

2017 National Health Research Forum

Mary Woolley:

Good morning. Please, take your seat. We want to get started here. We have such a fantastic program, I'm sure you agree. So, we want to get right into it. Welcome to Research!America's National Health Research Forum. I'm Mary Woolley, President of Research!America. And on behalf of our board, and if our board members just kind of either stand up or wave your hands. So many of you are here. Thank you. And, our extraordinary staff. My colleagues on staff, take a bow, you all. They're not all in the room.

[applause]

We thank you for being here today. And to those who are not in the room, thank you for joining the webcast, which is made possible by WebMD. This year's straight talk program has a provocative theme. I think you would agree. Is a disease-free world within reach? Disease-free world. And we've invited our panelists and speakers today to share their insights on whether we're getting steadily closer to meeting that aspiration, or whether we're slipping further away. And what are the conditions, the challenges, the opportunities that can speed medical progress and get us to that goal. How can we make significant strides in prevention and treatment, halt the progression of disease, and combat threats like the opioid epidemic, Alzheimer's disease, cancer, cardiovascular disease and so much more? Big questions, to be sure. And I'm sure we're going to get some straight talk.

Research!America, our member organizations and partners are actively advocating every day for robust funding for research and public health and for policies that drive private sector innovation instead of getting in the way. We are urging Congress to pass a bipartisan budget that would raise spending caps to help unleash the innovation that could bring us closer to cures and the eradication of deadly and disabling diseases.

We also urge Congress to repeal the medical device tax once and for all. It's a barrier that is slowing down the very innovation that we need to develop state-of-the-art devices to support our wounded warriors and countless other patients. We're counting on all of the advocates for research to step up your game, contact members of Congress before decisions are made that will affect us all for a long time to come.

Please join us on a two-day social media push this coming Monday and Tuesday. It's the 11th and 12th of September to urge Congress to raise the spending caps. You can check that out on social media, Twitter, and Facebook for details. And I'm sure that our panelists will share examples of why it's important, to add to those you already know, to strengthen our national commitment to research.

Before we begin today's discussions, I want to thank our sponsors. First of all, to Pfizer, our lead sponsor today. To our panel sponsors, AdvaMed, Amgen, Celgene, Elsevier, Janssen Pharmaceutical Companies of Johnson & Johnson, PCORI, and UCB. And to our science sponsors, Astellas, The American Association of Colleges of Pharmacy, the American Cancer Society, the American Heart Association, American Public Health Association, Bristol-Myers

Squibb, and Sanofi. And to our media sponsors, PoliticoPro, you may have seen the ad yesterday in Politico, and WebMD, which is hosting today's live stream to viewers across the country. We hope all of you will join the conversation on social media using the hashtag #RAForum17. #RAForum17.

So, right now, without further ado, we're going to hear from our keynote speaker, Dr. Mikael Dolsten, President, Worldwide Research & Development of Pfizer, the lead sponsor of today's program. Please welcome Dr. Dolsten.

[applause]

And please enjoy your lunch.

Mikael Dolsten:

It's a privilege to be here, and it feels a little bit special as Research!America put forward such a challenge to all of us: is the disease-free world within reach? A very ambitious question. Well, from a science perspective, the opportunity has never been greater to take on such a bold challenge and ambition. We are at a true crossroads for scientific innovation from basic science to clinical medicines to technologies that allow diagnostics or digital devices to be used in health care. While we can dream about cures being within reach, it is not contribution from one group. So, the R&D ecosystem must commit to further acceleration working together over boundaries, and it is a real opportunity today, in this very exciting time, to start the journey with a more swift speed.

If we just look at the few years that have passed, we have seen some example of what we can accomplish. Triggered by the economic revolution, we have seen extraordinary gains in treatment of what was a chronic progressive and fatal disease, Hepatitis C. By novel antivirals and the pioneers among several pharmas contributed by Gilead.

We have been among, in Pfizer, among several American pharma that have advanced novel targeted therapy for cancer. And we're seeing in parallel the revolution of immune oncology. So, while we have been very proud of being mustering the cell cycle to give new hope for cure in the future for breast cancer patients, note that I'm sitting to a fellow colleague from J&J that have made fabulous contribution in blood cancers and more recently in the unleashing of the immune system against tumors. We can see an armamentarium of opportunities that give hope that a disease-free world for some patient may be within reach.

