Attachment—Additional Questions for the Record

Subcommittee on Health
Hearing on
"The Future of Biomedicine: Translating Biomedical Research into Personalized Health Care"
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The Honorable Frank Pallone, Jr. (D-NJ)

1. As you discussed in your testimony, discoveries in basic science have helped form the foundation for precision health. However, we know that the timeline from discovery to societal change is often long. Similarly, there appears to be a long trajectory for moving toward a scientific and medical model of prevention.

    a. What are the biggest barriers to implementing a system of precision health?

    Precision Health seeks to use emerging technologies and our ever-broadening base of biomedical knowledge to not just treat disease but to predict, prevent, and cure it precisely – and critically, in that order.

    While promising, there are a number of barriers. I'd like to outline the three greatest challenges that I believe we can, with federal support, respond to:

    1. Continued investment in basic science enterprise and infrastructure. Public investment in the basic sciences is the bedrock of biomedical innovation — upon which all medical advances are achieved. Yet, success rates for NIH funding applications have fallen — declining to 21% from 32% over the past two decades. This is not for lack of high-quality submissions. Quite the opposite, research proposals that federal agencies rate as excellent often do not receive funding due to resource constraints. Today, we see a wealth of high-potential research still sitting on the shelf.

    Continued strong support for basic science research is necessary and essential to the U.S.'s continued global position as a biomedical leader. As it has so many times before, investing in discovery pays enormous dividends over the long-term by laying the groundwork for transformative technologies, therapies, and cures.

    2. Increased collaboration and partnership across disciplines and industries. The development of vaccines for COVID-19 in record time stands as a monumental achievement made possible by interdisciplinary research

collaboration and partnerships across government, industry, and academia. At Stanford Medicine, we view such collaborations as a defining feature of Precision Health. Continuing to foster these relationships will require strong market incentives and robust investment in public-private programs focused on bringing promising discoveries from bench to bedside – a process that can often take decades and billions of dollars to achieve for a single new therapy.

3. More robust public health training programs to help anticipate and respond to community needs. Well-established evidence shows that 60% to 70% of the factors that determine health are social, environmental, and behavioral in nature. Yet, the U.S. health care system's focus is on treating individuals who are sick instead of preventing disease and maintaining health at the community level.

In 1994, only 1% of U.S. physicians had received formal public health training. Today, public health remains a fraction of our nation's nearly $4 trillion health care budget—with funding projected to fall below 2.5% of total spending by 2023.

COVID-19 has underscored the unfortunate ramifications of bifurcating the fields of medicine and public health. Under our current system, the pandemic has laid bare glaring racial health inequities, overwhelmed intensive care units, and a national vaccination rollout that launched in fits and starts and encountered public hesitancy.

While we are already seeing significant advances in health care because of Precision Health, realizing its full potential will require a strategic change in our overall approach to health care, including with increasing investment into the field of public health.

b. What role do basic and translational research play in the future of precision health?

Basic science research underpins every major biomedical advance – from diagnostics to vaccines to cancer treatments and potential cures for disease. As we strive to realize the promise and potential of Precision Health, continued robust investment in basic research remains critical.

The federal government's general funding of the basic sciences through the NIH has been integral to this country's leadership in research and development of next-generation medicines. Continuing to enhance this investment is essential if we are to remain a global leader in this space. Supporting basic science research allows us to expand our understanding of human biology, open new fields of study, and create a foundation of knowledge that enables breakthroughs that will define the future of patient care – including how we predict, prevent, and cure disease.

Translating basic discoveries into real-world innovations is the next critical hurdle. Too many scientific breakthroughs have withered in the "valley of death" and failed to reach patients due to a lack of funding and long-term support needed to clear regulatory review. This is why, in addition to research in the basic sciences, Stanford Medicine is equally dedicated to translational research. We are proud to work with the NIH's Clinical and Translational Science Awards (CTSA) Program via Spectrum, the Stanford Center for Clinical and Translational Research and Education. Spectrum works across Stanford Medicine to help improve the quality, speed, and impact of researchers working to get more treatments to more patients.

Stanford Medicine has also supported the recent creation of the Arc Institute to foster interdisciplinary translational research. This independent, nonprofit research organization launching in Stanford Research Park has established education, research, and funding collaborations among Stanford University, University of California, Berkeley, and University of California, San Francisco. With an initial focus on complex diseases, including neurodegeneration, cancer, and immune dysfunction, the Arc Institute aims to enable faculty from these three Bay Area universities to freely pursue the research that they feel will be most impactful over an eight-year span. Ten initial donors have pledged to contribute over $650 million to the Institute.

Translating groundbreaking research is critical to Stanford Medicine's Precision Health vision and is why I also strongly support the creation of an Advanced Research Projects Agency for Health (ARPA-H). Having a national agency dedicated to more efficiently moving promising discoveries from lab bench to bedside is a crucial function needed to realize the full potential of life sciences innovations that we see occurring almost daily.

