

DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH

Testimony before the
House Committee on Appropriations
Subcommittee on Labor, Health and Human Services, Education, and Related Agencies

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Good Morning, Chairwoman DeLauro, Ranking Minority Member Cole, and distinguished Subcommittee Members. I am Francis S. Collins, M.D., Ph.D., and I am the Director of the National Institutes of Health (NIH).

I am joined by Christopher Austin, M.D., Director for the National Center for Advancing Translational Sciences (NCATS), Patricia Flatley Brennan, R.N., Ph.D, Director of the National Library of Medicine (NLM), Helene Langevin, M.D., Director of the National Center for Complementary and Integrative Health (NCCIH), Eliseo J. Pérez-Stable, M.D., Director of the National Institute on Minority Health and Health Disparities (NIMHD), and Bruce Tromberg, Ph.D., Director of the National Institute of Biomedical Imaging and Bioengineering (NIBIB),

I want to thank the Committee for its work on the Labor-HHS funding bill for FY 2020 that passed the House in June. We are grateful for your ongoing bipartisan support in helping NIH to continue our longstanding commitment to leading the world in biomedical research that will turn discovery into health.

Madam Chairwoman, I remember that, in April, you announced your intention to hold hearings with NIH Institute Directors who have not testified before the Subcommittee recently. We very much appreciate your and your colleagues' interest in having some of those Institutes and Centers (ICs) represented here today in effort to add some more detail to the very big picture that is biomedical research at NIH.

Unlike ICs that are primarily focused on research for specific diseases or disorders, many of which you have heard from often, our panel today comprises those that oversee a broad spectrum of research that is either disease agnostic, or improves the overall scientific and operational processes that lead to discoveries. It is an honor to be here today to talk about some of the research that is supported through these five ICs.

National Center for Advancing Translational Sciences (NCATS)

Nationwide, we have witnessed unprecedented advances in basic and fundamental science; however, the translation of research discoveries into treatments and interventions that improve human health in many instances is a slow and failure-prone process. The National Center for Advancing Translational Sciences (NCATS) was created to directly address this issue by improving the translation of discovery to health for the benefit of all biomedical research. NCATS is focused on improving the scientific and operational processes for refining and accelerating translation, the process of turning observations in the laboratory, clinic, and community into interventions that improve the health of individuals and the public — from diagnostics and therapeutics to medical procedures and behavioral changes.

For instance, through the flagship Clinical and Translational Sciences Award (CTSA) Program NCATS works collaboratively with more than 50 biomedical research institutions nationwide to improve clinical translation and to develop a cadre of trained investigators through sustainable translational science career development pathways. In the Trial Innovation Network (TIN), NCATS is developing, demonstrating the effectiveness of, and disseminating scientific and operational innovations to dramatically increase the efficiency and effectiveness of clinical

studies. With the participation of the CTSA Program hubs, Trial Innovation Centers, and Recruitment Innovation Center, the TIN works to understand and mitigate the delays and failures that can result in enormous losses to the health and lives of patients, the careers of investigators, and the advancement of science and medicine.

As another example, now in its tenth year, the Toxicology in the 21st Century (Tox21) program is a four-Federal agency collaboration among NCATS, the National Toxicology Program at NIH's National Institute of Environmental Health Sciences (NIEHS), the Environmental Protection Agency (EPA), and the Food and Drug Administration (FDA). Working to identify pre-clinical translational failure that results from unanticipated adverse effects of a new drug in humans, Tox21 fosters the systematic understanding of toxicity and the development of new testing systems. Tox21 researchers have developed new testing paradigms, a public database of more than 100 million test results on over 10,000 drugs and chemicals, and computational algorithms that are remarkably accurate in predicting the potential toxicity of a new compound. These publicly available data are now beginning to inform regulatory decisions about safety.

Additionally, NCATS is placing priority in advancing and accelerating treatments for rare diseases. There are about 7,000 diseases officially defined as "rare," or affecting fewer than 200,000 people in the United States; only a few hundred of these diseases have any approved treatment. Added together, rare diseases are anything but rare; they affect 25 million people in our country alone, and approximately 50 percent of rare disease patients are children. Families generally must cope with a years-long odyssey to a correct diagnosis, only to find that 95 percent of the time there is no effective available treatment. These too-often disabling and fatal diseases are devastating and costly for patients, their families, and the Nation.

NCATS is applying its collaborative translational science model to transform understanding, diagnosis, and treatment of rare diseases. NCATS' fundamental approach is to shift from considering each rare disease in isolation to identifying and developing treatments for rare diseases based on their commonalities. NCATS invests resources and expertise at the points where research is most difficult and therefore often abandoned.