We have patients that are born with faulty genes and have a projected life of disability and possible fatal outcome. We have been proud to be partnering with American biotech companies to advance gene therapies. And we've seen very recent accomplishment in clinical giving hope that we may be able to cure some of those genetic difficult diseases. But how can we really move faster, be bolder, and aim high for disease-free future for more and more patients?

I had an opportunity to participate in the blue ribbon panel hosted by former Vice President Biden, and I was inspired by the moonshot goal of a decade's worth of progress in five years. While it may be an opportunity to start a journey to stretch beyond that, to think about more than

a decade's worth of progress in less than five years but for many more patients than just cancer patients. And that is the real opportunity here. To take that inspiring, bold move but to think about the many patients, whether it's in neurological disease, muscular skeletal disease, psychiatric disease, infectious diseases; all of them should be benefiting from us taking this bold goal on.

So, what do we need to achieve in order to make it happen? We need to address new development paradigms. We need to ensure sustained funding levels for NIH and the regulatory system built for the 21st Century. And, of course, that these discoveries of new medicines has a health care system that ensures great patient access.

Well, when not all pieces are in place, setbacks may occur and actually, quite recently in Europe, the first approved gene therapy was pulled off the market due to lack to access, sufficient reimbursement, and investment around that therapy. So, it's really on all of us to ensure that we deliver for patients an integrated system of innovation.

We have tried to up our aspiration and inspire now to deliver up to 30 approvals of new medicines in the next five years. We're rethinking, in our company, the development process to bring therapies much faster forward and hopefully to see on average that we will see medicine instead of close to 10 years development time, maybe five years or less. We're looking at ways to perform small efficacy studies early in the clinic to identify the compounds to see the problems or to fail fast.

And to look at ways to leverage big data that allow us to see new patterns, get new insights to human disease so that we can select the right medicine for the right patient with a much better precision. Well, to achieve a more than a decade's worth of progress in less than five years, we need to work together to make sure that NIH can continue its role as a catalyst in the innovation system. To foster the great basic research that can provide medical insights and move forward consortium initiatives that bring everyone to the table. Such as, accelerating medicine partnership that has been launched to Cancer Moonshot and *All of Us*, the one million American precision medicine initiative.

I had a personal opportunity to work with Francis Collins that I think will attend later today and see the drive and commitment when we come together, to take on as a team, these extraordinarily important challenges. At the same time, NIH needs to be able to, through the grants across America, force the next generation of science talents so that our journey doesn't last a decade, but many decades and lasts centuries. Today, the funding that has happened over the last few years, in public and private investment, have made the U.S. a leader in bio-medical R&D and more than half of the thousands of medicine in global development were originated in the US. But we need to make sure that the past success becomes an even greater success of the future and to have a well-funded public sector, working with a vibrant private sector that has the right policies and incentives to succeed. And all of you are so important in making this happen.

When I think of a decade's worth of progress in less than five years, for all patient, not just for cancer patients, FDA has done a pioneering effort in breakthrough therapy pathways that has benefited many cancer patients and some rare disease patients. But if we, today, embrace the

broader goal of aiming to achieve the same aspiration for all patients, we haven't seen the same impact of the FDA to accelerate development and regulatory approval for other patient groups. Patients that suffer from pain, neurological disease, diabetes, infectious diseases. We also would welcome very much the FDA to partner with NIH and with companies to make sure that we can find novel surrogate markers that are predictive for disease and can allow new medicines that show promise to come much faster to patients in urgent need in order to have years of wait for therapies based on traditional ways of getting approvals that are very lengthy.

If there is our steadfast partner in drug development with a lot of deep expertise, we're encouraged by the early work of Commissioner Dr. Scott Gottlieb, that I think is also attending here today. And we hope the work of Dr. Gottlieb with the agency would help to implement the provision of the 21st Century Cures Act to further accelerate regulatory and development of new medicines. To achieve more than a decade worth of progress in less than five years, we also need to think about the critical role of electronic medical records.

