DEPARTMENTS OF LABOR, HEALTH AND HUMAN SERVICES, AND EDUCATION, AND RELATED AGENCIES APPROPRIATIONS FOR FISCAL YEAR 2024

THURSDAY, MAY 4, 2023

U.S. SENATE,
SUBCOMMITTEE OF THE COMMITTEE ON APPROPRIATIONS,
Washington, DC.

The subcommittee met, at 10 a.m., in room SD–192, Dirksen Senate Office Building, Hon. Tammy Baldwin (chairwoman) presiding.

Present: Senators Baldwin, Murray, Durbin, Shaheen, Schatz, Capito, Moran, Kennedy, Boozman, Britt, and Collins.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

STATEMENT OF DR. LAWRENCE TABAK, ACTING DIRECTOR

ACCOMPANIED BY:

DR. DOUGLAS LOWY, PRINCIPAL DEPUTY DIRECTOR, NATIONAL CANCER INSTITUTE

DR. JOSHUA GORDON, DIRECTOR, NATIONAL INSTITUTES OF MENTAL HEALTH

DR. RICHARD HODES, DIRECTOR, NATIONAL INSTITUTE ON AGING

DR. NORA VOLKOW, DIRECTOR, NATIONAL INSTITUTE ON DRUG ABUSE

OPENING STATEMENT OF SENATOR TAMMY BALDWIN

Senator BALDWIN. Good morning. I want to welcome everyone to the Senate Appropriations Subcommittee on Labor, Health, and Human Services, Education, and Related Agencies hearing on fiscal year 2024 budget request for the National Institutes of Health, and today I am happy to welcome Acting Director Tabak and his colleagues and I will introduce you all before the testimony begins.

These hearings are essential for our subcommittee to assess our country's needs for the coming year. For NIH (National Institutes of Health), this means providing our scientists with what they need to conduct cutting edge research, to discover and develop treatments to help patients fighting disease.

As I happen to be the granddaughter of an NIH-funded scientist, my grandparents raised me and I understand what an important role biomedical research plays not just in treating and curing dis-

ease but also in bolstering our economic growth and ensuring that America is a global leader in innovation.

We cannot afford to have NIH's potential limited or even worse have its legs cut out from under it. Yet that is precisely what the House Republicans have proposed to do with their fiscal year 2024 budget caps in the bill that they passed last week.

Cutting spending as they have proposed would mean slashing approximately 22 percent from programs next year that support a range of programs, including supporting our veterans, keeping our communities safe and healthy, and doing vital research to find cures for illnesses and diseases.

It would mean a cut of over $10 billion in fiscal year 2024 alone for life-saving medical research at NIH. An extreme cut like that would mean NIH could fund 5,000 fewer grants and would shutter hundreds of labs across the country. It would stall training for the next generation of researchers and result in fewer drugs being developed for cancer, Alzheimer's disease, diabetes, serious mental illness, and other devastating conditions.

This would slow progress to find treatments for disease and weaken America's competitiveness, particularly against China, and increase our reliance on foreign countries for clinical trials and drug development.

Fortunately, here in the Senate, Ranking Member Capito and I are focused on writing a bipartisan Labor/HHS (Health and Human Services) spending bill to move our country forward. We are committed to working together to find compromise.

Our communities are depending on us to continue providing the support needed to combat the opioid epidemic, the mental health crisis, and so many other challenges.

Every day across Wisconsin researchers at world-class institutions, like Marquette University, the Medical College of Wisconsin, and the University of Wisconsin System, are working around the clock and making ground-breaking discoveries.

I'm pleased to say this subcommittee has a proven track record of recognizing the tremendous importance of supporting our Nation's biomedical research community.

Acting Director Tabak, I'm pleased to see that the Administration's budget request for NIH would increase funding for the Cancer Moonshot and Mental Health Research, and I look forward to learning about the agency's plans to deliver new cancer treatments with fewer side effects and develop a precision psychiatric initiative, but I'm disappointed to see programs that aim to address maternal mortality, the opioid epidemic, Alzheimer's disease, and health disparities and develop a universal flu vaccine to name just a few, that those programs remain flat or are actually cut in the proposal.

I look forward to working with my colleagues to ensure NIH has the resources it needs across its 27 institutes and centers to continue the progress of recent years.

I have been glad to see NIH working to examine barriers to diversity among its researchers and within its clinical trials and increased career opportunities for groups that are underrepresented in biomedical research, but there is still a long way to go, and in

the meantime, these remain real problems with real consequences for research.

Finally, before I turn it over to Senator Capito, I want to mention an article published last week in Science revealing NIH's failure to discipline an investigator with a known documented history of sexual harassment.

In March of 2022, after years of urging NIH to take decisive action, this subcommittee wrote policy into law requiring institutions to inform NIH of disciplinary actions taken against harassers to ensure accountability.Yet, following a far-reaching investigation at Florida State University that resulted in a 131-page report detailing years of severe pervasive sexual harassment, NIH approved the transfer of an investigator from FSU (Florida State University) to San Diego Biomedical Research Institute and awarded him a new $2.5 million grant. Unsurprisingly, the abuse continued, driving at least one trainee out of the institution.

It is outrageous that NIH is complicit in this case of pass the harasser and I want to know what you're doing to hold the researcher and institutions accountable and how you will prevent incidents like this from happening again in the future.

So, Acting Director Tabak, I look forward to your testimony and appreciate your being here today.

In a moment, I will turn it over to Ranking Member Capito for her opening remarks. Following Senator Capito's opening statement, we will hear from Acting Director Tabak and after that Senators will each have 5 minutes for the first round of questions.

Senator Capito.

STATEMENT OF SENATOR SHELLEY MOORE CAPITO

Senator CAPITO. Thank you. Thank you, Madam Chair, and I agree with you. We need to do this together, work together. We have the Vice Chair here. So, she's riding hard on all of us as she is with the Chair. So, we are hopeful that we have a successful result.

Dr. Tabak, thank you for being here and for your role in performing the functions as NIH Director, really appreciate this. You've done it since December 2021 and have helped steer NIH through some interesting times. Maybe you'll write a book or something.

Dr. Volkow, thank you. Dr. Hodes, thank you. Dr. Gordon and Dr. Lowy, thank you for being here today to discuss some of the biggest health issues facing our Nation.

This is an important opportunity for us to hear about the NIH budget proposal and better understand the priorities for fiscal year 2024.

I've mentioned before that our jobs will be more challenging this year given the debt ceiling and fiscal challenges that face our Nation. Supported funding for biomedical research at NIH has long been a bicameral, bipartisan priority.

The budget proposes $48.8 billion in discretionary spending for NIH, including 21st Century cures and ARPA–H (Advanced Research Project Agency for Health). NIH funding has seen almost a 60 percent increase for the last 8 years and these investments are

for good reasons since NIH research affects every American in every way.

As I look through the dais, I think of all the people that I know in my home State who are affected by your different disciplines.

In West Virginia, NIH supports 952 jobs and a $142 million in economic activity during 2022 alone through the $49 million that were received in grants and contracts.

This year we need to prioritize areas of agreement, such as funding to find cures and treatment for cancer, including childhood cancer, and funding for our academic research institutions.

For example, in the fiscal year 2023 Omnibus, we reauthorized the Childhood Cancer Star Act, which I led with Senator Jack Reed and included in there $30 million to continue to implement it.

The Cancer Star Act directs the National Cancer Institute to advance childhood cancer research to better understand and track the disease and enhance support for survivors and those affected by childhood cancer. Childhood cancers are different than adults and this specialized research is very important.

West Virginia ranks above the national average both in new cancer diagnoses and deaths. So, I'm pleased that the budget devotes increases to the Cancer Moonshot and significant resources to the Advanced Research Project Agency for Health or ARPA–H to focus on finding cures and treatments for cancer.

Another area I greatly support is for the NIH Institutional Development Award or the IDEA Program. There have been few programs as impactful to my State as the IDEA Program and I'm disappointed that these awards are flat funded in the President's budget.

West Virginia University is one of 17 research institutions nationwide to participate in an IDEA, an Echo Program that was started in 2016. The collaboration between WVU (West Virginia University) establishes pediatric clinical trials throughout the entire State of West Virginia so that doctors and patients have access to the same treatments that are available at WVU's hospital in Morgantown.

WVU is also a leader in NIH COVID research. Dr. Sally Hotter with WVU is co-leading an IEDEA States Consortium Initiative to better understand the long-term effects of COVID.

The research capabilities at West Virginia University continue to prove that our West Virginia institutions can compete with any other institution in the country.

I'm disappointed in some of the overall funding levels in the NIH proposed budget. First, there are no new resources specifically for Alzheimer's research at NIH which Dr. Hodes knows is a great passion of mine. An estimated 6.7 million people 65 or older are currently living with Alzheimer's in our country and the national cost of caring for those Alzheimer's and other dementias is estimated to reach $345 billion, not to mention the emotional cost on our families and care-givers.

There's a lot of exciting research going on in this area. Alzheimer's and dementia-related research must remain a national priority.

Also, substance abuse challenges facing the Nation basically are receiving just lip service in this budget as the National Institute on Drug Abuse is receiving flat funding.

In 2021, fatal overdoses claimed nearly a 107,000 Americans. Dr. Volkow has visited my State and has seen firsthand how we are in the crosshairs of the opioid and addiction crisis.

Dr. Hodes, I know we are anxious to have you back in West Virginia and, frankly, I'd welcome all of you to visit West Virginia not just to see and learn but also to enjoy the State, as well, and meet the dedicated professionals.

I know we're dealing with a tight budget year this year, but investments in biomedical research are so important for the future of our country.

Listen. I want to thank all of you for what you do. I should have started with that because you're in an exciting time for research and exciting time for break-throughs, and we want to support you as well as we can.

So, thank you.

Senator BALDWIN. Thank you, Senator Capito, and I will now introduce our witnesses.

Dr. Lawrence Tabak is the Acting Director of the National Institutes of Health.

Dr. Joshua Gordon is the Director of the National Institute of Mental Health.

Dr. Richard Hodes is the Director of the National Institute on Aging.

Dr. Douglas Lowy is the Principal Deputy Director of the National Cancer Institute.

Dr. Nora Volkow is the Director of the National Institute on Drug Abuse.

I want to thank you all for joining us and underscore what Senator Capito just said. Thank you for what you do and how you have devoted your careers.

Acting Director Tabak, you may deliver your opening remarks.

SUMMARY STATEMENT OF DR. LAWRENCE TABAK

Dr. TABAK. Thank you, Chair Baldwin, Ranking Member Capito, and Distinguished Subcommittee Members.

I'm honored to be here today representing the National Institutes of Health.

Our mission at NIH is to seek fundamental knowledge about the nature and behavior of living systems and to apply that knowledge to save lives and improve health. Fundamental, translational, and clinical research are critical components of the biomedical research enterprise.

However, fundamental or basic research rarely makes headlines. Understanding how proteins fold or how gene activity is controlled doesn't often improve human health immediately, but fundamental research is essential to making breakthrough discoveries that lead to treatments and cures.

A paper published last Friday in the Journal of the American Medical Association indicated that NIH funding contributed to the development of 354 out of 356 new drugs approved by the U.S. FDA (Food and Drug Administration) from 2010 to 2019.

NIH supported the foundational evidence that pharmaceutical companies leveraged to develop life-saving drugs and many thousands of patents.

I've spoken to this subcommittee previously about how fundamental research from NIH supported scientists and collaborators positioned the United States to develop COVID–19 vaccines on an unprecedented timeline, but there are many other examples of how fundamental research has led to improvements in the health of Americans.

One such case is the breakthrough stroke treatment tissue plasminagen activator or TPA that resulted from decades of work conducted across biological disciplines. Researchers first found the enzyme on cells that line blood vessels in 1946. Three decades later, certain cancer cells were found to secrete TPA in large quantities and once purified the purifying enzyme dissolved clots in animal models.

A decade after that, using recombinant DNA technology NIH-supported clinical trials led to the approval of TPA to treat heart attacks and then in the 1990s TPA transformed the treatment of stroke, allowing most patients who are treated within 3 hours to make a full recovery with far reduced health costs.

Many of our most important advances have come when we were not even thinking about a direct application. Decades ago, NIH-funded research on how bacteria protect themselves from viruses, for example. No one involved could have predicted that this research would lead to tools that have revolutionized all of medicine.

Because of research on recombinant DNA in the 1960s, it became possible to produce drugs like human insulin and TPA for widespread use starting in the 1980s.

Continued investments led to the transformative approaches for gene editing, such as CRISPR. This highly-versatile technology has revolutionized how basic research is conducted and how diseases may be treated, including such things as sickle cell and antibiotic resistant urinary tract infections.

Discoveries build upon each other in ways that we cannot necessarily predict. Sustained public investment in fundamental research is essential to the discovery and development of new medical treatments.

To foster the application of fundamental research, NIH continues to support translational research studies and collaborate with industry to advance crucial interventions for the public.

As most of you know, Naloxone is a life-saving treatment that can quickly restore normal breathing when somebody overdoses on opioids. This drug is an essential tool in the fight against the opioid overdose crisis which claims 188 lives in the U.S. every day.

Injectable Naloxone was used for years but an easier intervention was needed. In 2013, scientists from the National Institute on Drug Abuse created a stable formulation of concentrated Naloxone for use in a nasal spray injector developed by an industry partner. Working together, they conducted clinical trials to evaluate the nasal spray formulation, providing the pivotal data to support FDA approval of Narcan in 2015, and just a few weeks ago the FDA approved Narcan for use without a prescription.

NIH-supported discoveries have affected nearly all of our lives from research studies that lay the foundation for future advances to clinical trials that evaluate potentially life-saving interventions.

Your continued support of our mission to help people live longer and healthier lives is crucial.

I thank you for your time and I welcome your questions.

[The statement follows:]

PREPARED STATEMENT OF LAWRENCE A. TABAK, D.D.S., PH.D.

Good morning, Chair Baldwin, Ranking Member Capito, and distinguished Members of the Subcommittee. I am Lawrence A. Tabak, D.D.S., Ph.D., privileged to be Performing the Duties of the Director of the National Institutes of Health (NIH). Thank you for the invitation to appear before you today so that I may provide you with information about our efforts in pandemic preparedness and our Fiscal Year (FY) 2024 budget request.

I truly appreciate the Committee's ongoing bipartisan support for NIH. As a result of this support, scientific advances have been made that reach people of all ages across the United States. From improving treatment options for substance use disorders to developing vaccines to prevent infectious diseases to discovering novel cancer treatments, the investment Congress continues to make in NIH improves the health of your communities.

The FY 2024 President's Budget builds on the Committee's investment in numerous public health challenges including maternal health, mental health, and health disparities research. In addition, it builds on the Reignited Cancer Moonshot,℠ continues efforts to develop a universal influenza vaccine, increases focus on substance use disorders, and prioritizes innovative nutrition research to reduce diet-related diseases.

STEADY PROGRESS ON PANDEMIC RESPONSE

The COVID–19 global pandemic demonstrated how fundamental research, and early-stage discovery, design, and development of vaccines and therapeutics can yield impactful results in a short amount of time. As we continue to address the effect of the pandemic on the public's health, a sustained investment in biomedical research is necessary to ensure our momentum on current vaccine and treatment options against future emerging infectious agents.

NIH was able to respond efficiently to the COVID–19 pandemic by capitalizing on decades of basic and applied research to facilitate the rapid development of vaccines, therapeutics, and diagnostics. These continue to be important tools to reduce the threat of disease. Over the past 3 years, NIH established networks and initiatives that are cornerstones in the study of and response to pandemic threats. This includes the Antiviral Program for Pandemics, the Rapid Acceleration of Diagnostics (RADx®) initiative, and the Accelerating COVID–19 Therapeutic Interventions and Vaccines (ACTIV) public-private partnership.

We are also grappling with a new public health challenge as we begin to understand the long-term effects of the COVID–19 pandemic, including Post-Acute Sequelae of SARS-CoV–2 Infection (PASC, also commonly known as "Long COVID") and the mental health effects of the pandemic. Furthermore, NIH continues to apply lessons learned during the COVID–19 pandemic to address other public health issues, including the recent mpox Public Health Emergency, and to help prepare for future pandemics.

CAPITALIZING ON VACCINE RESEARCH FOR UNIVERSAL INFLUENZA

Influenza viruses are deadly and costly pathogens that place a substantial health and economic burden on the United States and across the world each year. In the United States, the CDC estimates that the disease burden of influenza has resulted in between 9.2 million and 35.6 million illnesses, between 140,000 and 710,000 hospitalizations, and between 12,000 and 56,000 deaths annually since 2010, all of which results in an estimated $27 billion in health costs. Pandemic influenza—which occurs when a new, non-human flu virus emerges from an animal source with the capacity to spread readily from person to person—can pose an even greater threat. Current influenza vaccination strategies rely on the development of an annual vaccine targeting the circulating strains that are anticipated to spread in the United States. However, this approach does not always yield high levels of protection against seasonal strains and offers little to no protection against pandemic influenza viruses.

NIH seeks to develop a universal influenza vaccine that would generate robust, long-lasting protection against multiple subtypes of influenza, eliminating the need to update the vaccine each year and protect against newly emerging strains with pandemic potential. In 2022, a Phase 1 clinical trial began enrolling healthy volunteers at the NIH Clinical Center to assess the safety and efficacy of a novel universal flu vaccine candidate.[1] Building upon the success of mRNA vaccines developed during the COVID–19 pandemic, NIH is working to apply this platform to the universal influenza vaccine development. Additionally, NIH-supported researchers are actively identifying and developing novel adjuvants for influenza vaccines to increase their immunogenicity and effectiveness. Continued investment in this research will enable the development of more broadly protective and longer-lasting influenza vaccines. The FY 2024 budget request includes $270.0 million for universal influenza vaccine research, the same as the FY 2023 Enacted level.

A REINVIGORATED CANCER MOONSHOT

In FY 2024, the President's Reignited Cancer Moonshot Initiative[2] will support priority investments to advance the goals of the Reignited Cancer Moonshot which includes cutting America's cancer death rate by 50 percent over the next 25 years. Since its establishment in 2016, the Beau Biden Cancer Moonshot has supported over 250 research projects that pushed the boundaries of discovery and collaboration on behalf of cancer patients. The President's Budget includes an increase of $500.0 million for the Cancer Moonshot from the FY 2023 Enacted level, for a total of $716.0 million, with further increases proposed in FY 2025 and FY 2026 using mandatory funding.

Clinical trials play a prominent role in evaluating new cancer prevention, screening, and treatment approaches. NIH National Cancer Institute (NCI) funding will focus on doubling the number and increasing the diversity of people who enter NCI-sponsored clinical trials to develop new prevention, diagnostic, and therapeutic approaches at a more rapid pace. Funding will also support continued work towards increasing the pipeline of new cancer drugs. Additionally, the resources will fund a major trial to evaluate multi-center detection tests, the Cancer Moonshot Scholars program, and the NCI Telehealth Research Centers of Excellence, allowing the agency to sustain progress towards meeting the President's goal to end cancer as we know it. The FY 2024 proposal fully aligns with the following seven pillars of the Reignited Cancer Moonshot, which include diagnosing cancer sooner; preventing cancer; addressing inequities; targeting the right treatments to the right patients; accelerating progress against the most deadly and rare cancers, including childhood cancers; supporting patients, caregivers, and survivors; and learning from all patients.