Most rare diseases are genetic, caused by "misspellings" in DNA that are passed from one generation to the next. Advances in gene delivery and gene editing have recently re-invigorated gene therapy as a potential approach to treating genetically-based diseases. Unlike small molecule drugs, genes cannot enter cells, so they need to be transported in the body and into the diseased cell type by a "vector" carrier. While effective, this requirement for a vector greatly increases the experimental, regulatory, safety, clinical complexity, and cost of gene therapy, since both the carried gene and the vector are different in every development program. This significantly hinders gene therapy being expanded or "scaled up" to address the many diseases that potentially could be treated. To tackle this problem, and thus simplify gene therapy and make it more efficient and effective, NCATS is developing a Collaborative Rare Disease Platform Vector Gene Therapy Trial (PaVe-GT) program. Viral vectors will be well-characterized for their capacity and safety as gene delivery vehicles and tested as platforms to carry a variety of genes to treat multiple diseases. Initially, NCATS will support the testing of vectors as gene delivery vehicles for the treatment of at least three rare genetic diseases that share a therapeutic target tissue or cell type. If successful, NCATS will expand this strategy to

provide rare diseases researchers with a palette of vectors to treat many, and potentially all, rare genetic diseases.

National Library of Medicine (NLM)

Through its cutting-edge research, information systems, collections, and training programs, NLM plays an essential role in catalyzing basic biomedical science and data-driven discovery. NLM acquires, organizes, curates, and delivers up-to-date biomedical information across the United States and around the globe. NLM makes research results available for translation into new treatments, products, and practices; provides decision support for health professionals and patients; and aids disaster and emergency preparedness and response.

NLM is a leader in data science and open science, including the acquisition and analysis of data for discovery and the training of biomedical data scientists. As biomedical research becomes increasingly digital, NLM is expanding its data science and biomedical informatics research programs to improve access to digital knowledge assets, including research and bibliographic data, software used to generate or analyze research data, and models and workflows used in research. Making such materials findable, accessible, interoperable, and re-usable (FAIR), as well as attributable and sustainable, accelerates science, broadens opportunities for collaboration, enhances accountability, and increases the return on investments in research for research participants, science, and society.

NLM continues to expand the quantity and range of high-quality information readily available to scientists, health professionals, and the public. Every day, NLM serves more than 5 million users, receiving up to 15 terabytes of new data, adding value by enhancing data quality and consistency, and integrating new data with other information in NLM databases. NLM responds to millions of inquiries per day from individuals and computer systems and provides more than 115 terabytes of information, including more than 5.1 million published articles in PubMed Central (PMC), NLM's free full-text archive of biomedical and life sciences journal literature. On a typical day, more than 2.5 million users download articles from PMC.

NLM also maintains the Sequence Read Archive (SRA), the largest publicly available data repository, which includes more than 9 million records of next-generation genomic sequence data. Each month, 100,000 users download more than 2 petabytes of data. To improve access to and utilization of this data, NLM has uploaded the entire SRA data to two commercial cloud partners as part of NIH's STRIDES (Science and Technology Research Infrastructure for Discovery, Experimentation, and Sustainability) Initiative. This approach enables scientists, industry, and the general public to bring large-scale computing power to the data for novel scientific discovery.

National Center for Complementary and Integrative Health (NCCIH)

Through rigorous scientific investigation, the National Center for Complementary and Integrative Health (NCCIH) carries out its mission to define the safety and effectiveness of complementary and integrative health approaches – a group of practices and products that originate outside of conventional medicine but are typically used in conjunction with

conventional medicine. This diverse group of health practices includes natural products, such as dietary supplements, plant-based products, and probiotics, as well as mind-body approaches, like yoga, massage therapy, meditation, mindfulness-based stress reduction, spinal manipulation, and acupuncture. Integrative health care seeks to bring conventional and complementary approaches together in a safe, coordinated way.

Consumers often use complementary health approaches without understanding whether they work, or if they are safe, and without talking with a health care provider. Much of the information available to consumers is promotional, and not rooted in peer-reviewed, scientific evidence. NCCIH works to expand and share science-based evidence regarding complementary and integrative health approaches to inform health care decision-making by consumers, health care professionals, and policymakers.

The support of health and wellness is a priority of NCCIH. A small but growing evidence base suggests a potential benefit of complementary health approaches for the purposes of wellness, health promotion, and disease prevention. For example, music has been associated with several positive benefits. Music may enhance child development, improve adult function and well-being, and optimize the quality of life during aging. Many studies have shown that music may ameliorate the symptoms of a broad range of diseases and disorders that occur throughout the lifespan. However, more research is needed to determine where music therapy, in its many forms, can be beneficial and under what conditions. The exciting potential of this research has led to the formation of a trans-NIH Working Group, co-led by NCCIH. Together this working group developed a funding opportunity entitled “Music and the Brain: Research Across the Lifespan.” A set of 15 new awards has just been made. The aim of this initiative is to increase understanding of how music can affect health, with an emphasis on what happens at the neuronal level, and potential clinical applications.