On our own campus, we are currently leading several initiatives that function as a "mini-ARPA-H," so to speak, for accelerating translation. Our Innovative Medicines Accelerator (IMA), for one, seeks to allow high-potential ideas to progress to clinical testing – a challenge facing all academic medical centers. In addition to providing researchers with funding and other resources to support moving ideas to testing therapeutic candidates in animals, the IMA works closely with government, industry, and nonprofits to benefit from others' translational expertise.

Furthering the potential of the IMA, health care investment firm Deerfield Management and Stanford University announced in January the establishment of the Porter Alliance for Innovative Medicines. Designed to accelerate translational research into clinical therapeutics, Deerfield has committed up to $130 million and additional scientific and operational support to this collaboration to advance research coming out of Stanford faculty laboratories with a focus on drug prototypes emerging from the IMA.

As a nation, we owe so much to the basic science and translational researchers who have helped expand our understanding of human biology and brought better outcomes to patients. With continued and expanded federal support for basic science and translational research, I believe we will accelerate the extraordinary discoveries emerging in labs across the country and create a brighter future for people everywhere.

c. How will our health care delivery model need to change to adapt to a system of precision health?

Realizing Precision Health will require significant structural changes to health care delivery. True Precision Health accounts for the whole person and the many factors that influence their health: lifestyle, well-being, environment, genetics, underlying health conditions, and more. Our current system simply isn't architected to account for all of these factors, let alone coordinate the kind of care that can meaningfully apply insights across these many dimensions.

Therefore, a critical area that deserves more attention is also a practical one: how do we design an efficient and impactful Precision Health care model for patients? Among other considerations, this involves defining what kinds of cross-functional workflows, teams, and technologies are needed to enable coordinated, personalized, and holistic care. In 2019, Stanford Medicine initiated a pilot program called Humanwide—built on our Primary Care 2.0 model—to explore these issues.

The initiative brought together a broad team of primary care providers and specialists that sought to deliver Precision Health to a group of 50 diverse patients. Various health interventions were employed, including digital health monitoring, genetic testing, pharmacogenomics, behavioral health, nutrition, chronic disease management, and lifestyle coaching. Critically, this dynamic care team all had access to the same data and regularly huddled to discuss patients' individual needs and chart their progress.

The pilot offers an early blueprint for Precision Health and validates that this approach can work in principle. Moreover, it signals Precision Health's potential to identify previously undiagnosed conditions sooner, impact the onset of chronic disease, and tailor medications based on a person's genetic makeup.

The pilot also demonstrates how Precision Health can improve the experience of care for patients and providers alike. Patients appreciated the strong connection they felt to their care teams, while providers reported feeling more engaged in their work in a team-based model that emphasized prevention.

More research is needed in this area to determine how to practice Precision Health at scale and in different settings.

It is also important to underscore that our care models today are largely a reflection of our existing payment models. The vast majority of health care in the U.S. remains tied to fee-for-service reimbursement, a model that emphasizes volume (i.e., procedures performed, drugs prescribed, tests ordered) over value (i.e., health outcomes achieved). It is a system that is structurally biased toward treating disease after the fact instead of preventing it at the outset. Payment models must evolve to incentivize prediction and prevention at the same level as treating disease if we are to realize the full potential of Precision Health.

A final consideration is the importance of developing new evidence-based care standards for the coming era of personalized medicine. As we learn more about how a patient's health is influenced by personal factors, such as their DNA, creating new evidence-based standards for Precision Health is critical. The first step is enabling high-quality information sharing on the findings of personalized medicine research. Here, I believe that the NIH's *All of US* research program offers a valuable example. The program's emphasis on creating an open data sharing architecture — accessible to approved researchers to study the clinical application of its findings—is precisely the kind of model needed to ensure the development of new care standards can keep pace with the latest medical knowledge.

2. As a scientist, surgeon, and academic leader, you are a strong proponent of translational research. As such, you are well aware of the significant challenges associated with crossing the "Valley of Death" in basic and translational research. As technology advances and leads to breakthroughs in fields like defense and energy, breakthroughs in disease treatment and cures seem to lag behind.

    a. Are there any advancements in contemporary science that benefited from recent federal legislation to cross the "Valley of Death" in basic and translational research?

    The 21st Century Cures Act provided a robust framework of support for translational research through the $4.8 billion it authorized in new funding and by creating new regulatory pathways for achieving FDA approval for promising therapies and medicines.

    The Cures Act, for example, offers fast-track review for eligible regenerative medicine therapies and new antibiotics to accelerate approval for treatments that significantly improve upon the status quo. It also permits companies to submit data outside clinical trials in support of an application for approval of a drug or medical device. This "real-world evidence" includes data from exploratory drug trials and anecdotal clinical data that can be gathered in academic medical centers and small biotech companies rather than chiefly through large pharmaceutical manufacturers.

One modest example of a therapeutic that has benefitted from this change is a cold therapy device used to reduce post-operative pain in patients recovering from surgery to repair a sunken chest wall. The FDA previously approved the device for use in adults, but not in teens — a group for which conducting large-scale clinical trials can be exceedingly difficult. Primarily, this is due to the fact that pediatric patients with complex conditions make up a relatively small portion of the population.