ENHANCING NUTRITION RESEARCH AND FOOD SECURITY

The Office of Nutrition Research (ONR), within the NIH Office of the Director, focuses on advancing nutrition science to promote health, and to reduce the burden of diet-related diseases and nutrition health disparities. The budget includes an increase of $120 million to support nutrition research, including investments that will advance the goals of the White House National Strategy on Hunger, Nutrition, and Health. Resources will expand the efforts of the NIH Common Fund Community Partnerships to Advance Science for Society, and help to ensure diversity and inclusion in nutrition, health, and food security research. Funding will also allow NIH to focus on expanding and diversifying the nutrition science workforce and investing in creative new approaches to advance research regarding the prevention and treatment of diet-related diseases, including the Food is Medicine initiative and an Artificial Intelligence for Precision Nutrition program.

ONR is also collaborating with the NIH Institutes and Centers on a transformative research program examining the role of diet, food environment and related environmental exposures on the Developmental Origins of Health and Diseases. There is increasing concern that food environment, life stress, traumas, medications, health and nutritional status, microbiome ecology, and related environmental exposures are responsible for future diet-related disease risk. This discovery science program will also include a comprehensive study of human milk composition, dietary intake, and nutritional status measures and outcomes, answer mechanistic questions about the developmental origins of disease, and ultimately, lead to an optimized diet for the health of the mother and child.

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[1] www.nih.gov/news-events/news-releases/trial-potential-universal-flu-vaccine-opens-nih-clinical-center.

[2] www.cancer.gov/research/key-initiatives/moonshot-cancer-initiative.

REVOLUTIONIZING MENTAL HEALTH WITH PRECISION MEDICINE

With the FY 2024 President's Budget Request, NIH intends to direct increased attention towards mental health across all ages. Mental illnesses are the fifth leading cause of disability in the United States, accounting for 6.6 percent of all disability-adjusted life years in 2019. Exacerbated by the pandemic, suicide rates for youth have risen over the past 2 decades in the United States; in 2020, an estimated 6,643 youth ages 10 to 24 died by suicide.[3] Despite advances in the treatment of depression and other serious mental illnesses, there remain few evidence-based interventions that rapidly reduce suicide risk within healthcare settings. Finding the right treatment for a specific individual required a trial-and-error process that can lead to unacceptable delays in receiving effective treatment. The President's Budget includes efforts to apply the concepts of precision medicine to the field of psychiatry through the Precision Psychiatry Initiative. This initiative includes two component parts: (1) an innovation funnel to rapidly identify and assess biomarkers for the treatment for depression with the intent to lead to large-scale clinical trials; and (2) a data-driven refinement of precision diagnostics to study patterns of clinical trajectories and treatment response across large cohorts over time.

Serious Mental Illness (SMI) is a major, albeit less known, risk factor for COVID–19,[4] and people with SMI are more prone to SARS–CoV–2 infection and are more likely to require hospitalization and die from severe COVID–19. NIH supports research on many facets of mental health including rapid interventions to reduce severe suicide risk, funding adaptive interventions to optimize adolescent mental health treatments, and aggregating data to address mental health disparities research gaps. In response to the pandemic, NIH launched a project to support research focused on the social, behavioral, and economic impacts of COVID–19. The project supports research on the secondary effects of the pandemic, such as financial hardship, reduced access to healthcare, and school closures.[5] This initiative includes NIMH-supported research on: the impact of COVID–19 mitigation efforts on socioeconomic disparities in mental health and healthcare utilization; the effectiveness of digital health apps like Headspace as a just-in-time approach to immediate, personalized behavioral healthcare; the effectiveness of a digital platform on depression/anxiety symptoms of healthcare workers during the COVID–19 pandemic; and effectiveness, barriers, and facilitators to the implementation of a gold standard exposure treatment for post-traumatic stress disorder in healthcare system employee assistance programs serving frontline healthcare workers.

MAKING PROGRESS ON HEALTH DISPARITIES AND INEQUITIES IN RESEARCH

Building on investments made by this committee over the past several years, NIH hopes to continue the agency-wide effort to reduce health disparities across racial and ethnic minority, rural, low-income, and other underrepresented and marginalized populations. The President's Budget requests $95 million to sustain health disparities research across the Institutes and Centers that are developing and testing interventions appropriately tailored to the breadth of clinical and community services found in diverse settings and contexts.

UNITE, launched in February 2021, is an NIH-wide, collaborative effort comprised of five workstreams with distinct but coordinated objectives to tackle the problem of racial and ethnic equity in science while developing data-driven methods to promote diversity, equity, and inclusion across the biomedical and behavioral enterprise. To thoroughly address structural racism that may exist within the enterprise, UNITE works across three domains—Health Disparities and Minority Health Research, the internal NIH workforce, and the external biomedical and behavioral research workforce. Data gathering and analysis are central to all activities, and therefore evidence drives the work of UNITE. UNITE goals and charges are aligned with fundamental tenets of the NIH-Wide Strategic Plan for 2021—2025,[6] the NIH Minority Health and Health Disparities Strategic Plan 2021—2025,[7] and the NIH-Wide DEIA Strategic Plan for 2022—2026, released in March 2023.[8]

COMBATTING OVERDOSE AND ADDICTION

Opioid misuse, addiction, and overdose are among several widespread public health crises that were exacerbated by the pandemic. Since the pandemic, studies

[3] wisqars.cdc.gov/data/explore-data/explore.
[4] nimh.nih.gov/health/statistics/mental-illness.
[5] covid19.nih.gov/news-and-stories/covid19-ripple-effects.
[6] www.nih.gov/sites/default/files/about-nih/strategic-plan-fy2021-2025-508.pdf.
[7] www.nimhd.nih.gov/docs/nimhd-strategic-plan-2021-2025.pdf.
[8] diversity.nih.gov/about-us/strategic-plan.

have found increases in the use of illicit drugs including fentanyl, cocaine, heroin, methamphetamine, cannabis,[9] and most recently xylazine. Founded in 2018, the Helping to End Addiction Long-term (HEAL) initiative strives to address opioid addiction by developing new treatments and strategies to address both pain and opioid use disorder as well as advance healthy equity by acknowledging the environmental factors that contribute to drug use and chronic pain. In FY 2024, HEAL will focus on the health effects of taking multiple drugs together, find tailored treatment approaches, such as combination therapies, for different environments, and continue research on health disparities in treatment for opioid use disorder, neonatal opioid exposure and maternal health, and integrated pain and mental health treatments.

Opioid use is not the only alarming trend in addiction and overdose. The misuse of stimulants, such as methamphetamine, is also increasing, as are deaths attributed to combining opioids and stimulants. Improved prevention and treatment strategies are needed for both opioid use disorder and co-occurring conditions such as mental health conditions and polysubstance use for a range of at-risk populations and in various settings. Recently launched HEAL programs aim to develop safe and effective treatments, as well as define approaches to improve treatment access and retention in various settings.

PREVENTING MATERNAL MORBIDITY AND MORTALITY

Even during a global pandemic, NIH continued to focus on other long-standing yet urgent public health needs. The CDC estimates 1,200 women die each year in the United States of maternal causes, 80 percent of which are preventable, and thousands more experience severe pregnancy-related morbidity.[10,11]

To address this alarming trend, NIH established an agency-wide collaboration called the Implementing a Maternal health and Pregnancy Outcomes Vision for Everyone (IMPROVE) Initiative[12] which is an evidence-based approach to reduce preventable maternal and pregnancy-related deaths and associated health disparities for women at all stages of pregnancy. To build on the momentum made by the committee's previous investments, the FY 2024 President's Budget requests $30 million to continue the IMPROVE Initiative. In addition, the request also includes $3 million for the Eunice Kennedy Shriver National Institute of Child Health and Human Development to support research on mitigating the effects of COVID–19 on pregnancies, lactation, and post-partum health with a focus on individuals from racial and ethnic minority groups.

In summer 2023, IMPROVE will implement a national network of Maternal Health Research Centers of Excellence to support research projects that build on previous research and take innovative, community tailored approaches to address health disparities and risk factors for maternal morbidity and mortality. This research supports the development of earlier interventions to decrease or prevent negative maternal outcomes and promote maternal health equity.

NIH BUILDINGS AND FACILITIES

Facilities must co-evolve with science for NIH to achieve its full potential. A major component of the NIH Building and Facilities (B&F) program is the Repair & Improvement (R&I) program, which enables NIH to maintain and improve the performance of existing facilities throughout their life cycle. A key aspect of NIH's strategy is to sustain the condition of existing facilities to prevent premature deterioration and the curtailment of research. These investments help reduce the likelihood and consequences of building emergencies associated with NIH's Backlog of Maintenance and Repairs (BMAR) of nearly $3.8 billion across all campuses as of the end of FY 2022. NIH requests a funding level for B&F of $350.0 million, maintaining the FY 2023 Enacted level. This level is designed to address the pressing campus-wide infrastructure needs identified in the independent review of the facility needs of NIH's main campus in 2019 by the National Academies of Sciences, Engineering, and Medicine (NASEM). In addition to the B&F appropriation, NIH has received support for critical infrastructure projects in recent years from targeted allocations from the Nonrecurring Expenses Fund (NEF). In FY 2024, NIH is requesting a total of $120.1 million in NEF funding for five critical infrastructure projects on the Bethesda campus.

NIH plans to execute various modernization and repair projects to NIH's research hospital, replace research animal facilities with a centralized and more efficient fa-

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[9] https://nida.nih.gov/research-topics/comorbidity/covid-19-substance-use.
[10] www.cdc.gov/nchs/data/hestat/maternal-mortality/2021/maternal-mortality-rates-2021.htm.
[11] www.cdc.gov/reproductivehealth/maternal-mortality/erase-mm/data-mmrc.html.
[12] www.nih.gov/research-training/medical-research-initiatives/improve-initiative.

cility, improve facilities that advance computational and data science, replace temporary and obsolete administrative support facilities with permanent buildings, improve the energy and water efficiency of buildings, and support the co-evolution of science and buildings.

CONCLUSION

Turning discovery into health remains the central goal and mission of NIH. Improving health across the lifespan is essential to maintaining our country's greatest asset: its people. The NIH research community is fervently working on all fronts—from individualized medicine to societal level pandemic response—to foster new discoveries and catalyze breakthroughs in research. With the support of this Committee, NIH looks forward to tackling timely public health challenges through rigorous and innovative science in FY 2024. I look forward to answering your questions.

Senator BALDWIN. Thank you, Dr. Tabak.

We will now begin our round, first round of questions. I have several questions that I want to get to, but first, as I noted in my opening statement, the House Republicans last week passed a bill that would have devastating impacts on biomedical research.

HOUSE BUDGET CUTS

What they have proposed would require deep cuts to the NIH and would lock in those cuts over the next decade. I outlined a list of impacts I believed it might have on NIH.

Very briefly, is there anything that you would like to add about what a more than $10 billion cut would mean for NIH research, including if those cuts were sustained over the next decade?

Dr. TABAK. In addition to the numbers that you provided, Chair Baldwin, it would be a chilling effect on the entire biomedical research enterprise. It'll decrease interest in research careers and, as you well know in times of fiscal stress, disproportionately young investigators are the ones who suffer the most.

It really bodes poorly for the future of biomedical science.

Senator BALDWIN. Thank you.

BIOSAFETY INCIDENTS

Dr. Tabak, research that involves enhanced potential pandemic pathogens must be accompanied by safeguards and conducted under strict biosafety and biosecurity measures.

There have been two biosafety incidents involving the H5N1 virus at the University of Wisconsin, Madison, campus. The CDC (Centers for Disease Control and Prevention) considered a 2013 incident a serious exposure that required a researcher to quarantine for a week, which they ended up doing at home rather than at a dedicated quarantine facility.

NIH officials didn't find out about an incident in 2019 until 10 days after a trainee had been exposed. In March, the National Science Advisory Board for Biosecurity published a report recommending the U.S. expand the scope and impose stricter oversight of federally-funded research on dangerous pathogens. This includes NIH-funded studies overseas.

Dr. Tabak, how will the NIH increase its oversight of this research and ensure institutions are held accountable when incidents happen?

Dr. TABAK. So, as you know, the NSABB (National Science Advisory Board for Biosecurity) recently provided its report to HHS and this is informing ongoing discussions across the USG.

I can't presume what those discussions will yield but I can speak to what NIH is doing in the meantime.

First, we are considering how best to elevate the transparency and oversight of the decision process that we use at NIH that feeds into the HHS oversight function.

We are also developing approaches to partner more effectively with our applicant organizations by developing new materials which will clarify both institutional and NIH responsibilities in the process.

We're also performing a comprehensive review to our resisting recombinant DNA and synthetic molecules policies to ensure that we capture biosafety considerations related to emerging technologies, like CRISPR.

Senator BALDWIN. I appreciate your answer.

I just want to comment also that when we look at this oversight, we want to make sure that we don't prompt scientists to move their experiments to countries where there are less stringent requirements. It's a balance that we must reach.

Dr. Volkow, I'm concerned that this budget request leaves opioid research flat footed. Our communities continue to struggle with an opioid crisis and fentanyl is making it so much worse.

Fentanyl is 50 times stronger than heroin and a hundred times stronger than morphine and it has become the leading cause of death for people 18 to 45. In my home State of Wisconsin, synthetic opioids, primarily fentanyl, were identified in 91 percent of opioid overdose deaths from 2021 to 2022.

I've heard from families across Wisconsin of lost loved ones to fentanyl poisonings and overdoses. We have to utilize every tool in our toolbox, from stopping it from coming into our country to preventing its use to bringing an end to this national crisis.

Last October, the Wisconsin Department of Health Services distributed a 120,600 fentanyl test strips to organizations across the State to help prevent drug overdose deaths.

Doctor, what does research show about how effective fentanyl test strips are in a real-world setting?

Dr. VOLKOW. The data is actually showing that they are effective in changing the practices of people that are intending to use drugs when these come back negative and research is ongoing to actually strengthen the guidelines that can then inform the users on how to take these drugs in a more safe way and how to test them.

Senator BALDWIN. Thank you.

I see my time has ended. I'm going to turn it to Senator Capito.

Senator CAPITO. Thank you.

CHILDHOOD CANCER

Dr. Lowy, I wanted to talk a little bit about the childhood cancer that I spoke about in my opening statement. I talked about the Star Act, but I guess what I would ask you is where are you seeing the most promising advances in terms of being able to make advances in this pediatric cancer space and what are some of the differences or the top challenges that you have?

Dr. LOWY. Senator Capito, I really want to thank you and Senator Reed for the initial passage of the Star Act and its reauthorization this year and as you know, we are able as a result to support areas for cancer survivors, for improving our biospecimens, and then for collaborating with the Childhood Cancer Initiative to develop molecular characterization in more detail.

We hope that these and other advances will be able to improve the lives of children who develop cancer, both with improved treatment as well as with less toxicity. There have been several FDA approvals over the last few years but it's not enough.

Children who get cancer, as you know, terrible. Children who die from cancer, even worse. We are working hard at the NCI (National Cancer Institute) to support research that is specifically targeted to molecules that are able to interfere with specific abnormalities in a wide range of childhood cancers.

As you said in your opening statement, childhood cancers are not adult cancers in children but they are qualitatively different and we take advantage of that.

Thank you very much.

Senator CAPITO. Thank you. Thank you.

ALZHEIMER'S AND PARKINSON'S RESEARCH

Dr. Hodes, I want to ask you about the flat funding in Alzheimer's which makes absolutely no sense to me when we see the raging numbers. We know there have been a lot of breakthroughs recently, but I also wanted to ask you about Parkinson's disease because I think—I don't know that it's related to Alzheimer's, but it's a neurodegenerative disease.

Senator Murphy and I have just put a bill in that's leading legislation, National Plan to End Parkinson's Act, which would coordinate the research across the Federal Government and other ways.

So can you first talk about Alzheimer's and then the Parkinson's issue, on the Alzheimer's, the budgeting issue and then on the Parkinson's, what breakthrough kind of things are you anticipating, are you seeing within your research?

Dr. HODES. In terms of Alzheimer's disease research, we're clearly at a very exciting juncture, as many of you all have seen in the news, which, to be perfectly clear, the outcome of congressional support and NIH-funded research has led from translation of basic practice into clinical trials which are now showing effects for the first time.

The necessary funds to continue research in this area are important as we recognize it from the brains in people with Alzheimer's is really a very diverse disease. No one treatment is likely to be sufficient for all and promising reflection of what we have been able to accomplish, for example, are now some 59 early stage Phase 1 and Phase 2 clinical trials, only eight of which are targeted to amyloid. The other 51 are towards other diverse targets, such as inflammation, protein folding, and ultimately it's going to be the ability to personalize which of these is most effective for individuals.

So your question about budget and momentum reflects on the fact that if there were a limit in resources, we'd, of course, do our best to ration them appropriately but it would mean a slowing of

this whole and very successful pipeline from basic discovery for clinical trials research.

I'd also add that as we are seeing a time when clinical trial results are going to be translated into common practice in the communities, we are going to have to look very carefully at what happens when treatment reaches the community. Which individuals profit most? Who is most at risk for side effects? This is going to mean monitoring these outcomes in a way that we haven't done before.

To touch briefly perhaps on Parkinson's disease, the potential for a national plan equivalent to what has happened in Alzheimer's disease, I can only project could be as extraordinarily valuable as it has been for Alzheimer's disease.

I think you may be referring in fact to one particular discovery of a new sensitive means for a biomarker accomplishment in Parkinson's that shows the promise of detecting disease even before clinical symptoms and biomarkers as they have been in Alzheimer's disease are very critical to identification early to monitor the effects of clinical trials and to making the appropriate interventions available to the broadest diverse populations.

Senator CAPITO. Well, thank you. Just as a comment, thank you very much. I would agree now is not the time for us to take the foot off the pedal when we're starting to see these early breakthroughs that affect so many families across the country. Thank you.

Senator BALDWIN. Chair Murray.

Senator MURRAY. Well, thank you very much, Chair Baldwin, and Ranking Member Capito.

As Senator Collins and I have said from the start of these hearings, we are very determined to get back to regular order and make sure we pass the funding necessary to keep our families safe and healthy and keep our Nation competitive and that simply has to include providing robust funding for the National Institutes of Health.

If we want to continue to lead on the world stage, we have to continue our global dominance in biomedical research. Our Nation is the leading light here. I should know. I come from Washington State. We have many world-class institutions, and I couldn't disagree more with the House Republicans whose proposal to slash NIH funding would mean we will fall behind and fail to keep investing in these breakthroughs that have truly made a world of difference for patients across our country and across the globe.

We've got to build on that critical progress we've been making and ensure that our investments keep pace, not slash them as House Republicans voted to do.

You know, after a global pandemic that brought the world economy to a grinding halt and cost more than one million American lives, House Republicans are seriously suggesting that we slash funding for life-saving research.

So if we truly care about protecting families, we need to understand that this funding is just as critical as the investments we make in our military and we cannot forget the millions of families who are fighting cancer and Alzheimer's, substance use disorders, long COVID, and so much more.

We have to make sure that our investments reflect the reality that illness is one of our Nation's deadliest adversaries and biggest economic and national security threats.

As I mentioned, we saw that all too clearly during the COVID pandemic, but we also saw the incredible pace of discovery with COVID vaccines. It was no accident. It was made possible by our investments in research into mRNA vaccines in response to Ebola and other viruses and by a premier biomedical research enterprise that we have strategically built over decades and in the bipartisan pandemic response bill that I got signed into law last Congress, I'm glad that we were able to establish ARPA–H to continue strengthening our capacity for cutting edge research.

So I look forward to hearing from the witnesses today about the resources we need across NIH to continue supporting this life-saving work because at the end of the day, what we get for these investments are really important discoveries that keep our Nation competitive, that prepare us for pandemics and other health crises, and give families more time with their loved ones, and give patients hope for the future. That's not just worth the cost, it is priceless.

So I hope we all remember that as House Republicans have now voted for deeply serious and deeply dangerous cuts to cutting edge life-saving research, in the Senate we need to make sure that we are continuing to fund these important and critical investments.