In this digital age where information needs to be gathered and aggregated, we still have a very fragmented system. What if the day and age medical provide us insurance companies would come together and unite around one universal database that could give patients the deep insight of all the data to share with the physicians or others that participate to provide innovations over time? But we need, of course, to balance that with patient privacy and security.

Finally, this wonderful aspiration, let's think about what it could mean for patients and outcomes. For the many patient groups that would really feel that it's a disease-free world within reach is coming closer. And that there is hope of continued progress. We need equally to be open-minded and creative to ensure access while ensuring a healthy reimbursement ecosystem that allows full continued investment R&D. Access to leading care is one of the tenants of the health care system in this nation, and we need to make sure that all of these promising discoveries of new medicines become, as soon as possible, available for every patient suffering from those diseases.

More than a decade's worth or progress in less than five years, it can happen for many more patients if we can work together as a large team. We have come together in this nation many times to take on extraordinary challenges. We've done things that have been impossible anywhere else, and when I look across this room, I can see many brave, committed leaders that want to join our peers of the past that made extraordinary accomplishments.

So I do look forward to great conversation today. We can do it together and to take on the challenge of making steps forward to disease-free world within reach faster.

Thank you very much.

Mary Woolley:

Wow. I think you would agree that that was a perfect stage setter. I love the aspiration of a decade's worth of progress in five years or less. That could -- maybe we'll steal that for our title next year, Mikael. Just fabulous.

So I'm sure our first panel will be building on that concept and if they would come up now -- the

first panel. You're ready to go. The moderator of our first panel is Marilyn Serafini, a health care policy consultant and an award-winning journalist. Marilyn has been president and co-CEO -- excuse me, of the Alliance for Health Reform, now called the Alliance for Health Policy, a nonpartisan, non-profit organization dedicated to helping policymakers understand the foundations of health policy. She covered Congress, the White House and K Street for various publications including *Kaiser Health News* and *National Journal*.

And our panelists today are Dr. Anne Schuchat, the Principal Deputy Director for the Centers for Disease Control and Prevention; Seth Ginsberg, co-founder and president of Global Healthy Living Foundation; Gopal Khanna, Director of the Agency for Healthcare Research and Quality or AHRQ; Dr. Lucinda Maine, executive vice president and CEO of the American Association of Colleges of Pharmacy. We also have Congressman -- former Congressman Patrick Kennedy, also a former Research!America board member. Welcome. And we will be joined also by Governor Charlie Baker of Massachusetts, who will join the panel when he arrives.

So Marilyn, over to you.

Marilyn Serafini:

Great. Thank you so much, and thank you, everyone, for being here for this important conversation and especially to our experts on the panel today for being here. So we've just heard about a vision for a world without disease. So, how do we get from here to there? How do we achieve that? We've talked a lot about cures, but we're going to spend some time during this panel talking about preventing and managing chronic disease, and promoting better quality of life and how we do that without feeding the opioid epidemic, which is on everybody's mind.

So, we're going to start right off by identifying some of today's greatest challenges, and I'm going to turn first to Dr. Schuchat with the CDC. So, let's start by talking about a challenge that our new surgeon general has identified as the top priority and that's obesity. Which of course, feeds into diabetes, which of course, feeds into other chronic conditions. So, CDC data seems to indicate that we're not making a lot of progress in this area. Can you help us to understand the size and the scope of this problem and what the trend is?

Anne Schuchat:

Yeah. This is a tremendous problem. First of all, it's just a pleasure to get to be here again and to see all of you. Obesity is one of the toughest issues that we're facing. One out of three Americans is obese. Another one out of three is overweight. And both of those factors can lead to risk of many complex chronic diseases that shorten people's lives and reduce the quality of life that they have. We don't have perfect solutions for adult obesity right now. The most promising data we have is about preventing people from becoming obese and particularly trying to tackle childhood obesity with really making a difference in the early years.

There are lots of research projects ongoing right now to try to find solutions that will scale, but it turns out that reducing weight a little bit, not totally reversing obesity, but actually modest weight loss can really improve quality of life and reduce complications.