In this case, rather than conducting a large-scale trial, the UCSF-Stanford Pediatric Device Consortium worked with the device manufacturer to obtain real-world evidence to evaluate its safety and benefit. For pediatric patients treated with the device, routinely-collected electronic health records were used to help the FDA evaluate the risks and benefits. Ultimately, the FDA cleared the device for use in treating pediatric patients. This promising therapy for pediatric patients could have easily withered in the "valley of death" if a large-scale clinical trial was the only path to achieving regulatory approval.

Beyond the importance of these flexible pathways for translation, I would like to reiterate the value of the proposed Advanced Research Projects Agency for Health (ARPA-H), which would help bridge the divide from the research bench to bedside. It is a logical next step for scaling our country's substantial investments in breakthrough science.

3. This year marked the 20th anniversary of the project that we all know revolutionized modern medicine, the Human Genome Project.

    a. What has the Human Genome Project enabled us to do?

    In 2003, science achieved the remarkable milestone of sequencing the human genome. It took nearly 13 years, but the effort of an international team of researchers created the first complete map of human genes. This effort enables scientists and clinicians to read a patient's complete DNA makeup, including information about inherited diseases. The information made available through this technique has proven invaluable in furthering both research and patient care.

    Cancer exemplifies the power and potential of genomic sequencing. Though often referred to as a single disease, "cancer" is shorthand for more than 100 diseases with commonalities, as well as distinct characteristics. Sequencing cancer cell DNA allows researchers to identify which genes have mutated, better understand the disease's biology, and more strategically develop potential medicines. On the clinical side, DNA sequencing and the identification of genetic mutations help doctors to diagnose patients more accurately and determine the best course of treatment for an individual patient's cancer.

Though the initial sequencing took more than a decade, the science behind this breakthrough has accelerated exponentially. Today, genome sequencing is described as "rapid" when it is conducted in a few weeks. However, a new ultra-rapid genome sequencing approach developed by Stanford Medicine scientists and their collaborators led to diagnoses of rare genetic diseases in an average of eight hours. The fastest of these sequences took place in just over five hours, a world record.

Every minute is an invaluable resource for a very sick patient suffering from an unknown disease, and could potentially be the difference between life and death. Speed matters. Not only is the new genome sequencing method fast, a small sample showed that it may also potentially improve diagnostic rates of mystery diseases. The ability to have definitive answers within hours would have a transformative impact on medicine and the patients and families struggling to find answers.

Further, genetic sequencing has served as a critical part of the COVID-19 response at Stanford Medicine and worldwide. The Stanford Clinical Virology Lab, for example, has tracked SARS-CoV-2 variants of concern in the Bay Area using sequencing techniques. Having this information, specific to geographic regions, enables health departments to better respond to and mitigate the impacts of new variants as they emerge.

b. There remain significant ethical considerations related to CRISPR and gene editing technologies. What are the biggest opportunities where do we need to err on the side of extreme caution?

We've had the capability to edit genes for many years; however, CRISPR technology has transformed this field, due to its precision, comparatively low cost, and broad applicability. With older gene-editing tools, it could take months for scientists to design each customized protein needed for use. By comparison, RNA templates for CRISPR can be created in a matter of days and can be reprogrammed to target different genes.

CRISPR gene therapy is particularly well suited for diseases caused by mutations in single genes, such as cystic fibrosis and Huntington's disease. As an example, Matthew Porteus, MD, of Stanford Medicine is leading a clinical trial testing a CRISPR-based therapy for sickle cell disease, a blood disorder disproportionately affecting Black Americans that can cause excruciating pain and inhibit the flow of oxygen-rich blood to vital organs. In the therapy, CRISPR is used to repair a DNA mutation in stem cells from bone marrow that produce red blood cells; the newly modified stem cells are then returned to the patient's bloodstream with the aim of spurring the creation of healthy red blood cells.

Scientists at Stanford are also working on CRISPR therapies for treating cancer, including an FDA-approved technique for reprogramming immune cells to target and destroy cancer cells. In addition, CRISPR presents great opportunities for deepening our understanding of disease processes and enhancing precision medicine. For example, at Stanford, Joseph Wu, MD, PhD, and his colleagues developed a technique that uses CRISPR to determine whether a genetic mutation sometimes linked to a heart rhythm disorder is benign or disease-causing in individual patients.

As with all gene-editing technologies, it's imperative to give continuing, careful consideration to ethical concerns. Stanford bioethicists Hank Greeley, JD, a professor of law, and Mildred Cho, PhD, professor of pediatrics and medicine, are available for further discussion of these issues.

4. We have heard today about many of the great strides we have made in biomedical research, and the opportunities that lie ahead. However, we have not extensively discussed the field of pediatric research and the different considerations that apply to breakthroughs around pediatric diseases and conditions. A prime example of this is how long it has taken to develop and approve COVID-19 vaccines for children and adolescents. It is imperative that we invest in pediatric research if we are to address the greatest public health threats facing children in the 21st century, including obesity and malnutrition, diabetes, heart disease, cancer, infectious diseases, genetic disorders, asthma, prematurity, and now COVID-19.

    a. If getting adults to participate in preventative health and wellness has been difficult, what does the model of precision health look like for the pediatric population?