So I'm glad to be here today and speak to our witnesses and, Dr. Tabak, I am a huge supporter of NIH but I have to ask you a tough question today.

HARASSMENT

I have been pressing NIH for years about how to ensure that Federal dollars are not flowing to researchers who harass or bully or retaliate against or even create a hostile environment for their colleagues and for their students and how to ensure NIH workers themselves are not continuing to experience harassment.

So I have to say I am really appalled by recent reporting that an NIH-funded scientist who faced institutional disciplinary action because he was found to have sexually harassed colleagues was simply able to transfer his award from one university to another research institute where he then harassed a trainee in his new lab and, even worse, NIH awarded him a new $2.5 million grant.

That happened despite the fact that Congress directed NIH to make it mandatory for institutions to inform NIH when scientists or key staff are removed or otherwise disciplined due to harassment, bullying, retaliation, or hostile working conditions.

Despite NIH posting publicly that you require notification from all of your award recipients, despite NIH's knowledge of the investigation's finding, and I just have to say it is completely unacceptable.

So I need to ask you today what is NIH doing to fully implement the requirement under last year's law that such actions must be reported to the agency and how are you using that requirement to enforce workplace protections against harassment?

Dr. TABAK. Chair Murray, I want to assure you that we take this issue very, very seriously. We've handled over 650 allegations of

harassment, discrimination, and hostile work environments. We have dedicated staff addressing these allegations and about 30 percent of those allegations have been substantiated and in dozens of cases principal investigators were removed from grants.

The issue that you point out this morning of so-called pass the harasser problem, we, of course, are well aware of that and the specific case. Unfortunately, the original institution was not completely forthcoming about the extent of the investigator's behavior and it was only after the individual's grant was allowed to transfer to the second institution that we became aware of the greater severity of what the issues were.

We are now working with the second institution to understand what the most recent allegations are and I can assure you that if these allegations are sustained, we will take immediate action as required.

Senator MURRAY. Okay. Well, I want to follow up with you. I'm out of time, but I want to find out how you are making clear to these institutions and your grantees that these behaviors are not being accepted and what you're doing to make sure that our NIH workers themselves are not experiencing harassment because at the end of the day, innovation isn't just driven by programs, it is driven by people, and we need the best and the brightest, and if this is what they see around them, we are going to lose them. So this is critical.

Thank you.

Senator BALDWIN. Vice Chair Collins.

Senator COLLINS. Thank you very much, Chair Baldwin.

Before I turn to my questions, I'm going to make a few comments.

First, I want to thank each of you for your extraordinary work. In my judgment, there is no investment that pays greater dividends to American families than our investment in biomedical research and that is why I've been such a strong supporter of NIH and I will continue to be one.

I think we're very fortunate that all of those who are on this committee share that view, including the Chair and the Vice Chair of this subcommittee.

ALZHEIMER'S FUNDING

That is why I am puzzled at the flat funding for Alzheimer's research. We have made real investments to help the 6.7 million Americans aged 65 and older who are currently living with Alzheimer's and those who care for them and we know that this number is on a trajectory to double by 2060.

Alzheimer's is also one of our Nation's most costly diseases and it's one of the leading causes of death among seniors. As the Senator representing the oldest State in the Nation, this is of particular concern to me and as a person who lost her father, her grandfather, and two uncles to this devastating disease, I know personally what this means to American families. So I hope that we can correct the flat funding and continue the trajectory that we have been on.

Now let me turn to my questions. First, Dr. Hodes, I want to commend the National Institute of Aging. You have been essential

in your institute in sustaining the progress that we have been making and we've seen an exciting new class of treatments, one announced just yesterday that is similar to another that has been approved under the accelerated process of FDA that could delay or slow the onset of Alzheimer symptoms.

In a statement last year following the release of Phase 3 lecanemab data, NIH said, "Although NIH did not fund this study, our decades of research paved the way for this Alzheimer's trial that notably met its primary and secondary endpoints." I agree.

That's why I'm so frustrated that these new therapies based on sound science approved by the FDA are not reaching patients because of CMS's (Centers for Medicare and Medicaid Services) inexplicable determination that they are not reasonable and necessary for seniors and here's my real concern.

While this is being finally sorted out, it is so sad because these treatments are most effective when they're given early when people are in the early stages of Alzheimer's. So the patients who would benefit the most are not receiving access to this medication.

Dr. Hodes, in your view, what would broader access now to these disease-modifying therapies mean for patients?

Dr. HODES. Well, thank you for the question, and, of course, the FDA and CMS have the regulatory authorities that are distinct from NIH, but from an NIH perspective, as you said, the therapies that have become available now are the clear outcome result of research supported by NIH.

In fact, lecanemab, one of the drugs, is now being studied in three trials directly funded by NIA (National Institute on Aging), one of which, for example, is treating individuals before any symptoms, so an even earlier stage than before a so-called secondary prevention trial.

Through these, we're trying to work for exposure to more diverse populations and in terms of what this could mean to the public, we are preparing for when final FDA approvals and CMS coverage occurs so we can monitor and ensure that we understand in populations that are diverse, rural, urban, racial, ethnic, which are likely to differ and just which treatment, what time is best, that we have the infrastructure and the trials in place to optimize their impact on society.

This is the next stage, having first found successful interventions to learn from these first leads and to optimize them. So I agree with you the impact on the broad population can be huge and it's our research commitment to make sure that we are prepared to assess this.

Senator COLLINS. Thank you.

EFFECTS OF CANNABIS

Dr. Volkow, I am very concerned about the widespread use of extremely potent cannabis by our young people whose brains are still developing.

NIH research has sought to better understand the relationship between marijuana use and psychiatric disorders. Given recent trends in recreational cannabis use and increased potency, is more research needed to better understand the short- and long-term ef-

fects of cannabis use on mental health and is NIH or its grantees investigating cannabis-induced psychosis?

Dr. VOLKOW. Thanks very much for that question.

Yes, indeed, we are very concerned about the increased use of cannabis with very high content of THC (Delta-9-tetrahydrocannabinol) and also by the increased in regular use. So what we are seeing in the United States is an increase in the number of people that are using cannabis regularly at very high doses. This is particularly important because it is the high doses that are associated with psychosis.

It's a very important area of research to try to understand under what conditions the use of marijuana can result in psychosis and importantly chronic psychosis. So, yes, we are prioritizing this as an area of research to try to unequivocally determine if there's a causal link between the use of cannabis and psychosis.

Researchers are also investigating the potential role that cannabis use can have in suicidal behavior. So we need to understand what may be consequence or not of the use of cannabis, but from what we know, we should be concerned and certainly be monitoring the trends.

Senator COLLINS. Thank you.

Senator BALDWIN. Senator Durbin.

Senator DURBIN. Thank you, Madam Chair. It's an honor to be here and want to thank all of you for your work.

BREACHING THE BRAIN BLOOD BARRIER

I would like to address an announcement this week in Chicago from Northwestern University. It was a breakthrough in their research related to the brain and it has a personal element to it. We lost two of the pillars of the United States Senate to glioblastoma, brain cancer, Senator McCain and Senator Kennedy.

I understand the treatment of this terrible disease is limited by and large to surgical intervention because of the blood-brain barrier.

Now I'm going to stop trying to sound like I've ever attended medical school or even got close to one, but in reading the news account of this Northwestern University breakthrough, it appears that they have now opened the blood-brain barrier to allow drugs to pass through to the brain, meaning that unusable chemotherapy drugs can now reach brain tumors. So there's an option beyond surgery or could be soon.

The process they created is known as Sonication and I won't go any further to try to describe it, but it also said in the article that this could have an application on Parkinson's as well as Alzheimer's.

Would someone please comment as to whether this was an NIH-funded research project and what the prospects may be?

Dr. TABAK. Senator, I don't know the answer to that and will have to get back to you for the record.

Senator DURBIN. Well,——

Dr. TABAK. It certainly is a breakthrough and unless one of my colleagues knows specifically. No. We'll get back to you for the record, sir.

MENTAL HEALTH FUNDING

Senator DURBIN. Second point I'd like to raise is a number of people said to me if you ever get NIH in front of you, ask them why they aren't putting more money into mental health research.

I noticed in your opening statement, you talk about precision medicine, but when we look at the scourge of mental illness in this country, particularly as it affects young people now in extraordinary numbers and percentages, could you give me some kind of point of reference as to how much is being invested in mental health or mental illness as opposed to physical illness?

Dr. TABAK. Dr. Josh Gordon could answer that question, sir.

Dr. GORDON. When we're talking strictly dollars here, we're talking that the National Institute of Mental Health's budget is about two billion. There's a couple billion dollars more in NIDA (National Institute on Drug Abuse) and NIAAA (National Institute on Alcohol Abuse and Alcoholism).

But, of course, the crisis isn't about dollars, it's about people. We are in the midst of a national mental health crisis and we have to respond.

You noted in particular two priorities that we are highlighting in our research response and are highlighted by the President's agenda: precision psychiatry and youth mental health.

On the precision psychiatry space, we know that we need to do a better job in psychiatry in matching patients with treatments and we also know that we're on the cusp of being able to do for mental health, at least for some parts of mental health, like depression and schizophrenia, what the NIA has done for Alzheimer's, that is, develop and prove biomarkers can work and can be used in the clinic to help guide clinical decisionmaking and to innovate treatments and so we are spearheading—in the President's budget, we are proposing two large initiatives in precision psychiatry, one aimed more generally at mental health and one aimed at depression.

On the youth mental health space, again we know from a lot of different studies what to do, but we need to do a better job of figuring out how to implement things like suicide prevention programs and mental health prevention programs and early detection and early prevention treatments for psychosis in youth, in schools, and through digital health and through other settings that we know can reach children. So those are two of our priorities in those areas.

Senator DURBIN. Many any of the cities across America face what Chicago faces with gun violence, particularly from young people. I went to the Cook County Juvenile Facility where teenagers are being held waiting for trial, many of them accused of murder. They spend 1 to 3 years in this building. They've created a high school in the building for these teenagers. It looks like a regular high school inside, gymnasium, cafeteria, classrooms, and such, and when I asked the counselors what do you find when you sit down and talk to these young people who are on trial for murder and accused of gun violence, they said, well, we find the full menu of mental illness, but the one recurring theme is trauma. They've

been exposed to trauma in their lives and it's really changed the way they look at the world.

Senator Capito and I have a bill on this issue looking at trauma, ACEs (Adverse Childhood Experiences). It just seems to me that when we talk about youth mental illness, this is the most obvious frontline challenge that we face.

What should we be doing now that we're not doing when it comes to trauma exposure?

Dr. GORDON. You're a hundred percent correct that trauma is at the root of much mental illness not only in childhood but in adulthood, as well.

We know we need to do a better job of building resilience to trauma. One of the earliest findings in trauma research was that successful navigation of trauma in childhood can lead to resilience to a range of mental health consequences later in life.

So that's really been the focus of much research at NIMH (National Institute of Mental Health) and really needs to be the focus of implementation moving forward.

Senator DURBIN. I would just say in closing that I've been proud of this subcommittee and what it's achieved in terms of funding for NIH research. The 2 percent figure sent to us by the Administration is a true disappointment. I mean to tell the President as much.

The idea that the Republicans have suggested in the House of a 20–25 percent cut in NIH funding is scandalous.

Thank you, Madam Chair.

Senator BALDWIN. Thank you.

Senator Moran.

Senator MORAN. Chairman, thank you. I wish you and the Ranking Member well and will pledge to be a good member of this subcommittee to see that we achieve good results for NIH and other things.

Impact of Increased Funding

One of the examples of not in every instance if you spend money do you necessarily get a better result, but there is plenty of evidence that at NIH that does occur.

Dr. Hodes, I would highlight particularly the increasing total amount of money.

Dr. Tabak, I highlight that to you and what has happened, but in the area of Alzheimer's, I think we've seen significant difference and perhaps you could tie it to the additional resources that this subcommittee, this Congress has provided to NIH. I would be happy if you'd like to confirm that more resources do make a difference, Dr. Hodes.

Dr. HODES. I'd be happy to confirm that they have made a difference. The enormous progress we've seen could not have happened at this pace without the increased support and investment in research and similarly we'll do our best to continue the momentum of this with whatever resources are available.

Senator MORAN. Could you put that in personal terms what it might mean for a family or an individual who has been diagnosed with Alzheimer's?

Dr. HODES. Well, I think with the reduction and limitation in resources, we do our best, of course, to be good stewards of what resources we have, but inevitably it would slow the progression from

most basic discovery to the identification of new diagnostic, therapeutic, and preventive measures. We haven't spoken as much about prevention as we have treatment but that's another one of the very high priorities in which we've made great progress, the continuation of which is going to be dependent upon resources.

Senator MORAN. Thank you for the reminder about prevention.

DOWN'S SYNDROME

I chair the Down Syndrome Caucus in the Senate and one of the things that I appreciate is the opportunity. We have one of the institutes that have a role to play in that research. The relationship between Down Syndrome and Alzheimer's is still being developed and understood and hopefully providing information and a path forward.

Anything that I ought to know maybe, Dr. Tabak, about what's going on in the realm of Down Syndrome and how our caucus and my colleagues and I can be helpful in not only the research that's going on but in assistance to individuals and families?

Dr. TABAK. Well, with the continued leadership and support of the Congress, we have expanded our work with individuals with Down Syndrome. For example, the INCLUDE Initiative, which stands for Investigation of Co-Occurring Conditions.

As you know, people with Down Syndrome are more susceptible to certain types of disease and are less susceptible to others and so there's something to be learned for the general population as well as those with Down Syndrome.

We are in particular trying to enroll more people with Down Syndrome in typical clinical trials so that we have a better understanding of what interventions that we use for the general population would have on individuals with Down Syndrome.

We've already alluded to the intersection between Down Syndrome and Alzheimer's disease and, of course, Dr. Hodes is best prepared to speak to that specific point if you are interested.

Senator MORAN. Dr. Tabak, let me suggest to you that if NIH would provide me with information about how to encourage additional individuals with Down Syndrome to participate, we'd be glad to take that on as a project in educating our constituents. It's beneficial to them and beneficial to NIH.

Dr. TABAK. Thank you. We really appreciate that.

Senator MORAN. And we may suggest that we have a Down Syndrome Caucus meeting in which we pursue that and other issues that are going on.

Dr. TABAK. Thank you.

CANCER FUNDING

Senator MORAN. Dr. Lowy, I raised this issue a year ago with Dr. Tabak and I want to highlight this again.

I'm concerned about the competition that will occur for cancer research funding. So we have funding at the Advanced Research Project Agency, ARPAA, and I want to make sure that it doesn't come at the expense of basic clinical research at NCI.

We also have ARPA–H and the Cancer Moonshot Initiative, and I'm looking for a commitment by you and by NIH that there will

be a prioritization that NCI competitive cancer grants will be funded in fiscal year 2024.

Dr. LOWY. Senator Moran, thanks to you and the committee and the long-term strong support, we were able in fiscal year 2023 to increase the pay line for our large awards from the 11th percentile to the 12th percentile. This will mean more than a hundred additional grants than we were able to do in 2022.

It is still not enough. As you know, there has been tremendous opportunities for cancer research and so researchers are flocking to the NCI in large numbers, larger than in other areas, and therefore although we're supporting many more investigators than we did previously, our pay lines or success rates are not where they should be.

Turning to your specific question about these other entities, I can assure you that we interact regularly with them. For example, with ARPA–H, Dr. Bertagnolli and Dr. Wegrzyn, who is the head of ARPA–H, meet regularly, but we also are communicating directly with various possibilities of research that could be conducted by ARPA–H versus research that will be more appropriate for NCI and to work collaboratively and together to make this a reality.

Senator MORAN. Thank you.

Chairman, I wish that Dr. Collins was here to hear Dr. Lowy say that researchers are flocking, flocking to the NCI and I would look at that photograph of this young lady whose grant wasn't adopted and she was ending her career in research. It was something that captured me a long time ago on this topic about individuals that we lose when the money's not there.

Thank you.

Senator BALDWIN. Senator Shaheen.

Senator SHAHEEN. Thank you, Madam Chair and Senator Capito, for holding this hearing, and thank you to all of you for your work every day and for being here.

OPIOID EPIDEMIC

Dr. Volkow, you've been to New Hampshire. You know what a challenge we've had in my State of dealing with the opioid epidemic. 2022 was the worst year for overdose deaths since 2017 in our State, and I understand that in your testimony you discussed the important work of the Heal Initiative.

Can you talk about what's being done to address vaccinating individuals against substance use disorders and what other promising medications you're seeing?

Dr. VOLKOW. Yes, thank you very much, and, indeed, the funds from the Heal Initiative have enabled us one thing. For example, to expand very much the medication development pipeline and that includes development and research on vaccines and monoclonal antibodies.

So there is ongoing research on different strategies to develop vaccines that are targeting fentanyl, oxycodone, heroin, or multiple drugs at the same time. In parallel, we are investing also significant amount of resources to get monoclonal antibodies because those will be able to deliver higher titers.

These interventions are targeted to monoclonals to help prevent and reverse overdoses from fentanyl as well as with other drugs.

In terms of investments, we have a whole pipeline that goes from repurposing of medications that may be useful to result in better outcomes for the treatment of opioid disease disorders as well as completely novel targets that will be able to help people that are addicted not just to opioids but to multiple substances. That is a goal at the basis of the molecular mechanisms linked with addiction.

Also, an area that I think extraordinarily exciting is the utilization of narrow modelization by which we can actually strengthen or weaken certain sequence or hobs in the brain that are found to be associated with addictive behaviors and there many of the developments that have enabled us to go increasingly more precisely are part of the Brain Initiative which is another brain fundamental.

METHAMPHETAMINES

Senator SHAHEEN. How about methamphetamines?

Dr. VOLKOW. Methamphetamines, we don't have any medications that have been approved by the FDA. So it is a major priority for us. It can be very exciting.

Currently, we are doing clinical trials Phase 1 and Phase 4 monoclonal antibodies against methamphetamines because we don't have anything to reverse an overdose, but we're also working on vaccines for methamphetamines.

We are also doing research in terms of clinical trials taking advantage of medications that when combined have already shown to be beneficial in reducing craving and withdrawal. So this is an area that requires again investment of research and partnerships with industry so that we can bring these developments and translate them into the clinic.

Senator SHAHEEN. And are we talking about 5 years, 10 years, beyond that in terms of having something that we think is going to actually be marketable?

Dr. VOLKOW. I would actually like to say that there are so many lower hanging fruit, like the repurposing of medications. What I would hope that we could have them in the clinic if the FDA approves the indications, say, within 5 years.

For the issue of monoclonal antibodies or vaccines, this is a completely new adventure and there is no antecedent of approval by the FDA of vaccines or monoclonals which is likely again to result in a longer trajectory to get them from the research. Now they are in humans, some of these toys, into the clinic, but I predict this is going to be longer-lasting, but there's also an area where we are investing and that is the use of devices and that enables us to translate problems much faster because the level of safety that the FDA requires is much lower.

So we are investing on multiple roads to get more rapid and then also in the long term things that can be transformative.

Senator SHAHEEN. Well, thank you, very much appreciate your work.

DIABETES

Dr. Tabak, I'd like to switch to another illness. Senator Collins and I have been—we chair the Diabetes Caucus in the Senate and we've been looking at how we can continue to support the research

to address diabetes, and I understand that right now we have beta cell- and stem cell-derived islet replacement therapies that are actually showing promise for cures.

My daughter told me she had been to a conference where she met a man who had benefited from that therapy. He had been diabetes-free for 3 years.

Can you talk about what NIH is doing to support that and any challenges? I understand also that FDA has been an obstacle in getting approvals. Can you speak to that and what we need to see from FDA in order to see this research actually bear fruit?

