal Research

Network test drugs and devices already available. Novel data and big data can contribute to advancing understanding of people with disabilities, and socio-behavioral research and market access will inform research. Two respondents suggested careful evaluation of the dosing and timing of interventions through post-market surveillance to assess for risks of medications and device use.

Additional areas of inquiry were recommended, including research on technologies for caregiver burnout, implementation science, and barriers to reproductive methods. Many respondents asked for continued support of the federal Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC) to further research on therapeutics used by these populations.

Additional Ideas, Topics, and Overarching Themes Raised in the Responses

Within their comments, 85 respondents requested that their concerns apply across all six of the themes proposed by NICHD or provided additional topics and general comments for consideration. Several recommended the development of additional themes, such as on infant and child development to inform Theme 4, disability research informed by people with disabilities, and on the development of multi-purpose contraception. A few commented that the themes overlap, and others said that the themes were weighted toward pregnancy-related research.

Several respondents suggested that children's health should be at the core of all of NICHD's research, applying to all six themes and defined broadly to include biological, behavioral, cognitive, and social aspects (a "whole child" approach). Many respondents stated that behavioral and social science needed to be integrated more thoroughly throughout the entire plan. Others suggested that model organisms be included throughout the strategic plan, that genomic and genetic diversity should underlie all themes, and that a comprehensive focus on IDD is needed across all themes. Many of the respondents discussed the broad, systemic need for research that includes a health and social disparities component and recommended that this be specifically stated in all areas of NICHD's research plans; addressing potential for bias and discrimination should specifically be integrated into the design of all studies, including basic research. Other comments urged more attention to global health issues.

Some respondents proposed additional research ideas to be added to the strategic plan priorities:

- Biology of brain development
- Integration of epidemiological studies and animal/cell models
- Childhood nutritional needs
- Disparities in pediatric injury
- Pediatric physical and mental illnesses
- Health needs and assimilation of immigrant children
- Reproductive health education in schools
- Demographic disparities affecting gynecological health
- Factors that influence access to care and rehabilitation services

Comments also included many suggestions for approaches to expand NICHD's research capabilities, such as developing statistical and bioinformatic approaches to identify novel genetic interactions, including those that may underlie behavior. Among the other suggestions were to increase support for interdisciplinary team science; population science; greater reproducibility; effective dissemination of research results; data sharing, harmonization, analysis, and security; using machine learning and artificial intelligence methods; use of electronic health records and continuous physical monitoring; and development and use of innovative research designs when randomized clinical trials are not a good option for certain studies. Others wrote that NICHD should also support research on health care delivery and implementation science, engaging with the populations it serves.

Respondents made a few suggestions about potential partnerships to achieve these goals, including collaborations with other NIH Institutes and Centers, and partnering with pharmaceutical companies, international agencies, and foundations. For example, one commented that NICHD should explore collaborating further with the Health Research and Services Administration on issues related to maternal mortality. Another suggested that partnerships could be used to engage in more regular conversations with the child health research community.

Infrastructure/Funding

Respondents submitted many recommendations about how to facilitate NICHD's research priorities in the future. The majority of the comments supported continued funding for current infrastructure, such as NICHD's research networks. Numerous comments supported continued and increased funding for the Maternal Fetal Medicine Units network; others mentioned the Neonatal Research Network (although one comment proposed dismantling it), the Reproductive Medicine Network, the Pediatric Critical Care Network, and the Contraceptive Clinical Trials Network. Some comments recommended specific investments in the National Center on Medical Rehabilitation Research, the Human Placenta Project, Xenbase, critical care, emergency care, and biomarker mapping.

Several respondents described their concerns about funding for longitudinal studies, particularly long-term cohort and population studies, and large-scale data collection efforts, with one suggesting that NICHD create an infrastructure aimed at integrating interdisciplinary science. NICHD was also urged to invest in developing common data platforms and increase support for research using animal models.

Some respondents mentioned particular mechanisms, asking NICHD to increase the number of R01 grants and K career development awards, continue the U cooperative agreements (expressing concerns about recent changes), and reinstating the P01 program projects. One commenter recommended that funding opportunities be developed to broaden and diversify the next generation of pediatric scientists.

To implement the strategic plan, one respondent suggested focusing on the practice of science, data management, and technology utilization, while others stated that research should be targeted toward developing clinical guidelines and standard of care. Recommendations were made to

create an office within NICHD on clinical trials, policy rules for writing funding opportunity announcements, and updating its systems and processes. Others suggested inclusion of pregnant women in clinical research and creating a study section on reproductive health.

Training

Of the 22 comments submitted related to research training, the majority called for training the next generation of scientists. Some specifically requested that NICHD focus on training a more diverse group of scientists to reflect more diverse perspectives and populations. One respondent suggested creating training pipelines for new scientists aligned with each of the themes proposed in the RFI, a few others called specifically for pediatric research, obstetrician-gynecologist, and population science training. Training programs should be focused on addressing critical national shortages in academic physician scientists. One respondent stated that NICHD should take the lead on developing and piloting training programs on the recruitment and retention of pregnant women, children, and individuals with physical and intellectual and developmental disabilities into clinical research, suggesting that this program might be a possible partnership opportunity with the intramural research division.

Several respondents requested more workforce and other opportunities for trainees, including increased support for fellowships and professional conferences. One expressed concern for the recent shift from institutional mentoring awards to individual awards.

Conclusion

NICHD would like to thank all respondents for their thoughtful comments. This feedback will help to inform deliberations about NICHD's future research directions.