    In 2005, four times as many American children had a chronic condition than those in 1960. Today, more than 40% of school-aged children have at least one chronic health condition, according to the CDC. These conditions often have long-term impacts on health and well-being. But not all populations bear this burden equally; people of color are disproportionately affected.

    These disturbing data illuminate the urgent need for Precision Health approaches. Research shows that instilling healthy behaviors in children not only prevents chronic disease in the near-term, it also produces better outcomes than attempts to alter unhealthy behaviors later in life.

    Stanford Medicine's recently established Office of Child Health Equity (OCHE) utilizes a three-pronged approach to bring Precision Health solutions to the pediatric populations that need them most:

    1) **Policy Participation** — OCHE focuses on drivers of inequities and advocates for health policies that reduce child and maternal health disparities.

2) **Community Engagement** — OCHE works with community partners to respond to pressing child health issues and community-identified needs. The office focuses on collaborative, community-driven approaches, including partnerships with local schools, businesses and institutions. These collaborations engender trust, improve access to health services, and help us identify additional opportunities and strategies to improve community health.

3) **Equity-Oriented Research** — OCHE conducts rigorous research to advance clinical evidence that helps reduce child health disparities. The office has also partnered with the Stanford Maternal and Child Health Research Institute (MCHRI) on a new grant program: Research on the Structural Racism, Social Injustice and Health Disparities in Maternal and Child Health Pilot Grants.

With children, preventive care often involves helping them to develop healthy habits and to manage external forces that could potentially cause harm. In this vein, Stanford scientists investigated the benefits of a school-based health and mindfulness curriculum for elementary and middle school-aged children living in low-income communities. Their research found that at-risk children who received training in techniques to manage stress gained more than an hour of sleep per night compared to their peers — countering the potential negative effects of poor sleep on a child's cognitive, emotions, and psychosocial development.

For behavior change, Stanford research has shown that "stealth interventions" can have an extraordinary impact on the health and well-being of children. For example, Tom Robinson, MD, found that culturally-tailored dance classes targeted to young Black girls in low-income neighborhoods in Oakland, CA, contributed to lower total cholesterol and LDL cholesterol levels, produced beneficial changes to insulin levels, and reduced symptoms of depression. Significantly, 85% of the families stayed in the study for two years.

Another study by Stanford Medicine researchers showed promising results from multifaceted interventions targeting childhood obesity over three years. The trial, which focused on Latino children in low-income communities, could help inform policy and care approaches to reducing childhood obesity in populations at high risk for the condition.

Through a focus on public policy, equity-focused research, and community engagement, Stanford Medicine aims to ensure that more and more people, including the youngest members of our country, benefit from Precision Health.

5. In your testimony, you spoke to the difficulty of securing research grant funding. You cite that since 2000, NIH grant applications have doubled, but the success rate has declined from 32 to 21 percent. You also mention the additional challenges presented by the COVID-19 pandemic, which may have led to lost research productivity decline in investigators. Yet, there is a silver lining in that many more college students are

considering a career in health and science, presenting an opportunity to expand the workforce.

a. Since 2015, NIH appropriations have increased annually by over $1 billion, and they are on par to continue to increase. Still, amid significant increases in funding and grant applications, application success has declined. What are the barriers for researchers in securing funding through the NIH?

   Congress's long-standing bipartisan support of the NIH has funded groundbreaking research across every field of biomedicine. From this investment, we have seen staggering advances that have enhanced our fundamental understanding of human biology and brought forth novel diagnostics and therapies.

   Yet, as noted in the question, success rates for NIH funding applications have dropped to 21% from 32% over the past two decades. Perhaps more telling, research proposals that federal agencies rate as excellent often do not receive funding due to resource constraints. These challenges illustrate the high volume of high-quality research taking place across our country. There is tremendous potential sitting on the shelf.

   Though one might classify this situation as a good problem, it means we are not fully realizing the potential of our country's bright, innovative, and motivated scientists. As I did at my testimony in December, I encourage Congress to further its support of the NIH. Not only would this investment strengthen a strength, it would prove transformative for the health of future generations.

   Additionally, I recommend increased investment in interdisciplinary research, which continues to receive less funding, on average, despite its essential role in innovation and solving our nation's most pressing and complex health challenges. Fields from genomics and chemical engineering, to immunology and behavior science, to biology and public health, all benefit from a robust exchange of ideas, datasets, and peer-reviewed research.

   Finally, I applaud and encourage innovative grant application processes and awards that cater specifically to young, unpublished, and underrepresented minority researchers in science and medicine. Many young and underrepresented researchers cite the complexity and difficulty of the application process, as well as their lack of name recognition, as significant barriers to success. The NIH is well aware of this issue and has found that the average researcher does not receive funding as a Principal Investigator until their 40s. As this is a problem for both the future of science and for researchers that are underrepresented in clinical research, I recommend continued innovation in the processes that award grant funding. To that end, I strongly support the NIH's Next Generation Researchers' Initiative.

b. Respectfully, institutions like Stanford do not have the same financial constraints that other universities and medical schools do, such as Historically Black Colleges and Universities and Minority Serving Institutions. What can be done to increase grant application success for Black investigators and other researchers from underrepresented universities?