Dr. TABAK. We don't view them as being an obstacle, but it's certainly——

Senator SHAHEEN. That's my term. You don't——

Dr. TABAK. But certainly, we need to partner with them.

Senator SHAHEEN. Thank you.

Dr. TABAK. The challenges are to protect the newly-transplanted islet cells, regardless of what their origins were, from attack from the human immune system, and so we're using different approaches.

For example, we're encapsulating them as a barrier. We're also trying to genetically engineer the islet cells so that they're not recognized as being foreign. These are the types of approaches that will take things to the next level, but as you point out, the findings are very, very promising.

Senator SHAHEEN. So that we could actually see a cure in the foreseeable future for diabetes?

Dr. TABAK. The results are very promising.

Senator SHAHEEN. That's okay. You don't have to repeat that. I can use that. Thank you.

Thank you, Madam Chair.

Senator BALDWIN. Thank you.

Senator Schatz.

Senator SCHATZ. Scientists and their hedging. Thank you very much, all of you, for being here.

Social Media Use

Dr. Gordon, I don't have to tell you that we're facing a youth mental health crisis. The Surgeon General has called out a link between this crisis and social media use and said that 13-year-olds are too young to join social media.

Last week I introduced a bipartisan bill with Senators Cotton and Britt and Murphy to empower parents and protect kids on social media.

NIH has recognized these risks, too, and you are requesting an additional $20 million to continue to study the impact of social media on children.

Dr. Gordon, I know that correlation and causation are not the same thing, but does a spike in mental health challenges in kids correspond with increased social media use?

Dr. GORDON. First, there has been a spike. I actually wouldn't call it a spike. I would call it a mountain with a slope that really started 5 years ago or more increased rates of suicide deaths in children, increases rates of depression and anxiety.

So it's there, no question, and certainly the COVID pandemic has played a role, and there is evidence to suggest that social media

can be a harm for children's mental health. There's been a number of studies funded by NIH, including NIDA, NIMH, and the Eunice Kennedy Shriver National Institute of Child Health and Human Development, which have shown some of these negative impacts. Adolescents, for example, who discussed self-injurious behaviors through social media were more likely to have a suicide attempt, adolescents who place higher levels of importance on social media use and self-image report higher levels of depression symptoms. The list of findings goes on and on.

It is important to recognize, though, that social media can also be leveraged for positive impacts on mental health. For example, customized moderated social media platforms have been used to effectively deliver a wide variety of social supports and mental health treatments.

Senator SCHATZ. Because my time is limited, first of all, I agree with everything you said and thank you for that.

I'm going to reduce one question for the record, which is how you're going to use the $20 million in the President's budget.

But I'd just point out that, yes, there are plenty of beneficial uses of social media, especially for kids who are feeling alienated, but there are, in my view, no beneficial uses of the predictive algorithm that boosts content into people's brains, especially children's forming brains, and let's just take one moment to understand the business model.

The business model is engagement equals revenue and the algorithm has discovered that the way to get engagement is to upset kids.

So publicly-traded companies have a fiduciary obligation to run an algorithm that is systematically upsetting generations of children and so we shouldn't wonder why this is happening. This is happening. It is true that kids can find affinity groups and learn things and, you know, my kids certainly learn to do arts and crafts and fix bikes and there's all kinds of cool stuff on social media but none of that is coming from the predictive algorithm. All of that is coming from the search function. So I just wanted to make that kind of technical point.

Dr. Tabak, one of your priorities is to reduce health disparities and to build a diverse workforce. I was disappointed to see that the budget request makes no mention of the Native Hawaiian community, even as Native Hawaiians face 14 fewer years of healthy life than other groups.

What can NIH do to increase the representation of Native Hawaiians as investigators in community-based research?

Dr. TABAK. Well, one of the approaches, of course, is to launch studies that seek to understand the nature of these disparities in the health communities.

We recently announced a funding opportunity announcement for Native Hawaiians, Pacific Islanders, that collaboration, to support a population-based study to look at the key health gaps and we're committing about $44 million over the next several years.

Getting studies of this type into the communities often will attract people from those communities to participate and that's sort of an on-ramp, if you will, into health-based careers. So that's one approach.

Senator SCHATZ. Thank you. Thank you.

PSYCHEDELIC THERAPY

Dr. Volkow, 60 years ago the United States was producing research on psychedelics as therapy for addiction, chronic pain, and mental illness. This, as you know, research was cut off as a matter of public policy as part of the War on Drugs, and I know that there has been a pivot to sort of relook at these not to make an assumption that any of these things are medicines.

There's a process for that determination, but I think all of your agencies are now starting to relook at the potential therapeutic benefits of some of these pharmaceutical substances that have now been made contraband and used almost exclusively, you know, as very illegal recreational drugs.

Can you provide us an update on where we are on psychedelics research?

Dr. VOLKOW. Yes, thanks very much for this question on psychedelic research effectivity halted for many years, and as the evidence is starting to emerge that shows significant potential in terms of therapeutics for certain conditions, like severe depression or post-traumatic stress disorder and also preliminary research showing benefits for the treatment of addiction, we're actually engaging the scientific community to try to understand how basically psychedelic drugs can be potentially utilized for the treatment, how they affect the brain, and also how to deploy them in ways that are going to be safe and very effective.

So this is an area of great interest. Both NIMH and NIDA are partnering and trying to expand and accelerate.

Senator SCHATZ. Thank you.

Senator BALDWIN. Senator Boozman.

Senator BOOZMAN. Thank you, Madam Chair and Senator Capito, for this really important hearing, and thank all of you all for being here and just the great work that you do and the remarkable careers that you've had through the years.

NCI DESIGNATED CANCER CENTER

Dr. Lowy, the University of Arkansas for Medical Sciences, UMS, in Little Rock has been doing incredible work expanding its Cancer Institute and working towards applying for NCI designation.

As you know, there are 71 NCI-designated cancer centers in 36 States across the country with the closest to Arkansas being in Memphis, pediatrics only, Dallas, and Oklahoma City.

NCI-designated centers receive the large majority of the available NCI funding for research in clinical trials, giving them a unique advantage over non-designated centers. It's critical for all areas of the country to have access to quality cancer research and clinical trials.

What are the NCI's plans for supporting NCI-designated cancer centers in areas in the country where there are none, such as Arkansas?

Dr. LOWY. Senator Boozman, thank you very much for this question.

As you point out, there are 14 States that do not yet have NCI-designated cancer centers. To some degree, this is compensated for

by some of the NCI-designated cancer centers having outreach beyond their States. For example, the University of Utah and Wyoming just as an example, but Arkansas is one area where it would be wonderful if the University of Arkansas Cancer Center were able to meet the requirements that NCI has for NCI designation and our Office of Cancer Centers has interacted with the Cancer Center as recently as a couple of months ago to—we would really welcome the possibility of the Arkansas Cancer Center coming in for this important area.

While waiting for that, it's important to recognize that NCI supports other parts of the cancer research enterprise, such as the Community Oncology Research Program, which has more than 2,000 areas or places where people can enter clinical trials, including in Arkansas.

Thank you.

Senator BOOZMAN. We appreciate that and we do appreciate your help and you all have been really good in helping in getting us where we need to go.

CLINICAL TRIALS ENROLLMENT

One of the problems that we've got is with the finding enrollment for clinical trials. Arkansas, 41 percent of the population is rural and so that makes it just that much more difficult.

The budget request includes a $500 million increase for the Cancer Moonshot with one of the goals of the funding being to boost recruitment in clinical trials that NCI sponsors and/or supports.

What can we do to do a better job of accessing cancer trials in Rural America? How can we help you?

Dr. LOWY. Senator Boozman, this is a very important issue because there are so many parts of the United States, not just Arkansas, where rural populations are even at higher risk of developing cancer and unfortunately over the last 20 years, although mortality rates for cancer has gone down for people in rural areas as well as in urban, the rate of decrease now is slower for people in rural areas compared with urban.

NCI has had a number of meetings. In the very near future we are going to be providing research awards for areas of chronic poverty which are one of the potentially rural areas which have particular high incidence of mortality from cancer.

One of the good news, one of the few areas of good news for the pandemic has been the expansion of telemedicine and also the streamlining of clinical trials to make it easier for people in rural areas to enter and participate in those trials.

Thank you, sir.

Senator BOOZMAN. Well, thank you, and we do appreciate those efforts, and anything we can do to help you, we would be pleased to do. So we look forward to visiting with you.

Thank you all again very much. Thank you, Madam Chair.

Senator BALDWIN. Thank you.

Senator Kennedy.

Senator KENNEDY. Thank you, Madam Chair.

Dr. Tabak, nice seeing you.

Dr. TABAK. That's fine. Thank you, sir. Tabak.

Senator KENNEDY. By the way, I think the NIH is an extraordinary institution. You and your colleagues, your work is breathtaking.

DIVERSITY AND INCLUSION

But I want to ask you about one of your programs, Doctor. In 2020, you created a program called The Faculty Institutional Recruitment for Sustainable Transformation, and basically under the program, you gave 12 institutions $241 million, a lot of jack in anybody's book, and you directed the grant applicants to use the money to demonstrate a strong commitment to promoting diversity and inclusive excellence when you hire people. Okay?

Two of the institutions to which you gave money, one was University of South Carolina to hire faculty members and public health and nursing and the other one was University of New Mexico to hire faculty members in neuro-science and data science, two great institutions.

South Carolina and New Mexico issued rules to administer the money that you gave them and they both said that we are going to punish candidates who apply for jobs with us with this money that you gave them who espouse "race neutrality."

In other words, both of those institutions said we're going to give a very low score for anyone who states, "An intention to ignore the varying backgrounds of their students and treat everyone the same."

So they took your money and they said we're hiring faculty members and any applicant who says we don't believe in racial prejudice. We think everybody ought to be treated the same gets an F.

Did you know that?

Dr. TABAK. I'm not familiar with the specifics like you are mentioning, Senator.

Senator KENNEDY. Would you look into it?

Dr. TABAK. I certainly will. This program is an important effort by NIH to create a more highly diverse workforce.

Senator KENNEDY. I agree with that. It's a good idea. Do you know anybody against diversity?

Dr. TABAK. Well, unfortunately, sir,——

Senator KENNEDY. I don't.

Dr. TABAK [continuing]. I have run across a few over the years, but——

Senator KENNEDY. I'm sure there's some out there, but I think most fair-minded people agree with diversity.

Dr. TABAK [continuing]. Our effort is to create an environment where people from all backgrounds in every different dimension will be safe and welcomed to conduct high-quality biomedical research.

Senator KENNEDY. And I agree with that, but here's what I'm getting at. Do you think it's fair for the University of New Mexico and the University of South Carolina, two extraordinary schools, to say to an applicant who's borrowed hundreds of thousands of dollars to get her Ph.D. and who comes forward and they say how do you feel about race and they say I believe in racial equality, I believe everybody should be treated the same. They get an F. They're

dismissed summarily. Do you think that's fair to do that with your money, with taxpayer money?

Dr. TABAK. Again, sir, I can't speak to the specifics of these institutions. I will look into it.

Senator KENNEDY. Well, would you—if it's true, do you support that?

Dr. TABAK. Again, I'd have to see what exactly it is——

Senator KENNEDY. But if it's true, do you support it?

Dr. TABAK. What we are trying to do, sir, is create inclusive environments because unfortunately far too often certain individuals do not succeed in obtaining faculty level positions at universities.

Senator KENNEDY. But if I hire somebody—suppose—can I as an American legally, constitutionally, morally say I'm only going to hire Asian Americans? Anybody else of any different ethnic background need not apply. Is that moral? Is that constitutional?

Dr. TABAK. Well, God knows I'm not a lawyer, but, sir,——

Senator KENNEDY. Well, but you're a human being.

Dr. TABAK. [continuing.] To get to a faculty level position is a multistep process and very often highly-qualified candidates are never even considered because of where they train, where they're from, or what they look like.

Senator KENNEDY. Yes. But do you think——

Dr. TABAK. And none of that is fair.

Senator KENNEDY. Do you think—I don't think you're answering my question. Do you think it's right for an institution using money that you gave them to say if you believe in racial equality and you say you want to treat everybody the same, say a big old hook comes out around their neck and pulls them off the stage and they say I'm not going to be hired? Do you think that's right?

Dr. TABAK. I just don't—I would need to understand the context, sir, and I really don't know what these institutions are saying to candidates and I will certainly find out.

Senator KENNEDY. Well, I'm going to follow up. I want to know.

Dr. TABAK. Fair enough.

Senator KENNEDY. I mean, that's how they spent taxpayer money that you gave them and I'm going to follow up and I wish you would, too. This disturbs me.

Because I don't think that's lawful.

Dr. TABAK. We will certainly get back to you, sir, with what we find.

Senator BALDWIN. Thank you, Senator Kennedy.

Senator Britt.

Senator BRITT. Thank you, Madam Chairman.

DIGITAL PLATFORMS AND MENTAL HEALTH

I wanted to talk today obviously about the crisis in this Nation with regards to mental health.

Mr. Tabak, when you look at what is happening, it's clear that NIH has also identified this crisis as being one that is plaguing communities across this great Nation.

The White House in 2023, the Mental Health Research Priorities, those even showed they speak to digital platforms in terms of their effectiveness to treat mental and behavioral health outcomes.

However, there are plenty of NIH studies that show how social media and screen time likely have a negative effect on mental health, particularly youth mental health.

Now let me tell you something. As a momma of a 13- and a 14-year-old, this is something that is particularly important to me. I look at how young people are having to grow up right now. I know as someone who went through middle school and high school as a young woman that it's tough. I can't even imagine the additional pressures that they feel given having a screen at their fingertips all of the time.

I think the reports are shocking and I don't think the numbers lie. Last year, one in three high school girls said that they seriously considered suicide and actually one in nine or almost nine percent, one in 10 high school students reported actually attempting suicide in the last 12 months.

Folks, I ran for the Senate as a momma on a mission. I said that my children and other people's children and grandchildren should be able to achieve the American dream. If we do not take a hold of what is happening right now with social media and our youth, it is going to be so far gone we cannot get it back.

My question to you is what is the NIH doing to address the damage of social media and what effect it is having on our children and our children's mental health?

Dr. TABAK. So, Senator, on a personal level, I have a grandson who's the same age as your children. So I completely understand.

Senator BRITT. Thank you.

Dr. TABAK. If I may turn this to Dr. Josh Gordon, who's the Director of NIMH, to answer you specifically.

Senator BRITT. Absolutely. Thank you.

Dr. GORDON. To add to that personal, I have children who are 20 and 25 who grew up with social media. I saw them wrestle with it and the challenges they are in, and I can absolutely from that personal perspective understand the situation.

Senator BRITT. And I think if you look at the correlation, so from 2011 to 2019 the CDC says that depression amongst our children, our high school kids more than doubled. It is no coincidence that that actually coincides with the exact time where we had a rise in social media.

Dr. GORDON. For that matter, not just depression but suicide deaths have been dramatically increasing in children and children who are even younger than used to typically die. So we're seeing dramatic increases in the rates in pre-teens which is incredibly disturbing.

So what are we doing about social media and mental health? We and the National Institute of Child Health and Human Development both have programs in understanding the impacts of social media and, importantly, looking specifically at what aspects of social media use correspond with negative outcomes from the mental health perspective and trying to figure out how we might intervene and especially trying to support families and parents in working with children to figure out how to avoid the negative consequences of social media and how to regulate social media use at the family level.

So we have a range of different programs in this research that we've been supporting with specific dollars appropriated by this subcommittee in the past and we will continue to support that work.

Senator BRITT. I hope that you will all continue to work on this, to pay close attention. Our children are counting on us.

I want to follow up on what Senator Schatz said earlier. We have introduced a piece of legislation along with Senator Cotton and Senator Murphy to help with this. It's bipartisan. It prohibits children from under the age of 13 from using social media, which is consistent with what social media companies say that they already do. It requires a parent or guardian's permission for children ages 13 to 17 to create an account, so very simple, and the last thing is it requires social media companies to verify that quickly but it also does not allow them to utilize algorithms against our children.

So between 13 and 17, when they're on social media, they would not be able to be targeted by algorithms pushing them into what we know to be so many deep dark holes and so I am hopeful that this body will act. I am hopeful that we will come together and actually do something to put parents back in the driver's seat and to protect our children. I will tell you they are counting on us.

Thank you. I yield my time.

Senator BALDWIN. Thank you.

We will begin a second round, hopefully quick and painless.

XYLAZINE

So I wanted to start where I left off with you, Dr. Volkow. In March, the Drug Enforcement Agency announced it had detected a drug called Xylazine in nearly a quarter of all confiscated fentanyl in 48 States.

The combination of these drugs have proven to be very deadly, but the tools that we have to combat fentanyl overdoses, like the test strips we were talking about and Naloxone, may not help us in this situation.

So I wonder if you could talk about the impact that Xylazine has on the medicines that we use for overdose reversal and how NIH research is adapting to new and deadly ingredients that are being added to opioids.

It seems like, you know, every other day we hear about a new challenge with regard to other additives or things that are harmful in different ways.

Can you talk a little bit about Xylazine and how you're adapting your research?

Dr. VOLKOW. It's very important problem that has grown actually very, very fast. I would say in the past 3 or 4 years. So the first thing that we needed to understand is why more and more of the drugs, particularly fentanyl and heroin, were sold mixed with Xylazine, and what appears to be happening is that Xylazine basically expands the duration of the effects of fentanyl or heroin.

So it allows the dealers to actually basically create the product that has the characteristic that may be more reinforcing and therefore greater value.

It's become very challenging because whereas Naloxone serves to reverse an overdose from fentanyl, the response when you combine

these two drugs are not the same. So current research is ongoing to try to determine both in animals and animal models and in humans what should be the optimal target to try to prevent the deaths associated with the combination of fentanyl and Xylazine.

They act by very different mechanisms. Fentanyl inhibits respiration and breathing, so you don't have oxygen in your blood, but Xylazine also by a different mechanism that doesn't engage the same receptors is decreasing oxygenation.

So you have when you combine these two mechanisms that are exacerbating the outcomes which is why in some instances when you use Naloxone, Narcan, to reverse the overdoses, you don't get adequate responses and research is ongoing to develop therapeutics that can actually help in those overdoses.

Senator BALDWIN. Thank you.

NEXT GENERATION RESEARCHERS

Dr. Tabak, I was proud to author the Next Generation Researchers Act with Senator Collins to improve NIH opportunities for new and early stage researchers.

Since this bill was signed into law as part of the 21st Century CURES Act, NIH has increased funding for early stage investigators by 63 percent, and I'm proud of this progress but there's still a long way to go.

The average age of the first-time RO1-funded investigators remains 42 years old. Today, more than twice as many RO1 grants are awarded to investigators over 65 than to those under 36 years old. In the 1990s, those figures were reversed.

So we all know that diversity in the biomedical workforce leads to research innovation, higher quality work, and more participation in clinical trials by people from underrepresented groups. Yet inequities persist, and a study published in February shows that whenever there's an uptick in NIH funding, it creates more inequity.

Women and people of color face increased barriers and an uneven playing field to obtain funding.

So, Dr. Tabak, tell me how NIH is working to support more early stage investigators, including women and those from diverse backgrounds.

Dr. TABAK. Well, thank you for your leadership in this area and certainly we have made some progress, but as you point out, we have a ways to go.

Our target has been a minimum of 1,100 new early stage investigators each year. Last year we were able to fund over 1,600 which is the good news. But you're quite right. Those who already have support have advantage. It's just that simple and so we have set up some additional programs which we hope will level the playing field.

For example, there is the Katz Award where no preliminary data is required for the application. That may seem counterintuitive, but, in fact, what it does is it liberates the applicant from the work of their former mentor, their former Ph.D. advisor or postdoc advisor so that they can come with their best ideas and don't need to have enormous resources to create the preliminary data that's needed to really just support things for a great new idea.