According to a 2012 National Health Interview Survey (NHIS), Americans are spending approximately \$30.2 billion per year on complementary approaches to improve their overall health, manage symptoms of chronic diseases, and/or counter the side effects of conventional medicine. Pain is one of the leading reasons Americans turn to complementary health approaches. Current drug-based treatment options are only partially effective and can have serious side effects.

Responding to this need, NCCIH supports safety and efficacy trials of nonpharmacologic pain management approaches, as well as research on the basic biology of pain and pain processing in order to understand how these approaches can influence pain. NCCIH’s role in the HEAL (Helping to End Addiction Long-term) Initiative builds upon the leadership they have demonstrated in supporting research on nonpharmacologic treatments and pragmatic trials embedded in health care system delivery. NCCIH is leading two HEAL programs – Behavioral Research to Improve Medicated Assisted Treatment (BRIM) and Pragmatic and Implementation Studies for the Management of Pain to Reduce Opioid Prescribing (PRISM).

As another example, NCCIH along with other NIH, Department of Defense (DoD) and Department of Veterans Affairs (VA) partners launched the NIH-DoD-VA Pain Management Collaboratory (PMC) in 2017. The PMC focuses on nonpharmacologic approaches for pain

management and related conditions in military and veteran populations. The PMC currently funds 11 pragmatic clinical trial research project grants and a resource coordinating center, totaling approximately \$81 million over six years, with the NCCIH contributing more than half of these funds. The studies will not only show if specific nonpharmacologic approaches are effective for pain management, but also how they can be integrated into a healthcare system. This initiative may lead to new pain management practices within the DoD and VA and support the use of nonpharmacologic approaches for pain management in the general population.

National Institute on Minority Health and Health Disparities (NIMHD)

I know that many Members of the Subcommittee have interest in examining individual factors and systems in which we live, learn, work, and play that influence health status. The National Institute on Minority Health and Health Disparities (NIMHD) leads scientific research to improve minority health and to reduce health disparities. That research has evolved from a basic descriptive understanding of what health disparities are and who is most affected to discovering the complexity of factors involved in health and its outcomes. NIMHD works to transform the field of minority health and health disparities by building on evidence-based advances in promising areas such as genomics, behavioral and social science, and health information technology that could be beneficial in improving the health of racial and ethnic minority populations, people living in rural communities, individuals of low socioeconomic status, and sexual and gender minorities who often experience poorer health and greater disparities in health outcomes.

In the United States, it is estimated that 700 women die yearly from pregnancy and delivery complications,ⁱ and approximately 50% of these deaths are preventable.ⁱⁱ Maternal mortality rates (MMR) have increased from 17 deaths per 100,000 births in 1990 to 26 deaths per 100,000 births in 2015. Additionally, significant racial disparities in pregnancy-related mortality (PRM) persist. Black and American Indian/Alaska Native women experience the highest rates of PRM, at a rate that is three to four times higher than that of White women. NIMHD is funding research to examine postpartum hemorrhage (PPH), a leading contributor to maternal morbidity and mortality in the United States. Researchers aim to investigate racial and ethnic differences in PPH management (e.g., medications administered, blood transfused, surgical interventions used) and the timing of those interventions as a way of identifying more targeted interventions. NIMHD will examine how environmental, sociocultural and behavioral factors influence health outcomes in PRM, including the importance of patient-clinician communication, implicit and explicit biases in care, and the quality of health care.

Another example of NIMHD's work includes studying the interaction between epigenetic and biobehavioral determinants of preterm birth in African American women. Recent findings discovered that DNA methylation in the SLC9B1 gene in late second and early third trimesters can predict fetal intolerance of labor (FIL) or fetal distress at delivery, the most common indication for emergency Caesarean section, which is associated with increased risk of an insufficient supply of oxygen reaching the unborn baby and excessive acidity in the blood following deliveryⁱⁱⁱ. These findings could set the basis for a diagnostic test to identify pregnant women at elevated risk for FIL well in advance of delivery.

To highlight another area, NIMHD established the Surgical Disparities Research Initiative to support investigative and collaborative research focused on understanding and addressing disparities in surgical care and outcomes in minority and health disparity populations. Despite overall improvements in surgical care, surgical disparities remain a persistent concern in the healthcare system, and an understudied issue in health disparities research.