Advancing equity within our community, among those we serve, and broadly in the field of medicine is at the heart of Stanford Medicine's mission. Critically, this commitment to inclusion, diversity, and health equity (IDHE) involves fostering opportunities for underrepresented groups in medicine.

Launched in 2021, Stanford Medicine's REACH Initiative (Racial Equity to Advance a Community of Health) is dedicated to training a new generation of biomedical leaders who will actively promote equity and social justice – while working to reduce society's devastating health disparities.

Through REACH, we are investing in postbaccalaureate research programs to provide underrepresented minority students with the valuable clinical experiences needed for competitive medical school applications. This serves not only to diversify admissions into Stanford School of Medicine, but all medical schools.

In addition to prioritizing diversity in admissions, we believe we can advance equity by working directly with underrepresented universities. REACH has forged partnerships between Stanford and all four Historically Black Colleges and Universities with medical schools, which will enable student and faculty exchange programs, as well as robust collaboration and sharing of scholarship and ideas. These efforts build on a 2017 initiative that established a partnership between Stanford and Meharry Medical College in which we share research and mentorship resources. This initiative includes hosting Meharry students at Stanford for sessions on cutting-edge research and innovation.

To expand on and encourage valuable research with underrepresented institutions, I believe that grants specifically encouraging such cross-institution collaboration are warranted. This would not only create more opportunity for minority researchers, but also incentivize institutions with significant research resources to collaborate more frequently with underrepresented universities. In my view, this type of work greatly benefits all involved.

Last, to improve grant application success, we support the expansion of grant programs that specifically seek out and support the research of faculty from underrepresented groups. For instance, at Stanford Medicine, our Office of Faculty Development and Diversity sponsors an annual fellowship funded through our Hispanic Center of Excellence grant. This fellowship helps to advance the careers of junior faculty from underrepresented backgrounds as well as those with academic research in health disparities. Additionally, fellows are

invited to participate in training opportunities that will advance their career development at Stanford.

Programs and grants such as these increase the likelihood of application success for researchers from underrepresented backgrounds, through direct support and by bolstering their research portfolios.

c. How has Stanford increased the diversity of their medical student population and what more can Congress do to create opportunities for these communities?

Inclusion, diversity, and health equity (IDHE) are core values at Stanford Medicine. We work diligently to integrate IDHE into all that we do, from recruitment and leadership development programs to education, research, and community outreach initiatives focused on health equity. As a result of our ongoing efforts to diversify recruitment and admissions, about a third of our current MD and PHD students are from underrepresented minority groups.

One important initiative to support these students is our progressive funding model for tuition and living expenses, which was made possible by a generous matching gift from the late philanthropist and Stanford alumnus John Arrillaga. The funding model ensures that students from underrepresented backgrounds, first-generation students, and students with demonstrated financial need can graduate from the Stanford School of Medicine with little to no student debt. More than half of the award packages offered to our recent incoming class included full tuition and at least some living expenses. In total, $90 million in new scholarship funding is expected to go toward debt elimination for medical students with need over the next 10 years.

We also agree that creating more opportunity in science and medicine for diverse communities is critical. To ensure the broadest possible pipeline of students — and eventual physicians, researchers, and health care leaders — we believe in high school and undergraduate outreach and development programs that inspire underrepresented students from a young age to pursue clinical research and pre-medical education.

In line with this objective, we offer a wide range of educational and internship programs to engage high school students from diverse communities in the surrounding Bay Area. And at the undergraduate level, our REACH program is prepared to support more than 700 first-generation and underrepresented minority students and clinical trainees over the next five years. We believe this type of sustained investment in outreach and education programs in underserved communities can help students gain valuable experience for their applications and, ultimately, contribute to diversifying the medical student pipeline.

These engagement programs should not end once students gain admission to medical school. It is critical to provide ample training, mentorship, and leadership

development opportunities for students to increase representation in leadership and bring more focus to health equity at that level. At Stanford, this takes shape in various initiatives such as our LEAD (Leadership Education in Advancing Diversity) program. This 10-month program allows residents and fellows to develop skills to address IDHE issues, to produce leaders in academic medicine dedicated to IDHE, and to improve the culture of medicine.

Overall, advancing inclusion, diversity, and health equity in medicine is a complex issue that requires dedicated effort at every stage of the medical career pipeline. Programs for younger students should focus on engaging them in education and clinical research opportunities they are passionate about, while initiatives for medical students, residents, and established clinicians should also develop leadership skills and provide career opportunities.

The Honorable Anna G. Eshoo (D-CA)

1. Has your organization engaged with AI-related efforts of the federal government? If so, please share any of your comments or recommendations that you believe would be useful for the Subcommittee on Health with respect to enabling biomedical innovation.

   Stanford Medicine believes that artificial intelligence (AI) and machine learning are central to the future of biomedicine. AI has the potential to be a catalyst for rapid drug discovery and finding new indications, advancing diagnostics, and supporting clinical decision making at the patient bedside. Our Center for Artificial Intelligence in Medicine and Imaging (AIMI) is one of the many institutes exploring how to leverage AI for the benefit of patients and clinical care. We are grateful for Rep. Eshoo's leadership in this area, especially on the establishment of the National Artificial Intelligence Research Resource Task Force, on which our Stanford University colleague Fei Fei Li, PhD, sits.