We have the NIH Pathway to Independence Award. It's the Skip the Postdoc Award. You go right from graduate school into a faculty level position. It's not for everybody but there are talented people out there for whom this is just an ideal circumstance.

We are also looking at the NIH Director's New Innovative Award Program where, of course, we are trying to incentivize young people with great ideas to come into our system and this is gradually bringing in people from outside of the traditional biomedical research disciplines.

The good news about this pool of early career investigators is they are enriched for both women and people of color. There are more young people of color. There are more women in this early stage cohort than in the general cohort, and so if we keep pushing to fund more and more of these early career investigators, we are going to see a shift in that right direction that we all hope to achieve.

Senator BALDWIN. Thank you.

Senator Capito.

Senator CAPITO. Thank you.

ARPA–H

I wanted to ask about ARPA–H. In the fiscal year 2023 Omnibus there was $1.5 billion for ARPA–H and moved them under the NIH umbrella and then this new budget is asking for an additional billion dollars.

I'm a supporter of the goals of ARPA–H to be high-risk/high-reward, partnering with the private sector, but I don't really understand why ARPA–H is going up a billion and yet most of the other biomedical research being done at NIH is pretty flat funding.

Dr. Tabak, can you describe how NIH and ARPA–H can complement one another and your perception of this and where is ARPA–H fitting into the overall organization?

Dr. TABAK. So ARPA–H is an independent entity within the NIH superstructure. They have taken advantage of a number of our administrative systems so that they don't have to reduplicate, you know, sort of basic business systems and things of this nature.

The inaugural director, Dr. Wegrzyn, has been putting together her team. They've been onboarding over a hundred folks now. The key to their business model, if you will, is the recruitment of program managers who come with them unique ideas for bold and creative projects that they would like to see supported.

They have been sorting through some 250 candidates thus far. They have hired a few to begin with. They've just recently released a broad agency announcement for research to improve health outcomes across patient populations, communities, diseases, and health conditions.

The ARPA–H leadership has been engaging with the rest of the NIH leadership on a regular basis. We certainly want to avoid duplication——

Senator CAPITO. Right.

Dr. TABAK [continuing]. Or we want to incentivize shared engagement with one entity doing one aspect of a problem and the other entity doing another and so, you know, this is a bold new idea about how to fund biomedical research which we think will

complement what we do at NIH and we're looking forward to continuing to work with Dr. Wegrzyn and her colleagues.

Senator CAPITO. Well, I would hope, you know, the complementary aspect of it certainly and we see all the expertise on the panel and all the folks behind the expertise that we see here seated today certainly makes sense.

So we'll watch that as it fully develops and thank you for that explanation.

Last week the Republicans on Energy and Commerce launched an investigation into the NIH use of public relations communications services worth about a billion dollars since 2018 contracts to 10 public relations companies.

As I was reading this, I was thinking wow, that's a lot of money, a lot of money, and, you know, for 10 companies that's a lot of money, but then when I started thinking about the years and the fact that it had initial funding of $500 million and then was doubled to a billion under COVID, the COVID pandemic, and you and I talked about this on the phone, you know. There's a lot of people who have moved through COVID confused as to the best way to have achieved this, the best way to cope with it, you know. You're seeing all second guesses. Should we have closed the schools, should we not have closed the schools? Is it contagious? Can I get it from touching this? All the different things that we went through during that period.

NIH PUBLIC RELATIONS SPENDING

So I guess I have a two-fold question. First of all, I don't think we got our bang for the buck for NIH spending this much money in public relations because I think the confusion is partially owned by NIH and other health—you know, we could look at who else owns part of this.

We've never really been through this. You know, we don't really know. It was a hundred years ago, the influenza of 1918, you know, might have had some similarities.

But we can't sit here and say this is never going to happen again or could never happen again. So I guess my question is, as you look—first of all, will you keep us here at the Senate, at the subcommittee in the loop as to what that investigation uncovers with the vast amounts of dollars there? So I would like a yes. Thank you.

The other thing I would say is what is NIH doing to do a lookback in this area—I'm not talking about vaccine development or anything like that—of communicating to the American people how you could improve that part of the reaction to COVID and it's going to play into long COVID and everything else as we move forward.

So are you all doing a full analysis of what your reactions were? Are you going to make that public? When can we expect to see that?

Dr. TABAK. So as you well know, our mission is to translate and communicate research findings in a way that's understandable to all of our stakeholders, patients, families, healthcare providers, and again it's all done with the goal of improving health and so we are taking a look back to see how——

Senator CAPITO. In a formal way are you making——

Dr. TABAK. Well, I think it will become more formal, but initially we're sort of doing a landscape because—and again not to make excuses because we have to own, how it came out, okay, and I accept that.

But, of course, we were dealing with something that was ever-evolving and as you know, as you learn more and more, your message can be more and more precise and so we are looking back to try and figure out how things might have been done better with an eye towards what happens the next time because you're right, there will be a next time about something.

Senator CAPITO. There will be, and like if we look at like Dr. Volkow's area of expertise, it was thought initially, oh, well, if people can do telemedicine in this area with their—and then you saw the numbers go up. So maybe that wasn't true, you know. So it had a whole different dynamic.

If you look at mental health, huge issues there, and so I think we've got to do a really deep down analysis, but I think where we really need to—and you all are doctors and thank goodness you are, but sometimes we need to communicate in plain language what is actually going on and what you need to do and you can play a big role here with all the research.

Thank you all very much.

Dr. TABAK. Be happy to do that, yes.

Senator CAPITO. Thank you.

Dr. TABAK. Thank you.

Senator BALDWIN. So this will end our hearing today. I want to thank all of our committee members who attended for their thoughtful questions and thank you to all of you, Dr. Tabak, Dr. Gordon, Dr. Lowy, Dr. Hodes, and Dr. Volkow all for being here and sharing your expertise with us today.

ADDITIONAL COMMITTEE QUESTIONS

For any Senators who wish to ask additional questions, questions for the record will be due on May 12 by 5 p.m., and the hearing record will also remain open until then for members who wish to submit additional materials for the record.

[The following questions were not asked at the hearing, but were submitted to the Department for response subsequent to the hearing:]

QUESTIONS SUBMITTED TO DR. LAWRENCE TABAK

QUESTIONS SUBMITTED BY SENATOR TAMMY BALDWIN

Dr. Lawrence Tabak, Acting Director, National Institutes of Health (NIH)

Question. Swine are an optimal model species for investigation of a large number of human diseases and have made valuable contributions to almost every field of human medicine. Swine share anatomic and physiologic characteristics with humans that make them ideal models for research. In addition the anatomy and physiology make pig organs likely candidates for xenotransplantation. The NIH-funded National Swine Resource and Research Center was established in 2003 to develop the infrastructure to ensure that biomedical investigators across a variety of disciplines have access to critically needed swine models of human health and disease.

Can you provide an explanation of the benefits of designating a second NIH-funded national swine research center? Specifically, please share what the benefits would be of partnering with an academic institution that has existing medical imaging platforms dedicated for swine research use.

Answer. The National Institutes of Health (NIH) has long acknowledged the value of and invested in swine as a model organism for biomedical research. The NIH Office of Research Infrastructure Programs (ORIP) within the Office of the NIH Director (OD), in partnership with the National Institute of Allergy and Infectious Diseases (NIAID) and the National Heart, Lung, and Blood Institute (NHLBI), has supported the National Swine Resource and Research Center (NSRRC) at the University of Missouri since its creation in 2003. The NSRRC serves researchers across the nation by supporting swine-based research across multiple disciplines, providing valuable services to the research community and creating new genetically-engineered swine models in collaboration with investigators. The NSRRC has facilities and laboratories with advanced biosecurity to ensure animals remain pathogen-free from 14 specific pathogens. In addition, the NSRRC serves as a central repository by importing, maintaining, preserving, and distributing swine models and wildtype animals, cells, tissues, and organs to investigators throughout the country while ensuring the highest possible level of animal care and model quality. The NSRRC also serves as a source of information and training related to the use of these animals in biomedical research as models of human health and disease for the broader research community. The NSRRC performs its own cutting-edge research to advance technology in this area. Its inventory of live animals includes more than 20 genetic backgrounds.

The establishment of a second center would require substantial upfront financial and resource investment in equipment, infrastructure, animal care, maintenance, and ongoing research support. The existing NSRRC serves as a valuable resource for researchers, and it is at the forefront of providing swine models to the biomedical research community. The NSRRC's activities have been significantly expanded since its inception, including an $8 million NIH C06 Construction grant in FY 2022 to expand animal housing. This expansion has allowed more efficient use of the existing space and will permit the NSRRC to widen its exploration of applications of new swine models in various research fields and extend its training activity on the use of swine models. The enhanced capacity will also allow the interdisciplinary team of scientists that operate the NSRRC to enhance establishment and characterization, including phenotyping, of existing and newly developed swine models. The NSRRC partnering with an academic institution that possesses the necessary imaging equipment and expertise would be more cost-effective compared to establishing and maintaining imaging capabilities independently. Partnering with an academic institution would also foster interdisciplinary collaboration by bringing together experts from different fields such as imaging, veterinary and comparative medicine, and swine research. We believe that a partnership between an academic institution and the current NSRRC would be of greater benefit with less upfront costs than establishment of a second center.

Question. The Subcommittee's Joint Explanatory Statement (JES) for fiscal year 2023 included explicit recommendations on the implementation of funding for the Clinical and Translational Science Awards (CTSA) program. The JES expressed concerns about disaggregation of the CTSA Hubs and stated the agreement's support for maintaining the size, scope, and historic mission of the CTSA program. The agreement also maintained that no funded CTSA Hub should receive less than 95% of the funding it received in previous awards.

How will the National Center for Advancing Translational Sciences (NCATS) implement the explicit instructions in the FY 2023 JES?

Answer. NCATS leadership reached out in writing to House and Senate Appropriations Staff within 30 days of budget enactment, per the report language. Then on Monday, February 6, 2023, NCATS leadership, along with the NIH Budget Officer, met with House and Senate Appropriations Staff to provide an update on the Clinical and Translational Science Awards (CTSA) program as requested. Based on the discussion and outcome of the briefing, NCATS will continue with its existing funding opportunity announcements and will keep Appropriations Staff apprised of funding plans and any updates to the program, as previously requested. NCATS also encouraged the Appropriations Staff to reach out at any time to discuss the program.

Question. Geroscience offers exciting potential to address a wide range of aging-related diseases and conditions—including Alzheimer's, cancer, cardiovascular diseases, osteoporosis, and many others. Several NIH Institutes and Centers (ICs), as well as the Cellular Senescence Network within the Common Fund, recognize the promise of this approach by supporting research in this field. The comprehensive nature of the research, the number of ICs involved, and the possible applications to many diseases and conditions make it especially critical to track how much funding NIH is allocating for geroscience and for which purposes. This is why Congress asked NIH to submit a report on geroscience to the House and Senate Appropria-

tions Committees within 180 days of enactment of the fiscal year 2023 appropriations bill, which will occur next month. Congress also encouraged NIH to consider launching a trans-NIH initiative that would guide and enhance future research on geroscience.

Please provide an update on the report and plans for such an initiative.

Answer. The required report on geroscience activities across NIH is under review and will be transmitted to Congress in the coming weeks. Geroscience research is a priority across NIH, with more than 20 institutes and centers (ICs) actively involved in this area of research. These ICs participate in an NIH-wide Geroscience Interest Group, which meets monthly to discuss updates from researchers in the field, discuss potential research initiatives, plan future geroscience events, and explore gaps and opportunities in the field.[1] In April 2023, the group hosted the fourth Geroscience Summit, which brought together researchers and clinicians interested in geroscience and aging to explore the state of the science, including identification of research gaps and opportunities.[2]

Question. Urinary incontinence associated with lower urinary tract symptoms affects millions of women. Research to date has shown that the efficacy of treatment for the different types of urinary incontinence associated with lower urinary tract symptoms varies widely depending on individual patient characteristics and symptoms, and that a personalized treatment plan for these conditions has been found to be most effective. There are knowledge gaps around the etiology of these symptoms which are impeding the development of effective treatments and successful utilization of precision medicine for patients with lower urinary tract symptoms.

What needs to be done to advance scientific knowledge of the etiology of lower urinary tract symptoms to enable a personalized precision medicine approach for the treatment of these conditions and how will the NIH and NIDDK accomplish this?

Answer. NIH is dedicated to furthering an understanding of the various causes and manifestations of lower urinary tract symptoms (LUTS) with the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) as the lead institute for research in this area. NIDDK funds the Symptoms of Lower Urinary Tract Dysfunction Research Network (LURN), comprised of an interdisciplinary team of researchers, study coordinators, and medical facilities at six United States clinical sites and a data coordinating center. LURN aims to increase understanding of LUTS to inform strategies to better measure and manage the condition and improve patients' lives. Through development and use of detailed questionnaires, LURN aims to measure patient experiences, assess the wide range of symptoms, and characterize different subtypes of men and women with LUTS as a first step to developing precision medicine approaches. Through the NIH-funded Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) Research Network, NIDDK hopes to provide a better understanding of the underlying causes and distinct symptom profiles of urological chronic pelvic pain syndrome (UCPPS), which is characterized by chronic pain and diverse LUTS in men and women. Understanding that bladder health is an important aspect in the development of LUTS, NIDDK also supports the Prevention of Lower Urinary Tract Symptoms (PLUS) Research Consortium, to develop tools and strategies to measure and promote bladder health in women. This knowledgebase will inform individualized strategies for the prevention of LUTS in women. Additionally, NIDDK supports basic, translational, and clinical research into LUTS through funding of various other programs, centers, and investigator-initiated research projects. For example, the O'Brien Urology Centers are studying the pathophysiology of urologic diseases and conditions, and the Stimulating Urology Interdisciplinary Team Opportunity Research program supports investigator-initiated projects, some of which are studying how neurologic dysfunctions may impact various types of incontinence.

These activities are ongoing, and NIDDK continues to welcome investigator-initiated research in these areas. The knowledge gained from these studies will provide insight that can lead to more precise diagnoses and more effective, personalized treatment of LUTS.

QUESTIONS SUBMITTED BY SENATOR SHELLEY MOORE CAPITO

Dr. Lawrence Tabak, Acting Director, National Institutes of Health (NIH)

Question. Pulmonary fibrosis, or PF, means scarring in the lungs that, over time, can destroy the normal lung and make it hard for oxygen to get into the blood. There are over 250,000 Americans currently living with the illness. PF affects 1 out

[1] www.nia.nih.gov/gsig.
[2] www.nia.nih.gov/2023-fourth-geroscience-summit.

of 200 adults over the age of 70 in the United States. The prevalence of PF is on the rise with more than 50,000 new cases diagnosed annually and around 40,000 people dying each year from PF. There is currently no cure for PF. The average life expectancy for someone diagnosed with idiopathic pulmonary fibrosis, the most common form of PF, is just three to 5 years.

The National Heart, Lung, and Blood Institute (NHLBI) provides funds that are crucial to advancing pulmonary fibrosis research. In November 2022, the NHLBI brought together stakeholders to identify directions for research in PF. This meeting established the need for funding in several areas: improved research models, tools for earlier diagnosis, streamlined clinical trials, and enhanced focus on the genetics of PF, to name just a few.

A report on the outcomes of the Summit is currently being drafted.

I was pleased to learn that the National Heart, Lung, and Blood Institute (NHLBI) cosponsored a "Pulmonary Fibrosis Stakeholder Summit" last November that brought together leading PF researchers and patients to discuss a research blueprint for this devastating disease for the next 5 years. Can you or Dr. Gary Gibbons, Director of the NHLBI, comment on some of the key outcomes of this meeting and what you see as next steps in implementing strategies and approaches that were discussed?

Answer. On November 8 and 9, 2022, NHLBI, in co-sponsorship with the Three Lakes Foundation and Pulmonary Fibrosis Foundation, hosted a workshop entitled "The Pulmonary Fibrosis Stakeholder Summit." This workshop sought to identify scientific gaps and future basic and clinical research directions related to pulmonary fibrosis (PF) by providing a platform for investigators, sponsors, physicians, and patients to share innovative ideas for synergizing research efforts and ultimately improving patient outcomes for PF. Some key research gaps and opportunities that were identified during this workshop include:

—Development of Novel Models and Research Tools to Better Study PF and Uncover New Therapies
  —Development of models that recapitulate the evolution of PF from injury to fibrogenesis to the point where the disease no longer progresses, and to test drug candidates during the established fibrotic phase of disease in these models.
  —Expanding the practice of collecting fresh tissue and live cells at the time of routine clinical procedures and using standardized collection protocols to establish a central repository for research use of biospecimens across the fibrotic lung disease spectrum.
—Identification of Early Disease Risk Factors and Methods to Improve PF Diagnosis
  —Development of integrated molecular-, imaging-, and AI/ML-based diagnostic tools to predict individual risk factors and mechanistic drivers of disease progression from preclinical to advanced disease and convert those to optimal strategies for screening and surveillance of high-risk populations.
  —Increase diverse race and ethnicity representation in studies of genetic risk for PF onset and progression, and use that information to define guidelines for incorporating genetic testing into clinical practice for individuals with or at risk of PF.
—Advance Innovative Approaches to PF Clinical Trial Design
  —Development and validation of additional patient-centered endpoints for use in PF clinical trials to more comprehensively assess the success or failure of novel interventions to modify disease and/or improve patient quality of life.
  — Leverage more innovative statistical analysis approaches and clinical trial designs, including pragmatic, adaptive, umbrella, basket, and platform designs, to optimize participation in and enhance the output of PF clinical trials.

A workshop report is being prepared by the participants for submission to a scientific journal, with the hopes of disseminating this information to the broader community and stimulating new research in these areas to ultimately improve the diagnosis, care, and quality of life for patients living with PF.

Question. NIH recently has faced criticism surrounding research integrity from OIG reports that NIH had lax controls on its grants with EcoHealth and the subawards to eight subrecipients, including the Wuhan Institute of Virology.

The OIG found several deficiencies in the oversight of the awards. Some of these deficiencies include: EcoHealth's inability to obtain scientific documentation from WIV; and EcoHealth's improper use of grant funds, resulting in $89,171 in unallowable costs.

NIH resumed grant funding for EcoHealth despite OIG reported failures by EcoHealth surrounding previous NIH grant funding. Can you explain the decision process in determining resumed grant funding to EcoHealth?

What corrective actions have EcoHealth and NIH taken to date to address deficiencies identified by the OIG?

Answer. NIH takes its stewardship over the Nation's investment in biomedical research very seriously and routinely considers processes and measures for strengthening its oversight of Federal funds. NIH has implemented additional oversight measures regarding grants awarded to EcoHealth Alliance (EHA) to ensure that EHA's documented efforts to strengthen administrative processes meet NIH's requirements. NIH continues to actively monitor EHA's progress and is taking these further actions to ensure NIH meets its collective goal of supporting rigorous science to improve human health.

As background, awards to EHA aimed to advance our understanding of how pathogens can emerge from wildlife and spillover to cause disease in people. This includes research important for understanding how bat coronaviruses evolve naturally in the environment to become transmissible to the human population. This type of research is critical for the U.S. to prepare for how to respond if these pathogens do enter the human population. All awards were reviewed through NIH's two-stage review process and were determined to be scientifically meritorious during external peer review. Prior to funding, all awards were rigorously assessed by NIH to determine if any additional biosafety or biosecurity measures would be necessary.