Disparities in surgical care by race and ethnicity are partly due to a lack of standardized quality indicators to measure surgical disparities and access to surgical care. The Developing Disparities-Sensitive Surgical Quality Metrics is a project funded by NIMHD aimed at developing a standardized disparities sensitive metric on quality of surgical care that can be implemented in various hospital settings.

Cultural difference or incongruity is a factor often associated with the patient-clinician experience and relationship. NIMHD is funding a clinical trial involving eight academic medical centers to evaluate the effectiveness of the Provider Awareness and Cultural Dexterity Toolkit for Surgeons (PACTS), to assess surgical residents' knowledge, attitudes, and cross-cultural skills in caring for patients of diverse cultural backgrounds.

National Institute of Biomedical Imaging and Biomedical Engineering (NIBIB)

The National Institute of Biomedical Imaging and Bioengineering (NIBIB) is now in the middle of its second decade of significant progress in developing novel biomedical technologies to help diagnose, treat, and prevent illness. NIBIB's vision of improved health for all Americans is driven by the convergence of engineering and the physical and life sciences.

Recent scientific advances are giving us new tools to tackle challenging health problems. Sophisticated imaging techniques allow us to peer into the human body with pinpoint accuracy and even eliminate or repair unhealthy tissue. Developments in bioengineering promise to enhance the body's natural ability to recover from injury and disease, aided by a new generation of biotherapeutics. Transformative technologies are also being made possible with new types of materials and electronics. As one example, NIBIB-supported researchers created a small, flexible ultrasound patch that can be worn like a band-aid to accurately monitor blood pressure. The idea to utilize ultrasound technology in a wearable device is a new approach that could lead to other avenues for monitoring and diagnosing illness.

Flexible electronics, ink-jet printable materials, and harnessing the increasing computing power of smartphones are a few of the advances that will enable future discoveries and help propel them to become useful tools for medical practitioners and individuals. NIBIB's Discovery Science and Technology (DST) Program is helping to drive scientific progress and lead a path toward the future of medicine where faster, better, less costly approaches are more broadly applicable. In a test case of this type of technology, researchers designed a sensor platform to detect a protein biomarker (HER-2) for diagnosing one type of breast cancer. This test uses electrochemical detection, a method that measures electric currents that are generated from reactions in the test compounds. The benefits of the device are numerous: it can be manufactured for 25 cents, gives results in 15 minutes, and of great importance to patients, it uses a small blood plasma sample instead of tissue, thus eliminating the need for painful biopsy.

NIBIB-supported research in health informatics technology (HIT) is also building toward practical, patient-centered applications such as using data to help doctors make clinical decisions, developing technologies to monitor a patient's treatment in their own home, and improving medical images with the next generation of intelligent data analysis tools and support systems. Telemedicine and mobile health technologies are transforming healthcare delivery, with the potential to provide broader access for a range of illnesses to patients in their own homes or a nearby clinic. One experimental method of using telemedicine to help monitor patients in their own home is a system to detect a dangerous drop in white blood cells in patients receiving chemotherapy. NIBIB researchers developed a prototype tabletop device designed to be used easily at home, which operates by taking a video of blood moving through extremely small capillaries at the base of the fingernail just below the skin. From the video, the device can count the number of white blood cells, detecting a reduction in the normal number of white cells expected in just one minute – helping already compromised patients to avoid contracting infectious disease, hospitalization, and even death.

In closing, Madam Chairwoman and Members of the Subcommittee, I hope that our being here today will help to cultivate even further your knowledge of the great work being done at NIH. This is a time of remarkable opportunity for translating scientific discovery from numerous domains into improvements for Americans' health. On behalf of the panel here today, I thank you for your strong, consistent, and bipartisan support for investments toward making and applying those crucial discoveries.

This concludes my formal remarks. My colleagues and I welcome your questions.

ⁱ Centers for Disease Control and Prevention, **Racial/Ethnic Disparities in Pregnancy-Related Deaths — United States, 2007–2016 (September 6, 2019)**.

https://www.cdc.gov/mmwr/volumes/68/wr/mm6835a3.htm?s_cid=mm6835a3_w

ⁱⁱ Main & Menard, 2013. **Maternal mortality: time for national action**. *Obstet Gynecol*. 2013 Oct;122(4):735-6
PubMed ID: 24084528.

ⁱⁱⁱ Kumar PL, James PF. **Identification and characterization of methylation-dependent/independent DNA regulatory elements in the human SLC9B1 gene**. *Gene*. 2015 May 1;561(2):235-48. doi: 10.1016/j.gene.2015.02.050. Epub 2015 Feb 19. PMID: 25701605; PMCID: PMC4361323.