   Fully realizing the potential of AI in medicine will require sustained focus in several areas. For one, we must continue to develop a talent pool of highly trained data scientists in the U.S. Competition for data scientists remains extraordinarily high, and especially so for individuals with backgrounds that intersect the life sciences and data science. Academic medical centers have an important role to play in cross-training future leaders who are "bilingual" in these domains. At Stanford Medicine, for instance, many of our medical students take courses offered by the School of Engineering to foster this crucial skill set.

   Equally important is the focus on health equity and ethics. If not implemented thoughtfully, AI has the potential to amplify biases that exist in medicine and threaten to exacerbate health inequities. If you are interested, I would be glad to connect you with David Magnus, PhD, one of our leading bioethicists who can discuss these considerations in greater detail.

2. Please describe any legal, policy, technical, or other protections that protects the privacy of personal information used in research conducted by your institution.

   Stanford Medicine and all members of the University community are responsible for sustaining the highest ethical standards. It is a responsibility that we take very seriously in our research, and we have robust policies and programs in place to protect privacy and ensure compliance with all regulations governing clinical research.

   Our Office of Research develops policies and practices to advance rigorous and transformative research while ensuring compliance with federal regulations, state laws, and institutional policies, which you can read more about here. On this site, we detail numerous programs at Stanford that, among other objectives, standardize research best practices across our institution, offer extensive training to our investigators, and ensure compliance at every step of the research process.

   We pride ourselves on our rigorous Institutional Review Board (IRB) process, which evaluates all research involving human subjects at Stanford Medicine to ensure the ethical and equitable treatment of those subjects. This includes a comprehensive review of how any study will address patient privacy and the handling of sensitive data — including studies conducted in partnership with other institutions. The IRB can approve, require changes, or reject any research that does not meet our high standards for privacy.

   a. Do you believe the lack of a comprehensive privacy law reduces the desire of subjects to participate in biomedical research?

      Not necessarily. Between the Common Rule and HIPAA, along with the ability to place certain studies under a Certificate of Confidentiality, I believe there are adequate protections in place for patient privacy. Clinical trials take these protections very seriously and communicate them to prospective participants. In our experience, the lack of an additional privacy law has not been a key deterrent for potential research subjects. Though, further study of this issue is warranted.

   b. Do you believe federal privacy protections need to improve to protect individuals while also enabling medical research?

      Fortunately, academic medicine has multiple safeguards in place to protect research participants' rights, including their privacy rights, which align with and/or exceed existing regulations. Further alignment between existing laws, such as HIPAA and the Common Rule, would continue to protect patients while enabling biomedical research.

The Honorable Michael C. Burgess, M.D. (R-TX)

1. In your opening testimony, you described precision medicine as "an approach to predict, prevent, and cure." Clearly there is great potential for this approach to patient care. How can we ensure that patients have access to health care providers with specialized training in this area?

   I believe advances in virtual health have significant potential to expand patient care access in communities that lack specialists and other essential expertise.

   The dramatic rise of telehealth during the pandemic is well-documented. Like many other health systems across the United States, Stanford Medicine accelerated our expansion of this capability and saw an enthusiastic response from our patients. After experiencing a video visit, more than three out of four patients said that they were very or extremely likely to choose a video visit over an in-person visit. This format allows providers to see more patients and to see them more frequently and efficiently, increasing convenience, and bridge geographic distance for our patients.

   Though some types of care are more conducive to virtual visits than others, I believe it can be a powerful tool for connecting patients with specialists that they might not otherwise have access to. As health systems hardwire this format into health care delivery, however, we recognize that barriers remain that must be addressed.

   Many communities in the United States – particularly in rural areas — lack reliable broadband to support telehealth services. We are also mindful of the 'digital divide,' separating people with greater access to technology from those, typically in underserved communities, who do not. Access to the internet isn't the only barrier to using digital health technology. Digital literacy can also be a challenge and is something that can be addressed through thoughtful telehealth design to help those with limited digital experience navigate virtual care. Moreover, providing options for different languages and culturally competent care must be integral to the ongoing development of these systems.

   Waived requirements for telehealth services, enabled by the national Public Health Emergency (PHE) declaration on COVID-19, has been instrumental to the broad success that U.S. health providers and patients have experienced via this format. Recognizing that the PHE is temporary, we ask Congress to pass legislation updating requirements, so that telehealth can be a service that truly reflects the 21st Century.

2. In the hearing you elaborated on the benefits of integrating more personalized health care into practice. You mentioned the potential precision medicine has in reducing the cost of prescription drugs and treatments for patients by using pharmacogenetics to target the

most effective and efficient treatment. How can we encourage greater patient access to precision medicine?

As a matter of practicality, a patient today seeking the kind of personalized and holistic care we envision for Precision Health would have a difficult time finding it. That is because, at a national level, we have yet to design a scalable model for care that accounts for the many unique factors that influence a person's overall health.