After a detailed administrative review of EHA's management of these awards, NIH notified EHA of the need to implement a corrective action plan to ensure robust oversight and accountability to NIH. A summary of these communications and actions are as follows:

—On January 6, 2022, NIH provided Congress with a status update regarding an ongoing NIH Office of Extramural Research (OER) administrative review of EHA. At that time, NIH determined that EHA needed to improve specific areas of its administrative policies and practices representing shortcomings identified by the OER administrative review. Therefore, NIH placed immediate specific award conditions (SACs) on EHA's active awards while the grant recipient worked on developing a requested Corrective Action Plan (CAP) to address the identified issues.

—On August 19, 2022, NIH provided Congress with an update on EHA's implementation of the CAP. At that time, NIH determined that EHA had demonstrated it was working toward correction of the administrative and financial problems with a full implementation plan laid out in the CAP.

—NIH also identified one area of non-compliance under the grant R01AI110964 (R01) that could not be remedied with SACs. NIH had requested EHA provide NIH the laboratory notebooks and original electronic files from the research conducted at WIV. Since EHA failed to provide these records and WIV was unable to fulfill its duties for the subaward, NIH notified EHA on August 19, 2022, that it would be terminating the WIV subaward for failure to meet award terms and conditions.

—To maintain a higher level of oversight, NIH imposed additional SACs for all EHA awards for a minimum of 3 years. These SACs included doubling the frequency of the required scientific progress and financial reports EHA is required to submit to NIH. In addition, EHA is required to conduct onsite inspections of all its subawardees every 6 months to confirm that all terms of subaward agreements are being fully and appropriately executed.

NIH acknowledges prior cooperation and substantial improvement in EHA processes and recognizes EHA is still working on implementing corrective actions. However, given the seriousness of these challenges, NIH will provide additional oversight of EHA's management of its grant awards while EHA addresses the material deficiencies related to financial reporting and subrecipient monitoring. Accordingly, in 2023, NIH imposed four additional SACs on NIH awards to EHA. These include requiring EHA to develop or improve written policies to comply with the NIH Grants Policy Statement (GPS) and requiring EHA to receive prior approval of subaward written agreements from NIH to ensure EHA complies with all requirements in the NIH GPS.

In addition, NIH is removing EHA's eligibility for unrestricted advance drawdowns of funds—which means NIH is converting EHA from an advance payment method to a reimbursement method. This will require EHA to submit monthly reimbursement requests with a detailed list of actual expenses incurred and supporting documentation. The reimbursement method will provide NIH with stronger oversight of EHA's accounting and spending practices. Lastly, NIH is requiring EHA to obtain an independent third-party audit to conduct a comprehensive review of

EHA's accounting practices and financial responsibilities under the terms and conditions of the NIH awards.

NIH believes these additional monitoring mechanisms will allow NIH stronger oversight of EHA to ensure that the grant recipient meets the responsibilities required to receive Federal funding.

EcoHealth Alliance is not suspended or debarred at this time. The HHS Assistant Secretary for Financial Resources' office makes discretionary suspension and debarment decisions, not NIH. Any suspensions or proposed debarments are subject to the Office of Management and Budget guidelines to agencies under the Nonprocurement Common Rule in 2 CFR 180 for nonprocurement transactions (as further implemented by HHS at 2 CFR Part 376) or the Federal Acquisition Regulation 48 CFR Subparts 9.406—9.407 for procurement transactions (as further supplemented by HHS at 48 CFR Subpart 309.4).[3]

Question. Prion disease, which is caused by misfolded proteins in the brain is similar in some respects to Alzheimer's and related dementias. Creutzfeldt-Jakob disease (CJD) is a rare, 100% fatal, degenerative brain disease that causes rapidly progressive dementia.

Is NIH doing any specific research on CJD?

Answer. NIH supports dozens of studies on Creutzfeldt-Jakob disease (CJD) and other prion diseases such as transmissible spongiform encephalopathy, which are fatal brain diseases that occur in sporadic, infectious, and inherited forms, and are caused by misfolded cellular prion protein that propagates rapidly throughout the brain leading to widespread neuronal death. NIH-funded scientists are investigating the normal function of cellular prion protein, what triggers them to misfold and aggregate in neurons, how misfolded prion protein spreads throughout the brain, the mechanisms by which misfolded prion protein contributes to cell death, and how inflammation contributes to the disease process. NIH-funded researchers are also conducting preclinical studies in animal models of prion disease to investigate potential treatment strategies that prevent or attenuate prion misfolding, aggregation, and/or propagation; thereby slowing or stopping disease progression.

Question. Are there areas of research in the ADRD space that can help inform treatments or cures for CJD

Answer. Several neurodegenerative disorders, for example Alzheimer's disease, Alzheimer's disease- related dementias (e.g., Frontotemporal dementia, Lewy body dementias), and Parkinson's disease, share a core disease mechanism with CJD. Although the specific proteins vary between diseases, in all cases, proteins misfold and aggregate and spread throughout the brain, thereby initiating a cascade of cellular events that contribute to wide-spread cell death in the brain.

Ongoing research to understand the mechanisms by which proteins misfold, aggregate, and contribute to cell death as well as research to identify therapeutic agents that could prevent or attenuate prion misfolding, aggregation, and/or propagation could advance research on CJD, as well as other neurodegenerative diseases. Similar to understanding and intervening in prion misfolding, researchers are intently studying misfolding of beta-amyloid and tau (two proteins that are the cellular hallmark of Alzheimer's), as well as misfolding of the protein alpha-synuclein in the context of Lewy body dementia and Parkinson's. It is hoped that advances in any one of these specific areas could help inform treatments for CJD, and vice versa. In fact, research on prion disease has already facilitated major advances in other neurodegenerative diseases. Building upon an assay originally developed by the NIH Rocky Mountain Laboratories for prion disease, scientists have developed a test to detect the abnormal form of alpha-synuclein in the fluid that surrounds the brain of people with Parkinson's. The test requires greater validation, but current data suggests it has good accuracy in diagnosing a particular form of Parkinson's, even years before motor symptoms begin. Currently the test requires a spinal tap, but NINDS-supported scientists are working to modify the test so that it can be used with skin or saliva samples. NIH-funded researchers are developing similar tests for beta-amyloid and tau and are using these same technologies to develop a skin test for prion protein in people with sporadic CJD, which could enable early detection and early intervention.

QUESTIONS SUBMITTED BY SENATOR JERRY MORAN

Dr. Lawrence Tabak, Acting Director, National Institutes of Health (NIH)

Question. Dr. Tabak, at the end of 2020, Congress provided $1.15 billion for research on long COVID. Using this funding, NIH started the RECOVER program,

[3] www.ecfr.gov/current/title-2/subtitle-A/chapter-I/part-180.

which over the life of the program has received a lot of criticism. Concerns have been raised about NIH's lack of urgency and whether it is focused too much on open-ended research questions as opposed to testing treatments and moving therapeutics to clinical trials.

How significantly are you working with private industry to research and test treatments?

Answer. NIH is moving with deliberate speed to understand and clinically define this new post-viral condition, elucidate the underlying biologic mechanisms, and launch clinical trials testing treatment strategies. Recognizing the important role that the private sector plays in development and commercial availability of medical treatments, NIH has met with numerous industry representatives, including industry partners participating in the ACTIV public-private partnership, to review the RECOVER clinical trial program and invite interested groups to discuss potential public-private collaborations.

Question. How many contracts or grants do you have with industry on treatments?

Answer. We have executed confidentiality disclosure agreements with approximately twenty companies/industries to explore possible collaborations. In addition, as of May 4, 2023, there were five agreements under development with industry/private sector to support collaborations and provision of candidate interventions such as antiviral, neuro-stimulatory, and immune modulating interventions.

Question. How much funding has been obligated for public-private collaborations on treatments?

Answer. Four of the five RECOVER clinical trials involve public-private collaborations. As of May 4, 2023, NIH anticipates an approximate investment of $95 million for the conduct of these trials (exclusive of infrastructure costs and subject to adjustment in response to clinical protocol requirements). NIH support of exploratory Phase II studies to provide proof-of-concept and assess safety of candidate interventions across a broad range of interventions (e.g., immune modulators, antivirals, and neurostimulants) and patient populations provides the foundation for larger scale private sector studies.

Question. How many clinical trials are funded by NIH that are testing treatments for long COVID?

Answer. There are five clinical domains that make up the RECOVER clinical trials. These are: a) viral persistence and immune dysregulation; b) neurologic/cognitive dysfunction; c) autonomic dysfunction; d) sleep disorders; e) cardiopulmonary/exercise intolerance/fatigue. These domains were informed by data coming out of RECOVER cohort studies, input from clinicians, and questionnaires that identified some the most burdensome symptoms reported by patients.

Although there are five domains, that does not mean that there will only be five interventions tested. Rather, multiple interventions will be assessed in each clinical domain pending the availability of funds. In addition, trials in the five symptom areas will be run in parallel, which means we will not wait for one set to be complete before starting another one.

RECOVER clinical trials will utilize an adaptive platform trial design. This unique design will allow researchers to easily add different therapies to be tested and to stop interventions if these are proven ineffective. The trials are designed so that they will inform one another. This advanced methodology will enable the best treatments to get to patients on a quicker timeline compared to traditional clinical studies.

Question. How many of these trials are phase I, II, and III?

Answer. Currently the clinical trial portfolio comprises five Phase II trials, including exploratory trials as well as trials designed to pave the way to pivotal Phase III studies.

Question. How much funding has been obligated or committed for clinical trials?

Answer. As of May 4, 2023, NIH RECOVER obligated $171.5 million (inclusive of infrastructure) to launch a suite of clinical trials through the Clinical Trials Data Coordinating Center (DCC) at Duke Clinical Research Institute.

QUESTIONS SUBMITTED BY SENATOR CINDY HYDE-SMITH

Dr. Lawrence Tabak, Acting Director, National Institutes of Health (NIH)

Question. As our understanding of Alzheimer's and related dementias expands, we now have a better understanding that many of these neurological diseases have similar underlying mechanisms. For example, there are many similarities between Alzheimer's Disease (AD)/Alzheimer's Disease Related Dementias (AD/ADRD) and prion disease, which is caused by misfolded proteins in the brain. Alzheimer's Dis-

ease has already benefited from prion disease research, specifically research for Creutzfeldt-Jakob disease (CJD) a rare, 100% fatal, degenerative brain disease that causes rapidly progressive dementia. The specialized protein amplification techniques developed to study CJD are now being applied to Alzheimer's and contributing greatly to our understanding of that disease.

Will NIH consider prion disease, specifically CJD, as a research priority within AD/ADRD? If not, please provide a detailed explanation as to why not.

Will NIH intentionally expand the research the agency funds through the National Institute of Aging (NIA) to include prion disease, specifically CJD?

How does NIH consider updates to what the agency considers to be AD/ADRD to reflect the most current state of scientific understanding of these diseases and their underlying mechanisms?

Answer. The National Plan to Address Alzheimer's Disease and Related Dementias defines the specific diseases and conditions that are considered to be Alzheimer's or a related dementia.[4] Under the implementation approach that NIH uses to identify AD/ADRD research projects, any proposals that explore prion disease that also make a strong and clear scientific connection to AD/ADRD (e.g., disease mechanisms, etiology, health outcomes) are able to be considered for AD/ADRD funding. Currently, NIH uses AD/ADRD funds to support several studies that are exploring direct mechanisms of prion-related neurodegeneration. In FY 2023, NINDS released a funding opportunity announcement (FOA) inviting projects on Cellular and Molecular Mechanisms of Prion-Like Aggregate Seeding, Propagation, and Neurotoxicity in AD/ADRD (PAR–23–023).[5]

The National Plan to Address Alzheimer's Disease and Related Dementias (NAPA) defines the specific diseases and conditions that are considered to be Alzheimer's or a related dementia[6] NIH's AD/ADRD portfolio is wholly inclusive of these National Plan-defined conditions. In addition, other scientifically valid and closely related research conditions may also be eligible for AD/ADRD funding. NIA/NIH considers any meritorious grant application that is relevant to Alzheimer's and related dementias for AD/ADRD funding. NIH already uses AD/ADRD funds to support several studies that explore prion diseases, including CJD, in the context of dementia-related research themes.

The National Plan to Address Alzheimer's Disease and Related Dementias defines the specific diseases and conditions that are considered to be Alzheimer's or a related dementia.[1] As stated in the National Plan, "In addition to AD, this National Plan addresses Alzheimer's disease-related dementias (ADRD) consistent with the approach Congress used in NAPA. These ADRDs include frontotemporal dementia (FTD), Lewy body dementias (LBD—which include dementia with Lewy bodies and Parkinson's disease dementia), vascular contributions to cognitive impairment and dementia (VCID), and mixed dementias—especially AD mixed with cerebrovascular disease or Lewy bodies." While NIH's AD/ADRD portfolio is wholly inclusive of these National Plan-defined conditions, this does not exclude other scientifically valid and closely related research conditions from eligibility for AD/ADRD funding. As mentioned above, any proposals that make a strong and clear scientific connection to AD/ADRD (e.g., disease mechanisms, etiology, health outcomes) are able to be considered for AD/ADRD funding. Therefore, AD/ADRD appropriations are being used to support projects that explore AD/ADRD-related mechanisms or themes in conditions beyond those that are formally defined in the National Plan, for example in prion diseases, ALS, post-traumatic brain injury dementia, and Down syndrome.

QUESTIONS SUBMITTED TO DR. DOUGLAS LOWY

QUESTIONS SUBMITTED BY SENATOR TAMMY BALDWIN

Dr. Douglas Lowy, Principal Deputy Director, National Cancer Institute (NCI)

Question. Clinical trials are essential for determining whether new treatments work against cancer. But often there aren't enough staff who are qualified to support and administer these trials. This is especially true for trials that are testing complicated new technologies. In some cases, the staffing shortage is forcing trial sponsors to delay cancer trials or even abandon them. The FY 2024 President's Budget proposes a $500 million increase for NCI to expand and modernize cancer

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[4] aspe.hhs.gov/collaborations-committees-advisory-groups/napa/napa-documents/napa-national-plan.

[5] grants.nih.gov/grants/guide/pa-files/PAR-23-023.html.

[6] aspe.hhs.gov/collaborations-committees-advisory-groups/napa/napa-documents/napa-national-plan.

clinical trials to more quickly produce prevention, detection, and treatment measures. These investments are expected to double the participation of patients in NCI clinical trials, but we can't expand clinical trials without the staff to run them.

What is NCI doing to address staffing shortages for clinical trials?

Answer. The shortage of clinical research staff (e.g., research nurses, research coordinators, and regulatory staff), as well as healthcare workers, has diminished the capacity of the cancer clinical trials workforce. This is a major concern of the National Cancer Institute (NCI), as this deficit could lead to long-term consequences for the speed of NCI's clinical research programs. In November 2021, NCI directed a survey of NCI-Designated Cancer Centers to assess the ongoing impact of the COVID–19 pandemic on the capacity of Cancer Centers to conduct treatment trials. The results indicated that the pandemic has taken a toll on clinical trial resources and put even greater strain on the workforce who support clinical trials, causing many staff to leave their positions in academic or community research settings for higher pay, career advancement, and/or for the ability to work remotely.

NCI is taking steps to improve cancer clinical trials and to create flexibility for clinical trial sites. NCI has determined that it is possible to develop flexible, faster, simpler, less expensive, and higher impact clinical trials by focusing on four key areas: streamlining processes for trial design and execution, focusing on essential endpoints, setting up trials in a way that broadens rather than limits participant access, and increasing efficiency of data collection, which would help to alleviate demands on the clinical trials workforce.

These recommendations came from a report released by the Strategic Planning Working Group of NCI's Clinical Trials and Translational Research Advisory Committee (CTAC).[7] In alignment with these recommendations, in fall 2023, NCI plans to launch elements of a Virtual Clinical Trials Office (VCTO) supporting NCI trials conducted at NCI-Designated Cancer Centers and NCI Community Oncology Research Program (NCORP) sites to alleviate the strain on the cancer clinical trial workforce. VCTO personnel would work remotely to support local research site health professional staff. Initial services under consideration include eligibility screening, study coordination, and promoting enrollment of patients who are medically underserved. VCTOs may also assist with questions about informed consent and the enrollment process; regulatory support; and adverse event reporting. NCI recently solicited feedback from NCI-Designated Cancer Centers and received universally positive feedback from small and large centers and is collecting additional input regarding specific needs and conditions from individual sites. NCI has already supported the hiring of VCTO personnel and aims to identify up to six Cancer Centers and six NCORP sites to begin the pilot program in fall 2023, based on need, activation time, and accrual of underserved populations.

Question. According to the NCI FY 2024 budget justification, NCI has invested nearly $1.4 billion of the $1.8 billion in available Cures Act Cancer Moonshot funding to support over 240 research projects across more than 70 cancer science initiatives.

Given NCI received the largest proposed boost of all NIH ICs—nearly 7 percent—how is NCI prioritizing the proposed increase and what Cancer Moonshot initiatives will continue or end as a result of the drawdown in Cures Act Cancer Moonshot funds?

Answer. While Cures Act Innovation Funds for the Cancer Moonshot conclude in FY 2023, several Cancer Moonshot projects have timelines that extend beyond FY 2023. Flexibility to carry over funds allows NCI to support each project on the appropriate timeline. At the same time, NCI continues to plan for additional research to pursue new Moonshot goals in FY 2024 and beyond, as described in the FY 2024 Congressional Justification, and pending the availability of new appropriations.

Because Congress provided multi-year budget authority for Innovation Funds under the Cures Act, NCI will be able to continue to support certain Moonshot programs beyond the end of FY 2023. This important flexibility enables NCI to conclude certain Moonshot programs that have met initial goals, avoid any abrupt endings to ongoing projects, and maximize the gains these programs have made—including through the development of new programs to build upon progress made to date.

Approximately 90 percent of the funds appropriated for the Cancer Moonshot from FY 2017 through FY 2023 will be obligated by the end of FY 2023 to support continuing Cancer Moonshot programs including the Cancer Immune Monitoring and

[7] www.cancer.gov/about-nci/organization/ccct/ctac.

Analysis Centers-Cancer Immunologic Data Commons (CIMAC–CIDC) Network[8] and the Human Tumor Atlas Network.[9] NCI plans to deploy an additional $220 million after the close of FY 2023 to minimize any disruptions in the progress of Moonshot projects, including the Participant Engagement and Cancer Genome Sequencing (PE–CGS) Network,[10] projects focused on cancer survivorship transitions of care,[11] and research efforts aimed at developing new approaches to identify and care for individuals with inherited cancer syndromes.[12]

Other programs initially supported through the Cancer Moonshot include the Immuno-Oncology Translational Network (IOTN),[13] established to improve immunotherapy outcomes across the spectrum of adult cancers and to prevent cancers before they occur, and a related follow-on project, the Cancer Immunoprevention Network (CIP-Net),[14] which aims for a deeper understanding of immunoprevention and fostering a community of cancer immunoprevention researchers. Additional examples include the Fusion Oncoprotein Childhood Cancer Consortium (FusOnC2),[15] a collaborative group of transdisciplinary researchers focused on the molecular drivers of childhood cancer, and a subsequently-developed network to support projects to better understand fusion-drive cancers, identifying new drug targets and agents to disrupt fusion oncoprotein drivers for high-risk solid tumors and brain cancers. The projects noted above will be transitioned from Moonshot funding to regular funding mechanisms, pending availability of appropriations.

As described in the FY 2024 Congressional Justification, top priorities for NCI and the Cancer Moonshot in reaching the goal of reducing cancer mortality rates by 50 percent over 25 years include a significant modernization and expansion of NCI-supported clinical trials networks to support doubling patient enrollment and democratizing enrollment in clinical trials. Additionally, modernizing clinical trials infrastructure includes building a National Cancer Research Data Ecosystem to collect, integrate, and share data from clinical trials and a broad range of research studies—while protecting patient privacy.