However, at Stanford Medicine, we recently piloted such an effort through a program called Humanwide – built on our Primary Care 2.0 model. The goal of this initiative was to better understand the workflows, teams, and technologies needed to enable a Precision Health model. Various approaches were tested as a cohort of 50 diverse patients went through the pilot, receiving many different kinds of health interventions from a dedicated team of care providers, coaches, and specialists. This included the use of pharmacogenomics to match medications to a person's unique genetic make-up.

Though conducted at a small scale, the initiative signaled, among other health outcomes, that a Precision Health model could have value in prescribing more precisely tailored medications and potentially avoid adverse drug reactions that are influenced by a person's genetic make-up.

More research is needed to determine how this Precision Health model could be applied at a national scale, as well as the barriers that would need to be overcome, including challenges associated with reimbursement. Fee-for-service payment underpins most of health care today (i.e., most payment is tied to reactive "sick care"), while Precision Health would require a significant shift in payment toward predicting and preventing disease.

When thinking about access, fostering community partnerships is another crucial part of the solution. Sadly, as we have seen during the pandemic, access to quality health care, let alone Precision Health, remains a major obstacle in this country.

Closing these care gaps through collaborations involving care providers, community groups, and public health departments, will be an important first step to expanding equitable access to the kinds of medical advances I believe we will see take shape over the next decade.

a. Do you envision specialists, such as genetic counselors, playing a role in increasing access to these services? If so, how can our health care providers better utilize these specialists?

Our genetics have a significant bearing on life-long health, and we're learning more every day about how to incorporate this knowledge into care delivery.

Given that genetic screening is often the front door to personalized care, it underscores the importance of knowledgeable genetic counseling when interpreting results and advising patients on potential health risks.

Yet, physicians and those in training report not feeling prepared to incorporate this information into clinical practice. According to a 2019 survey of physicians, medical students, and residents commissioned by Stanford Medicine, only 21% of physicians and 7% of students and residents said they felt very prepared to use genetic screening for health risks in practice.

Academic medical centers play an important role in increasing clinician fluency in this domain, which by extension, will empower more productive collaborations with genetic counselors in developing care strategies for patients that are informed by DNA testing.

The Honorable Richard Hudson (R-NC)

1. Public engagement, understanding, and meeting the public's needs is key to optimizing the impact of biomedical research in our communities. How can we best communicate and engage with the public as to the outcomes and impact of biomedical research on their day-to-day lives? In this communication and engagement, how do we best minimize misinformation and maximize public trust? If applicable, please explain the strategies and tactics your organization or entity are utilizing to best communicate and engage with the public with regards to your biomedical research work.

   We place a high priority on helping our patients, our surrounding communities, and the general public access accurate and relevant information about medicine, public health, and biomedical research.

   The foundation for this communication is openness and transparency about our work. We publish regular reports on our research and clinical developments on a number of digital platforms, including news releases, conversational blog posts, longer-form magazine articles, and videos. We also invite members of our surrounding communities to campus for events supporting wellness through accessible presentations on the latest research and practical tips for healthy living.

   As important as it is to create a welcoming environment on campus and in our clinical spaces, we also recognize that fostering a strong relationship with the general public requires reaching beyond our own region. This has been particularly true during the pandemic, when safety precautions have limited in-person interactions and widely-accessible, understandable information has been in great demand.

Our partnerships with local organizations, state and county public health departments, and national and international public health groups have been instrumental for us in determining what information is most relevant for different audiences and how to connect with them in meaningful ways. To support health in underserved populations in our local community, for example, we worked with partners to participate in virtual information events and to create resources devoted to COVID-19, with FAQs, videos, model social media messages, infographics, and many other informational resources in both English and Spanish. We also established vaccination sites in areas hardest hit by the pandemic, and continued mobile services to reach individuals near their homes.

On a national level, our experts teamed with the Kaiser Family Foundation in a series of short videos focusing on frequently asked questions about vaccines from minority communities. To reach audiences around the globe, Stanford Medicine experts have created animated videos that are designed to transcend language barriers, communicating public health messages through engaging visual narratives. These videos enjoyed wide distribution through partnerships with international groups.

Several Stanford Medicine experts are available to speak further about countering misinformation, including Douglas Owens, MD, professor of health policy and chair of the department of health policy, and Yvonne Maldonado, MD, professor of pediatrics and of epidemiology and population health.

2. Public-private partnerships are a critical part of ensuring translational biomedical research continues to progress and achieve success. How can we better foster innovative public-private partnerships to maximize such progress and success? If applicable, please explain how your organization or entity is approaching the development and furthering of public-private partnerships.

Public-private partnerships are a catalyst for biomedical innovation. Stanford Medicine deeply values our collaborations with the government to advance translational research, including the work of the Stanford Center for Clinical and Translational Research and Education (Spectrum) with the NIH.

An area worth further exploration is the co-development of new initiatives between the government and various research and health care entities. The establishment of ARPA-H, for instance, could benefit from outside clinical, scientific, and industry advisors to ensure its objectives, funding models, and processes are aligned with the practices of the broader biomedical research community and oriented to address barriers that impact translation.

3. How can stakeholders – participants, patients, researchers, and providers – best work with state and local public health departments, as well as our communities, to maximize the public health impact and outcomes of biomedical research?