With the proposed FY 2024 Moonshot funding, NCI would continue successful Moonshot programs that support these FY 2024 priorities to accelerate progress, while also funding new initiatives to leverage progress made so far. Examples of continuing Moonshot programs include the Telehealth Research Centers of Excellence,[16] Acquired Resistance to Therapy Network,[17] and Cancer Moonshot Scholars.[18] These programs will make important contributions to expanding the scope of and access to NCI-supported clinical trials, provide new insights to overcome drug resistance, and fortify the cancer research workforce. The proposed Cancer Moonshot increase will provide critical resources to continue these and other programs and make progress toward a doubling of clinical trials enrollment, and toward the Cancer Moonshot mortality reduction goal.

The proposed Cancer Moonshot increase in FY 2024 aims to both support continuation of successful research initiatives launched with Cures Act funds and to launch the new efforts. These new initiatives and necessary expansions will help more people with cancer and at risk of cancer participate in NCI-supported clinical trials and will ensure data generated through these trials and through other NCI-supported research efforts is available to inform future discoveries.

QUESTIONS SUBMITTED BY SENATOR JOE MANCHIN, III

Dr. Douglas Lowy, Principal Deputy Director, National Cancer Institute (NCI)

Question. We know that the most important way to combat cancer is early detection, however in most rural areas its difficult to access healthcare, let alone cancer

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[8] www.cancer.gov/research/key-initiatives/moonshot-cancer-initiative/implementation/adult-immunotherapy-network#cancer-immune-monitoring-and-analysis-centers-cimacs-and-the-cancer-immunologic-data-commons-cidc.

[9] www.cancer.gov/research/key-initiatives/moonshot-cancer-initiative/implementation/human-tumor-atlas.

[10] epi.grants.cancer.gov/events/pe-cgs/.

[11] grants.nih.gov/grants/guide/rfa-files/RFA-CA-19-035.html.

[12] grants.nih.gov/grants/guide/rfa-files/rfa-ca-19-017.html.

[13] www.cancer.gov/research/key-initiatives/moonshot-cancer-initiative/implementation/adult-immunotherapy-network.

[14] prevention.cancer.gov/major-programs/cancer-immunoprevention-network-cip-net.

[15] www.cancer.gov/research/key-initiatives/moonshot-cancer-initiative/implementation/childhood-cancer-research.

[16] healthcaredelivery.cancer.gov/telehealth/trace.html.

[17] www.cancer.gov/about-nci/organization/dcb/research-programs/artnet.

[18] www.cancer.gov/about-nci/organization/crchd/diversity-training/cancer-moonshot-scholars-diversity-program.

screenings. West Virginia has a high cancer rate than the national average, and in particular has high rates of late stage cancer—such as colon cancer and lung cancer.

Dr. Lowy, what can be done to increase cancer screenings in rural America?

Answer. Increasing uptake of cancer screening is an important priority across the National Cancer Institute (NCI). NCI supports several key programs, partnerships, and individual research grants that aim to increase screening access and uptake. The "Accelerating Colorectal Cancer Screening and Follow-up through Implementation Science (ACCSIS)" Program is a Cancer Moonshot Initiative that supports research to improve colorectal cancer screening, follow-up, and referral for care among populations that have low colorectal cancer screening rates. The ACCSIS program focuses on underserved groups, including underserved racial and ethnic minority populations and people living in rural or difficult-to-reach areas. The program includes research centers in Appalachia (Kentucky and Ohio), Arizona, California (San Diego), Illinois (Chicago), New Mexico, North Carolina, Oklahoma, and Oregon.[19]

NCI is also supporting several research efforts to reduce barriers and increase uptake of cervical cancer screening, including in rural areas. Over half of new cervical cancer cases are diagnosed among women who have never been screened or are infrequently screened, reflecting barriers presented by socioeconomic disparities and geographic inaccessibility, among other factors.

NCI's Cervical Cancer 'Last Mile' Initiative is a public-private partnership that will help inform the accuracy and clinical effectiveness of self-sampling-based human papillomavirus (HPV) testing for primary cervical cancer screening. As part of the 'Last Mile' Initiative, NCI is supporting the "Self-sampling for HPV testing to Improve Cervical Cancer Prevention ('SHIP')" trial, which will include participants representing a wide diversity of socioeconomic and racial/ethnic groups and geographic regions, including both urban and rural populations across the U.S.[20] NCI is also supporting the "Multilevel HPV Self-Testing Intervention for the Increase of Cervical Cancer Screening Among Women in Appalachia" clinical trial, which studies how well an HPV self-testing intervention works for increasing cervical cancer screening among women in four Appalachia states (Ohio, Kentucky, West Virginia, and Virginia).[21] NCI and several Federal agencies have partnered to form the Federal Cervical Cancer Collaborative (FCCC), a Cancer Moonshot Initiative focused on reducing the persistent disparities in cervical cancer through more equitable cervical cancer vaccination, screening, and management among geographically isolated and economically and medically vulnerable populations. The FCCC aims to bring cervical cancer prevention and management guidelines into safety-net settings of care more swiftly.[22]

Activities to increase cancer screening in rural regions are also part of NCI-Designated Cancer Centers' Community Outreach and Engagement efforts.[23] For example, the University of Kentucky Markey Comprehensive Cancer Center, in partnership with community-based hospitals, is engaging in statewide collaborative efforts[24] to increase lung cancer screening and survivorship care, which has helped Kentucky achieve the second highest lung cancer screening rate in the country, leading to a 19 percent reduction in the diagnosis of late-stage lung cancers in the state. The Markey Cancer Center also includes a Patient-Oriented and Population Sciences Shared Resource Facility,[25] which supports an initiative to refine and assist with dissemination of materials designed to increase uptake of cervical cancer prevention among high-risk populations in primary care practices in Ohio, Kentucky, Virginia, and West Virginia.

Another NCI-Designated Cancer Center undertaking efforts to improve screening in rural populations is the University of Virginia Cancer Center (UVACC), which serves 87 contiguous counties across northwestern Virginia and West Virginia, where 30 percent of the population is rural.[26] Among the screening programs developed by UVACC are a Mobile Prevention Coach to provide free/reduced-cost mammograms, Pap tests, and HPV self-sampling tests to low-access communities; a Telehealth Lung Cancer screening program to provide radiology consults to rural hospitals, leading to a sustainable pathway to screening; and a CRC navigator program

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[19] healthcaredelivery.cancer.gov/accsis/.
[20] prevention.cancer.gov/major-programs/nci-cervical-cancer-last-mile-initiative.
[21] www.clinicaltrials.gov/ct2/show/NCT04411849.
[22] dceg.cancer.gov/news-events/news/2022/Federal-cervical-cancer-collaborative.
[23] cancercontrol.cancer.gov/research-emphasis/supplement/coe.
[24] ukhealthcare.uky.edu/markey-cancer-center/community/learning-opportunities/lung-screening.
[25] ukhealthcare.uky.edu/markey-cancer-center/research/srf/popsrf.
[26] med.virginia.edu/community-outreach-engagement/discover-the-community-we-serve/.

to enable a pathway to colonoscopy and increase the utilization of stool-based CRC screening.

NCI is also supporting the discovery, testing, and validation of new tests that may detect cancer more accurately and potentially reduce barriers to screening. The NCI Division of Cancer Prevention is in the process of creating a network to carry out widespread evaluation of cancer detection tests across populations. The Cancer Screening Research Network[27] is on track to begin in 2024, with sites representing different regions and populations across the country.

QUESTIONS SUBMITTED TO DR. JOSHUA GORDON

QUESTIONS SUBMITTED BY SENATOR TAMMY BALDWIN

Dr. Joshua Gordon, Director, National Institute of Mental Health (NIMH)

Question. A recent CDC survey found that teenage girls and LGBTQ youth are grappling with a mental health crisis. Suicide is the second leading cause of death in youth and young adults aged 10–24. Data show that almost 45 percent of LGBTQ youth seriously considered suicide in the past year, and that suicide rates for Black youth are on the rise. The FY 2024 President's Budget proposes at $200 million increase for mental health research. This funding would support a Precision Psychiatry Initiative focused on developing biomarkers for major depression and identifying diagnostics to better predict patient prognosis and optimize treatment.

How would identifying new biomarkers for depression deliver better, faster treatments to patients? And how could these investments help reduce suicide?

Answer. Effective treatments for depression exist; however, identifying the best treatment for a specific person experiencing depression remains a significant challenge. Treatments are often selected by trial and error, with providers and patients sometimes waiting months to see if a treatment is effective. As part of the Precision Psychiatry Initiative, the National Institute of Mental Health (NIMH) aims to support research to uncover why people with depression respond differently to different treatments and identify biomarkers—objective, measurable characteristics that indicate health or disease states—to define depression subtypes, which could greatly improve treatment selection. Using biomarkers, mental healthcare providers may be able to predict a patient's response to different treatment options, which will decrease the time-consuming trial and error process and provide people with a working treatment sooner. Since depression is one of the main risk factors for suicide, advancements in biomarker development to optimize depression treatment may help considerably reduce suicide deaths.

QUESTIONS SUBMITTED BY SENATOR JOHN BOOZMAN

Dr. Joshua Gordon, Director, National Institutes of Mental Health (NIMH)

Question. According to the CDC, rates of suicide among farmers are 1.5 times higher than the national average.

Farming communities are essential in Arkansas with almost 50,000 farms across the state.

I appreciate Congress and the Administration's support for expanding access to mental healthcare. However, I fear that farmers are often left out of the conversation.

How does the NIMH intend to tailor its mental health research to ALL Americans, especially the farmers that are core to our nation's agricultural mission?

Answer. The National Institute of Mental Health (NIMH) recognizes that farmers and others who live or work in underserved rural and frontier areas may experience mental health disparities—that is, increased risk for mental illnesses and suicide, as well as limited access to evidence-based mental health treatments and services. NIMH aims to address this serious and growing concern by supporting research to understand how mental health disparities arise and improve the delivery of mental health services and interventions in rural areas and other under-resourced communities. For example, in September 2023, the NIMH Office for Disparities Research and Workforce Diversity will sponsor a webinar titled "Coming Face to Face with Suicide in American Farming," with the goal of identifying knowledge gaps in this area. Also, NIMH recently published a set of priorities for mental health disparities research, which identified reducing suicide and suicidal behavior among rural populations as a top priority area. The NIMH Office of Rural Mental Health Research

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[27] prevention.cancer.gov/major-programs/cancer-screening-research-network-csrn.

collaborates with others in the Department of Health and Human Services to coordinate and support mental health research activities focusing on the unique strengths, challenges, and needs of individuals who live in rural and other underserved areas. Through these efforts, NIMH remains committed to advancing the goal of mental health equity and ensuring that NIMH-supported research benefits all Americans.

QUESTIONS SUBMITTED TO DR. RICHARD HODES

QUESTIONS SUBMITTED BY SENATOR SHELLEY MOORE CAPITO

Dr. Richard Hodes, Director, National Institute on Aging (NIA)

Question. Precision medicine-based approaches are being used in many fields. Some NIH Institutes, such as the National Cancer Institute, have embraced it significantly.

Can you comment on how precision medicine can be advanced for Alzheimer's Disease and other neurodegenerative diseases?

Answer. NIH is working to advance precision medicine for people living with Alzheimer's and other neurodegenerative diseases, including those living with mixed dementia, a condition in which more than one dementia pathology is observed to occur simultaneously in the brain. Essential to precision medicine is a dedication to ensuring research—from basic science through clinical trials—is inclusive so that findings are applicable to all populations, especially those most at risk for dementia. NIH funds several efforts to meet the need for therapeutics informed by precision medicine. As one example, NIH recently launched the second iteration of the Accelerating Medicines Partnership® Program for Alzheimer's Disease (AMP® AD) program in collaboration with the Foundation for the National Institutes of Health. In its first phase, this partnership involving government, industry, and not-for-profit organizations yielded the identification of more than 600 new potential disease mechanisms and risk factors (e.g., genes and proteins). This helps inform the development of a range of precision medicine treatment approaches by providing additional targets for drug discovery. The second phase builds on this success by collecting and analyzing additional data and samples from populations most at risk for Alzheimer's. Researchers in the program are using cutting-edge approaches to bring new medicines and support to patients by enhancing validation of novel, clinically relevant therapeutic targets and biomarkers.

NIH is also funding several projects at institutions around the country to accelerate the development of precision medicine approaches for Alzheimer's and other neurodegenerative diseases, including a recent funding opportunity to build infrastructure for precision medicine research on minority health and disparities in Alzheimer's and related dementias.[28] This effort is complemented by several workshops and research summits focused on identifying key gaps and opportunities for advancing precision medicine for Alzheimer's and related dementias.[29] These efforts are reflected in the broad range of drug candidates being tested in NIA-funded clinical trials. As a result of the substantial research progress achieved over the last several years in understanding how Alzheimer's and related dementias develop and worsen, the drug development pipeline has never been more diverse. Drug candidates now in NIA-funded clinical studies target multiple aspects of the disease process, from inflammation in the brain to disrupted sleep patterns to changes in hormone levels and more.

Question. How we can tap into dramatic advances in genomics in the past few years towards this?

Answer. Several NIH efforts are aimed at harnessing advances in genomics in broader, more diverse populations to enable a precision medicine approach to preventing and treating these diseases. Ten years ago, we knew of only 10 genes associated with Alzheimer's. Thanks to efforts like the NIH-funded Alzheimer's Disease Sequencing Project,[30] we now know of and are researching more than 70 related genetic variants, which offer a broad range of new targets for intervention, such as those involved in inflammation or metabolism or that are associated with growth factors and hormones. The Alzheimer's Disease Sequencing Project continues to identify new genes and gene variants that contribute to increased risk for or protec-

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[28] grants.nih.gov/grants/guide/rfa-files/RFA-AG-23-020.html.

[29] Examples include: 2021 NIH Alzheimer's Research Summit: Path to Precision Medicine for Treatment and Prevention; NIA-AA Symposium: Enabling Precision Medicine for Alzheimer's Disease Through Open Science; Microphysiological Systems to Advance Precision Medicine for AD/ADRD Treatment Virtual Workshop.

[30] www.nia.nih.gov/research/dn/alzheimers-disease-sequencing-project-consortia.

tion against the disease. This project also includes the Diverse Population Initiative—a targeted effort to sequence the entire genome of individuals from diverse communities to help identify shared and novel genetic riskfactors for Alzheimer's and related dementias across populations. Genomics data from this and other efforts are made available, with appropriate privacy and security safeguards, to the research community via a centralized data repository. These important genomics data can help advance precision medicine for dementia and other neurodegenerative diseases.

Question. The Labor-HHS Committee Report in the last two appropriations cycles contained language expressing concern about a correlation found between medications that are commonly prescribed for overactive bladder and the development of cognitive impairment and Alzheimer's Disease and Related Dementia (ADRD). The report language urged NIA to study these medications and other treatments for overactive bladder to determine their safety and efficacy, as well as their potential risks related to ADRD.

Has NIA initiated research on adverse neurocognitive effects of overactive bladder medications?

If research on these medications has not been initiated, what are the NIA's plans for studying the safety of the medications that are being prescribed to millions of Americans for treatment of overactive bladder?

Answer. NIA has supported and continues to support studies on the safety of drugs used to treat overactive bladder, including research investigating the adverse neurocognitive effects of these medications. As one example, NIA is funding research using a novel model to investigate dementia induced by a specific class of medications meant to treat overactive bladder.[31] NIA is also funding research evaluating the cognitive effects of overactive bladder medications in older women with incontinence.[32] Because these drugs may increase the risk of developing dementia, they may be important targets for deprescribing, a process meant to safely reduce or stop medication to minimize or prevent harmful side effects. Along with other research initiatives,

NIA is funding a clinical trial testing whether discontinuing use of anticholinergics, a class of drugs used to treat overactive bladder, improves cognition and lowers the risk of dementia, as well as other research on the impact of deprescribing on dementia risk.[33] NIA also funds the United States Deprescribing Network, an effort to enhance research on possible ways to deprescribe potentially risky medications and improve medication use among older adults. The Deprescribing Network itself provides funding for several pilot and exploratory studies, grant planning activities, and small collaboration grants.

NIH also funds studies of non-drug therapeutic approaches to treat overactive bladder. One NIA-funded research study is assessing brief mindfulness and non-invasive brain stimulation to reduce symptoms of urgency incontinence in women.[34] NIA also recently supported a study testing a novel, non-invasive nerve stimulation device for in-home treatment of overactive bladder.[35]

In addition, NIA has several broad funding opportunities available to fund meritorious applications proposing additional such research. Some of the current projects on dementia and overactive bladder are funded via these opportunities, which include support for:

—basic and clinical research
—small businesses (such as those developing non-drug therapies for overactive bladder)
—training and career development awards for the next generation of clinicians and researchers working in this area

NIA has funded and continues to fund studies on the safety of drugs used to treat overactive bladder, including those described above.

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[31] reporter.nih.gov/search/0lm26jQsukuQXix5r__QvGw/project-details/10258975.
[32] reporter.nih.gov/search/0lm26jQsukuQXix5r__QvGw/project-details/10343015.
[33] reporter.nih.gov/search/Shaj-qYerkm0U6DRn1S6tg/project-details/10129872.
[34] reporter.nih.gov/search/PWzY007ysEW1d1WslGSukQ/project-details/10259722.
[35] reporter.nih.gov/search/rmFNoL91xkamsqkkLW–QEQ/project-details/10219001.

QUESTIONS SUBMITTED TO DR. NORA VOLKOW

QUESTIONS SUBMITTED BY SENATOR JEANNE SHAHEEN

Dr. Nora Volkow, Director, National Institute on Drug Abuse (NIDA)

Question. Xylazine, a sedative only authorized in the US for veterinary use, has been detected in a growing number of overdose deaths and illicit drug combinations. It is commonly encountered in combination with fentanyl but has also been detected in mixtures containing cocaine, heroin and a variety of other drugs. From 2020 to 2021, the Drug Enforcement Agency found a more than 60% increase in xylazine-positive heroin tested at DEA labs in the Northeast, and xylazine-related overdose deaths also doubled in the Northeast over that same time period. As NIDA is aware, common opioid overdose reversal drugs such as naloxone are ineffective against xylazine, as xylazine is not an opioid.

Could NIDA please detail what research the agency is funding to find overdose reversal drugs, similar to naloxone, for xylazine?

Answer. Given the rapid recent spread of xylazine across the United States, NIDA has been quickly growing its research efforts to understand xylazine toxicity and to develop xylazine overdose reversal agents. Xylazine is a sedating agent that targets alpha-2 adrenergic receptors (A2R) in the brain and is approved by the United States Food and Drug Administration (FDA) for use as an animal tranquilizer. While not approved for human use, it is increasingly mixed with illicit opioids in the United States and has become implicated in a growing number of opioid-related overdose deaths. Case studies show that xylazine alone can cause slowed breathing and heart rate, loss of consciousness, and coma. Given that opioid misuse can cause similar symptoms, there is concern that xylazine and opioids may be an especially dangerous combination. While the opioid reversal agent naloxone should always be administered in cases of overdose involving xylazine laced opioids, effects specific to xylazine do not respond to naloxone.

The mechanisms of xylazine overdose in humans, alone or in combination with opioids, are not fully understood. In veterinary practice, xylazine sedation is reversed using A2R antagonists such as yohimbine. These antagonists may hold promise for reversing overdose in people exposed to xylazine; however, some of them lack specificity for A2R and can trigger adverse reactions, including paradoxically deeper sedation, observed in veterinary settings.[36] There is also concern that rapid, simultaneous reversal of xylazine and opioid overdose could trigger severe withdrawal symptoms. NIDA is supporting preclinical studies to characterize these mechanisms and identify safe, effective reversal agents for xylazine overdose. For example, NIDA intramural investigators are testing the effects of xylazine, with and without opioids, in a rodent model that they originally developed to identify stronger opioid overdose reversal agents.[37] Once these investigators establish the baseline effects of xylazine and xylazine-plus-opioids in this model, they will test the potential therapeutic effects of A2R antagonists, with and without naloxone.

To gain further insight into xylazine overdose and approaches to treatment, NIDA-funded investigators have been gathering data from people who have been exposed to xylazine. In a recent study of patients who presented to the emergency department with opioid overdose or toxicity, those who also tested positive for xylazine had lower rates of cardiac arrest and coma than those positive for opioids alone.[38] In addition, the two groups did not differ significantly in their length of stay in the ED, hospital admission, or mortality. Other studies have found that people heavily sedated or unconscious from xylazine are at high risk of being in environments where they are victims of violent assaults; so, xylazine sedation alone, without effects on heart or lung function, can incur serious health and safety risks.[39] Overall, these studies suggest that overdose and other outcomes associated with xylazine toxicity are more complex than anticipated based on xylazine's known pharmacology, and that it will be important to fully understand the full array of these outcomes as we work toward appropriate therapies, including overdose reversal agents. To that end, NIDA is prioritizing new research on the prevalence and outcomes of xylazine use and treatment of xylazine overdose in combination with other drugs.

Question. Could NIDA please detail the timeline the agency expects for those reversal drugs to be available for commercial use?

Answer. Research on potential xylazine overdose reversal agents has begun but is not yet at a stage in which a timeline to market availability can be predicted.

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[36] pubmed.ncbi.nlm.nih.gov/30372437.
[37] pubmed.ncbi.nlm.nih.gov/36828628.
[38] pubmed.ncbi.nlm.nih.gov/37014353.
[39] pubmed.ncbi.nlm.nih.gov/36846574.

As noted above, preclinical studies are underway to address whether A2R antagonists can also reverse xylazine overdose, alone and in combination with opioids. NIDA intramural investigators estimate that these studies will be complete in 6 months. If these studies show promise, there is potential to further accelerate the development of xylazine overdose reversal agents by repurposing the veterinary medicines already available, as opposed to starting over with new drug discovery and synthesis. We expect that forthcoming research will help further accelerate progress in developing treatments for xylazine use and overdose, including xylazine overdose reversal agents.

QUESTIONS SUBMITTED BY SENATOR JOE MANCHIN, III

Dr. Nora Volkow, Director, National Institute on Drug Abuse (NIDA)

Question. Recent estimates show more than 106,000 Americans, and more than 1,500 West Virginians, died from drug-related overdoses in the last year. West Virginia continues to have the highest rate of overdose deaths in the country with 90 deaths per 100,000 people, which is almost triple the national average of 31.5 deaths per 100,000 people. To combat this ongoing epidemic, the Administration released its National Drug Control Strategy. The Strategy highlights the need to expand the science behind recovery and directs the Office of National Drug Control Policy to partner with the National Institute on Drug Abuse, among others, to develop, prioritize and implement a Federal recovery agenda.

What are other ways that we can better expand access to substance use disorder treatment in rural America, particularly in West Virginia, where the overdose rates are the highest in the nation?

Answer. NIDA acknowledges the vital need to ensure rural access to evidence-based interventions and supports substance use research in rural communities. Through the Rural Opioid Initiative, a collaboration with the Appalachian Regional Commission, the Substance Abuse and Mental Health Services Administration, and the Centers for Disease Control and Prevention, NIDA has funded several projects aimed at assisting rural communities with comprehensive approaches to addressing drug use. Ongoing studies address opioid, stimulant, and tobacco use, spanning diverse approaches such as novel peer-delivered and technology-supported interventions, harm reduction approaches, and strategies that address social determinants of health and reduce stigma. The Kentucky Viral Hepatitis Treatment (KeY Treat) Study underway at the University of Kentucky, for example, is working toward reducing the health burden of hepatitis C infection associated with drug use in rural Kentucky.[40]

With funding from the NIH Helping to End Addiction Long-term Initiative® (HEAL), NIDA supports large research programs with rural components, conducted in real-world settings and in collaboration with a diverse range of stakeholders to ensure that the strategies being studied are sustainable and scalable. NIDA's Clinical Trials Network expanded its multi-site network for developing and testing treatment effectiveness with new nodes and protocols to expand the use of medications for opioid use disorder (MOUD) in rural settings and emergency departments, implement evidence-based models to optimize the delivery of MOUD, and prevent opioid use disorder (OUD) or progression to more severe OUD. Specifically, the CTN added the Appalachian Node,[41] representing a collaboration among the University of Pittsburgh, West Virginia University, and Pennsylvania State University. NIDA's HEALing Communities Study® is testing evidence-based strategies to reduce opioid-related overdose deaths, increase MOUD treatment, and reduce risky opioid prescribing in 67 communities within 4 states, including in rural areas highly affected by the overdose crisis. The recently launched Harm Reduction Research Network also aims to test and improve the effectiveness, implementation, and impact of harm reduction strategies in rural areas and other communities. Finally, through the Integrative Management of chronic Pain and OUD for Whole Recovery program (IMPOWR), a NIDA-led study aims to develop effective, equitable, and sustainable interventions for chronic pain and OUD to meet the needs of people in rural and Black communities. Findings from these studies will provide valuable insights into how specific rural communities can increase access to interventions for OUD through tailored approaches that meet individual and community needs.

Question. Far too many West Virginians are familiar with substance use and the impact it can have on loved ones, families and communities. However, the driving force behind the record numbers of overdose deaths we are seeing is illicit fentanyl.

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[40] www.ncbi.nlm.nih.gov/pmc/articles/PMC8258565/.
[41] www.ctn.pitt.edu/.

In the last year illicit fentanyl became the number one cause of death among Americans 18 to 45, surpassing deaths from COVID–19, suicide and car accidents.

We must act now to better understand substance use and ensure that we do not lose future generations to overdose. West Virginia may lead the nation in drug overdoses, but there are some very smart people leading innovative research projects to find treatments for substance use disorder.

Dr. Volkow, you have been to West Virginia, visited the West Virginia University's Rockefeller Neuroscience Institute, and have seen first-hand the work being done to study and find treatments for substance use disorder.

Dr. Volkow, how can NIDA continue to support research institutions that are studying the science of substance use disorder and working on treatments for substance use disorder?

Answer. Through a variety of NIH funding mechanisms, NIDA continues to fund meritorious applications submitted by researchers from diverse institutions to maximize its support of research. Notably, there are multiple NIH funding mechanisms geared toward increasing research infrastructure.

For example, the congressionally mandated Institutional Development Award (IDeA) program builds research capacity at institutions in states with historically low levels of NIH funding.[42] Similarly, Institutional Research Training Grants support institution infrastructure to enable the recruitment and training of graduate students and postdoctoral candidates.[43]

NIDA also uses novel approaches to bring a variety of institutions into the research enterprise. For example, with funding from the NIH HEAL Initiative, NIDA expanded its Clinical Trials Network, adding five new research nodes and supporting the development of new protocols to develop and test substance use interventions. In addition, through NIDA's Racial Equity Initiative, the Institute issued two notices of funding opportunity (NOFO) specific to Minority Serving Institutes (MSIs) which are underrepresented in substance use research, with companion notices for other research institutions. One opportunity focused on novel research to understand how structural racism impacts substance use and another aims to support visionary applications to study the intersection of substance use and racial equity. Applications submitted in response to these NOFOs are being reviewed and will be funded in FY 2023. NIDA is also currently participating in two novel NIH funding opportunities to further promote the diversity, breadth, and geographic locations of research programs.[44,45] Together, these efforts aim to encourage diversity and, in doing so, increase the scientific value and impact of research.

QUESTIONS SUBMITTED BY SENATOR SHELLEY MOORE CAPITO

Dr. Nora Volkow, Director, National Institute on Drug Abuse (NIDA)

Question. Last year, you [Dr. Volkow] wrote about the financial sense in investing in prevention. You said that "You can't put a dollar value on the losses American families have suffered due to the addiction and overdose crisis," but that certain prevention and treatment strategies can save costs for the healthcare system in the long run.

Can you tell us about the cost savings associated with drugs use prevention and addiction treatment?

Answer. Research has demonstrated that substance use prevention and treatment strategies are a good investment and reduce burden across many sectors of society, including healthcare, public safety and the criminal legal system, behavioral health, and education. These strategies are relatively inexpensive compared to the high costs incurred if substance use disorders develop and are left untreated.

NIDA-funded researchers have found that higher-risk adolescent behaviors, including substance use, accounted for more than 10 percent of all hospital charges to healthcare payors in North Carolina, suggesting there is significant potential for cost savings if barriers to preventative and treatment services are addressed.[46] Another analysis from researchers funded by NIDA showed that implementation of a structured prevention approach called Communities That Care had a sustained impact on reducing risky health behaviors and a continued positive cost benefit, with an approximately $602 investment in each child yielding an estimated $7,754 in savings by the time participants were age 23—a $12.88 return for each dollar in-

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[42] www.nigms.nih.gov/Research/DRCB/IDeA/Pages/default.aspx.
[43] researchtraining.nih.gov/programs/training-grants/T32-a.
[44] grants.nih.gov/grants/guide/pa-files/PAR-23-122.html.
[45] grants.nih.gov/grants/guide/pa-files/PAR-23-144.html.
[46] Ridenour et al., 2022 www.ncbi.nlm.nih.gov/pmc/articles/PMC8554188/.

vested. The return was over twice as great when the downstream economic benefits of completing college was included.[47] Other research studies have shown that addiction treatment is associated with a net positive cost savings, with one study showing greater than 7:1 ratio of benefits to costs, estimating substance use treatment costs at $1,583 while being associated with a monetary benefit to society of $11,487.[48] The primary drivers of these benefits are reduced costs associated with the criminal legal system and increased employment earnings.[49]

It should also be noted that NIH, with leadership from NIDA, is supporting two national studies—Healthy Brain and Child Development (HBCD) study and Adolescent Brain Cognitive Development SM Study (ABCD Study®)—that aim to provide research which can inform prevention service delivery. Specifically, HBCD identifies human brain, cognitive, behavioral, social, and emotional development beginning prenatally through childhood (e.g., age 9–10). The study will help predict and prevent some of the known impacts of pre/postnatal exposure to drugs or adverse environments, including risk for future substance misuse, mental disorders, and other behavioral and developmental problems.[50] The ABCD Study will determine how childhood experiences (such as sports, videogames, social media, unhealthy sleep patterns, and smoking) interact with each other to affect brain development, academic, health, and other outcomes. The results of the ABCD Study will provide a broad array of stakeholders including, families, schools, health professionals; and policymakers with information to promote the health, well-being, and success of children, which can lead to cost savings.[51]

Question. From February 2020 to June 2021, substance use caused a 9–26% decline in prime-age labor force participation. This is an issue that affects not only the workforce in my state of West Virginia, but working adults across the country.

Can you tell us about the potential effects that addiction treatment can have on employment and workforce readiness?

Answer. While NIH is not the United States government lead on labor force participation, we work closely with other Departments and Agencies to address health issues affecting the Nation. Work from other government entities has been summarize below.

According to the United States Bureau of Labor Statistics, the labor force participation rates (LFPR) of workers aged 25–54 declined substantially (around 3 percentage points) during the COVID pandemic. Recovery has been slow: As of January 2022, the rate was still about 1 percentage point below pre-pandemic levels, however, according to data for April 2023[52] the LFPR has fully recovered. A May 2022 study from the Federal Reserve Bank of Atlanta[53] had suggested that up to about one quarter of the post pandemic drop could be accounted for by increased problematic substance use in the workforce, highlighting the importance of maximizing access to substance use treatment in the workplace.

The implementation of effective and comprehensive addiction treatments could have transformational effects on workforce readiness, as employment is one of the most widely acknowledged social determinants of health and well-being among the general population. At the same time, it must be acknowledged that the relationship between problematic substance use and employment is complex. For example, that relationship is bidirectional: substance use can impact labor market outcomes and the experience of work can similarly influence substance use patterns.[54] Another important aspect in need of further research is the effects of remote working on mental health symptoms and substance use patterns in members of the workforce with psychiatric vulnerabilities.[55] Finally, research has shown that the type and rate of substance use varies quite dramatically by occupation and industry.[56]

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[47] Kuklinski et al., 2021 pubmed.ncbi.nlm.nih.gov/33837890/.

[48] Ettner et al., 2006 pubmed.ncbi.nlm.nih.gov/16430607/.

[49] Koenig et al., 2005 pubmed.ncbi.nlm.nih.gov/15797638/.

[50] heal.nih.gov/news/stories/healthy-brain-child-development-hbcd-study.

[51] nida.nih.gov/research-topics/adolescent-brain/longitudinal-study-adolescent-brain-cognitive-development-abcd-study.

[52] fred.stlouisfed.org/series/LNS11300060.

[53] www.atlantafed.org/-/media/documents/research/publications/policy-hub/2022/05/09/05—did-substance-abuse-during-pandemic-reduce-labor-force-participation.pdf.

[54] Addiction, employment, and the return to work. pen.library.ubc.ca/media/stream/pdf/52383/1.0347521/5.

[55] Cohen and Bloomberg. Fortune Magazine May 2023 fortune.com/2023/05/13/remote-workers-substance-use-disorders-return-to-office-mandates/.

[56] SAMHSA 2015. www.samhsa.gov/data/sites/default/files/report__1959/ShortReport-1959.html.

QUESTIONS SUBMITTED BY SENATOR JERRY MORAN

Dr. Nora Volkow, Director, National Institute on Drug Abuse (NIDA)

Question. Insomnia impacts approximately 25 million Americans, with one-third to one-half of servicemembers and veterans impacted. Insomnia is a significant societal problem with a considerable disease burden—including comorbidities of PTSD, anxiety, depression, and drug abuse. Currently, one of the most common insomnia prescriptions is benzodiazepines and z drugs (zopiclone/zolpidem)—that are recommended for short-term use, but are commonly used long-term, resulting in daytime impairments and lead to abuse. Treatment options exist that address chronic insomnia without dependence issues and decrease the likelihood of drug abuse—DORA class. Dual Orexin Receptor Antagonists (DORAs) work by blocking signals in the brain that stimulate wakefulness. DORAs have an excellent safety profile that does not suggest habit-forming behavior. Various research agencies are currently studying DORAs to help with insomnia-associated conditions (DoD for PTSD, NIH/NIDA for Sleep).

Currently, DORAs are schedule IV on the DEA Controlled Substance Schedule. Idorsia filed a Citizens Petition asking the DEA Administrator to initiate a rulemaking process to remove the DORA class medications from scheduling under the Controlled Substances Act (CSA) based on 8 years of real-world evidence that shows the class has an insignificant abuse profile and potential for abuse. The first step in the process for DEA to consider de-scheduling DORAs is for FDA to review the Citizen Petition and, if they concur with the scientific evidence, to then recommend to DEA that it begin the rule making process to propose de-scheduling the DORA class of treatments (which currently includes three products from three separate manufacturers).

The DORA class of drugs are also already available on the market in Europe without any of the restrictions or potential stigma that exist in the U.S. market.

Dr. Volkow, I know that NIDA has focused on finding non-addictive treatments for insomnia. This is particularly an issue for our servicemembers and veterans, who are significantly impacted by insomnia and may be prescribed drugs that can become addictive. Can you discuss the research NIDA has either already done or has planned in this space, particularly with the DORA class of drugs? Has NIDA identified priorities around finding the best treatments, at the lowest risk, for insomnia?

I also understand that NIDA is interested in research into the DORA class of drugs as a potential treatment for opioid use disorder. What relevant research do you have underway or planned on this topic?

Answer. Dual orexin receptor antagonist (DORA) medications block the activity of both versions of the brain's receptors for the signaling peptide orexin, which helps regulate sleep stages and wakefulness. NIDA research on DORA medications is not specific to veteran populations, though NIDA research does address this priority more broadly in the context of addiction, a field where the identification of pharmacotherapies (e.g., for pain and sleep disorders) with less potential for misuse constitutes a strategic research area. DORAs are a good example in this context as the orexin system plays a prominent role in health (e.g., sleep and appetitive behaviors) and disease (e.g., Parkinson's, depression/anxiety, and addiction). NIDA's significant investments in investigating potential applications for DORAs (in the broad context of addiction) illustrates this interest. Relevant projects in this space include studies to:

—Identify potential mechanisms of sleep disruption induced by methamphetamine use via investigations of the orexin system and the therapeutic potential of DORAs. The results of this project may lead to new and more broadly effective medications that will target both methamphetamine abuse and related insomnia;[57]

—Investigate the clinical potential of a potent and selective orexin 1 receptor (OX1R) antagonist (a medication that blocks the activity of only the orexin 1 receptor) (AZD4041/BPN–19302), which studies in rodents and non-human primates have shown can reduce the addiction-like behaviors that are relevant to those commonly found in opioid use disorder patients;[58]

—Evaluate the potential of the FDA approved orexin antagonist suvorexant to alleviate the adverse effects of opioid and methamphetamine co-use, including the sleep disturbances characteristic of this condition;[59]

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[57] reporter.nih.gov/search/A6Z2dnBww0SwLArh0G3z8A/project-details/10631661.
[58] reporter.nih.gov/search/TqdUrvtOv0GD2jHNie__YgQ/project-details/10469590.
[59] reporter.nih.gov/search/A6Z2dnBww0SwLArh0G3z8A/project-details/10577909.

—Identify new compounds to alleviate opioid withdrawal dependent sleep disruption in an animal model of oxycodone dependence;[60]
—Develop novel OX1R antagonists for the treatment of cocaine use disorder without the sleep-inducing liabilities seen with existing DORAs;[61] and
—Translate positive preclinical findings showing orexin antagonism has substantial promise for treating addiction into the clinical domain by administering suvorexant to people who smoke cigarettes with a tobacco use disorder as a means to facilitate smoking cessation.[62]

In addition, the NIH's National Center on Sleep Disorders Research (NCSDR), located within the National Heart, Lung, and Blood Institute (NHLBI), is currently supporting several clinical studies and clinical trials for the treatment of insomnia. As insomnia is commonly associated with, and exacerbates, other medical and psychiatric disorders, it is of critical importance to find effective therapies for this disorder. Currently, cognitive-behavioral therapy for insomnia (CBT-I) is the recommended first-line treatment for this disorder; however, research supported by NIH has shown that there are different "types" of insomnia. Depending on the type an individual may have, treatment can be personalized.

In summer 2023, NHLBI will launch its largest randomized clinical trial, with sites in the United States and Canada, to test both medication and behavioral interventions in individuals that have the different types of insomnia. NHLBI is also supporting a new hybrid effectiveness-implementation trial to use brief behavioral treatment of insomnia in socioeconomically disadvantaged adults in primary care.[63]

SUBCOMMITTEE RECESS

Senator BALDWIN. The committee will next meet in this room, Dirksen 192, on Thursday, May 11, at 10 a.m., for a hearing on the Biden Administration's Budget Request for the Department of Education.

Until then, this committee stands adjourned.

[Whereupon, at 11:40 a.m., Thursday, May 4, the subcommittee was recessed, to reconvene at 10 a.m., Thursday, May 11.]

[60] reporter.nih.gov/search/TqdUrvtOv0GD2jHNie__YgQ/project-details/10516885.
[61] reporter.nih.gov/search/A6Z2dnBww0SwLArh0G3z8A/project-details/10400321.
[62] reporter.nih.gov/search/A6Z2dnBww0SwLArh0G3z8A/project-details/9979831.
[63] reporter.nih.gov/search/zBDt0NIqqESUbopRoK8FzQ/project-details/10507411.