COVID-19 has demonstrated just how crucial it is for the medical establishment to reimagine its relationship with public health. For the past century, medicine and public health have more or less operated in isolation. Yet, we see that both perspectives are crucial to improving people's health and bolstering our nation's resilience to future pandemic threats.

I believe a combination of solutions will be required to bridge this divide and begin integrating these perspectives. For one, public health receives a fraction of investment when compared to our nation's $4 trillion health care budget. One projection estimates public health will fall below 2.5% of overall health care spending in the U.S. by next year. That is despite well-established evidence that 60% to 70% percent of the factors that determine our health are social, environmental, and behavioral in nature. These issues are at the heart of public health practice and suggest an alignment problem with how funding is allocated today.

It is well-documented that only a small fraction of physicians today receive rigorous training in public health, and fewer still pursue degrees in both disciplines. I believe that this is an important role that academic medical centers can play.

While Stanford and many other medical schools offer public health courses and the option to pursue dual-degree programs, this still puts too much onus on students to volunteer for these opportunities. Looking ahead, there is a significant opportunity to more natively integrate public health into the core curricula. But here, too, reimbursement remains an obstacle. Until we have a reimbursement system that rewards for outcomes and preventing disease, even the best-trained physicians will be limited in what they can accomplish.

In addition to bridging the gap between medicine and public health, designing future research programs that emphasize community engagement can be a powerful way to maximize health outcomes. One way to engage our communities in research about human health is to invite them to participate, as the NIH's *All of Us* research program has. Through this ambitious effort, researchers are compiling one of the world's largest and most diverse databases of health information, with the aim of informing studies on a variety of health conditions and advancing individualized care. More than one million people across the United States have been invited to contribute their health data over an extended period, to provide a robust and representative dataset. Through their participation, individuals can be connected to clinical studies that meet their needs, and broadly gain a stronger understanding of the research process. *All of Us* also was designed to include

participants in its design, implementation, and governance, with representatives serving on committees, boards, task forces that oversee the program.

The Honorable Janice D. Schakowsky (D-IL)

1. Publicly funded research from the National Institutes of Health (NIH) is at the heart of nearly every biomedical and pharmaceutical breakthrough, including mRNA COVID-19 vaccines. As previously noted, beyond the hundreds of thousands of lives saved, the United States would be in an even more challenging financial and economic position had it not been for the decades of research that preceded this devasting pandemic.

   Unfortunately, outside of the United States and a handful of other rich countries, only a tiny percentage of people have received shots in arms. Currently, over 130 World Trade Organization (WTO) member countries support a proposal for the WTO to provide a temporary waiver of intellectual property barriers that vaccine makers use to guard their monopolies. In May 2021, the Biden Administration announced support for a temporary waiver of these barriers; however, as of December 2021, the WTO has not provided text or any agreement to move forward. The E.U. and Germany appear to be blocking negotiations. Meanwhile, over 800,000 Americans and over five million people worldwide have died from COVID-19.

   A former Moderna chemistry chief revealed that with technology transfer and know-how-sharing, any modern factory should be able to get mRNA vaccine production online in, at most, three to four months.

   a. Do you believe that if other countries, particularly low- to middle-income countries, were permitted to manufacture the Pfizer and Moderna vaccines to vaccinate their populations, it would stop the development & spread of deadly COVID-19 variants, and effectively end the pandemic?

      Ensuring global access to vaccines remains absolutely critical to ending the pandemic and mitigating the spread of future COVID-19 variants. I am especially encouraged by the international community's recent efforts on this front and the pledge by the U.S. to donate 1.1 billion vaccine doses for global use before 2023. Still, there is more that can and must be done to ensure all are protected.

      The issue you raise with regard to manufacturing is an important question. Drug development, as the current model exists in the U.S. today, is one of extremes: high-risk and high-reward. Roughly 90% of all drugs fail clinical trials and never win approval.

      Market incentives, such as intellectual property rights, have historically been part of what fuels our nation's biomedical innovation engine. At the same time, these financial interests must absolutely be balanced with the needs of patients who

ultimately benefit from new drugs and therapies — particularly during times of crisis. How this balance should be struck to optimize for equity and innovation deserves rigorous study.

At Stanford Medicine, Michele Barry, MD, FACP, leads our Center for Innovation in Global Health and can speak with you further on issues of global health equity.

b. In your testimony, you also mentioned the toll, both physical and economic, of Alzheimer's Disease. Publicly funded NIH scientists across the country are working to find a treatment. If a breakthrough were found, do you believe it would be fair to Americans suffering from Alzheimer's Disease – who have paid into the research and development of the cure through taxpayer dollars – to pay $64,000 per year for a lifesaving treatment?

Balancing biomedical innovation with issues of access, cost, and outcomes for patients is one the more challenging issues we will navigate in the coming decades, as a growing number of precision therapies and cures achieve regulatory approval.

How these advances should be evaluated for clinical use and who pays for them are both areas that our faculty have explored extensively. If you are interested in a conversation, I would be glad to connect you to Kevin Shulman, MD, at Stanford Medicine, who can discuss this further, including considerations in the area of Alzheimer's disease.