We're focused right now on pre-diabetes. Again, one out of three Americans, or 84 million

Americans have pre-diabetes. And that's a condition that puts you at great risk for type II diabetes and heart attack, stroke, blindness. We've issued a big campaign about a year and a half ago that started. Go to, you know, doihaveprediabetes.org to see more about it. But it involves shameless exploitation of cute animals to try to help people figure out, you know, am I one of those people who has enough risk factors that I need to attend to it?

Obesity can seem hopeless, but as the surgeon general has promoted, there's simple steps people can take to try to improve their quality of life even if major weight loss doesn't occur. Control of, like, blood pressure, improving physical activity, improving healthy diet, modest weight loss can make a huge difference.

Marilyn Serafini:

Great. So, there are other important trends in disease and chronic disease that the CDC is reporting on.

Anne Schuchat:

Yeah. You know, the news for the past few decades, as you heard in the keynote, has really been good with huge decreases in deaths from heart disease, stroke, and cancer. From 2000 to 2013, we had a 38 percent drop in deaths from stroke. But you may have seen yesterday we reported that has now reversed, and we are starting to see, actually, an increase in deaths from stroke. What we think is happening is the obesity epidemic, uncontrolled risk factors like hypertension are catching up with us. And while the incredible medical breakthroughs that many of your companies or your research groups have contributed to has led to better treatment of strokes and a reduction of death from strokes over the past few decades, now we're seeing a reversal.

Three out of four states have seen increases instead of decreases. So, we have a lot more work to do, again, going back to controlling these terrible risk factors for chronic disease conditions and poor quality of life. The biggest thing, of course, that's going off that has all of our attentions is the opioid epidemic, and I know we're going to get into that in more detail.

Marilyn Serafini:

Absolutely. Seth Ginsberg. At the Global Healthy Living Foundation, you seek to help patients better manage pain. Everything from migraine to arthritis, osteoporosis. Talk a little bit about that. Help us to understand the scope of the pain problem.

Seth Ginsberg:

Sure. So, it's huge to very huge. Unfortunately here in the U.S., worldwide actually. But according to the Institute of Medicine, for example, over 100 million Americans report pain, and that might be discrete pain caused for example, post-operative or from malignancy, but it could also be the disease itself through headaches; right? And so -- or migraines. And as a result, the U.S. spends over half a trillion dollars a year in direct and indirect cost dealing with pain. And that is a number too large to fathom. And you know, reason enough to focus as much effort and bandwidth as possible on the subject as I know so many experts here do regularly, which is amazing.

But as an organization representing folks whose pain ranges, again, from post-operative

arthroplasty pain as a result of a joint replacement or prior to that from the osteoarthritis that led to the arthroplasty to folks who have migraines, you know? Fifteen, 16 million Americans are incapacitated due to migraines and headaches.

I know this firsthand as the caregiver, as the spouse of somebody who literally, unfortunately, because the pain -- the headache medicine was checked under the hull of a plane, which will never happen again, nearly needed to divert an airplane, you know, as a result of an incredibly horrible migraine. And so, as a result of that firsthand, but naturally, you know, representing patients, you know, throughout the U.S. living with this, you know, the spectrum of pain, it's an issue we need to tackle and we need to address head on, so to speak.

Marilyn Serafini:

Are we treating -- and by the way, I can relate to your wife on the migraines. Are we treating pain wrong?

Seth Ginsberg:

I would say we're treating pain okay and we need to treat pain much better. But instead of indicting the entire medical community for how we're treating pain, I'd prefer to look at the glass half full and look at all the opportunities we can, as a society, improve the treatment and the management of chronic pain.

Marilyn Serafini:

Okay. Great. So Gopal. How do we leverage data and analytics to understand the trends in health care and some of these trends that we're hearing about?

Gopal Khanna:

Well, the keynote speaker did the job for me. He talked about data and the significance and importance of it. And we at AHRQ are -- one of the three core competencies is data, how we bring data together, harmonize it, leverage it and through trends analysis, we've been doing that for a long time. And I'll give you an example. It was the analysis of the data we collect from the states that helped us identify the opioid problem a couple of years before anybody else even recognized how large and big that problem was.

So, data is extremely important not just to track but to identify and take a predictive approach so that solutions can be thought of from a policy point of view as well as the point of care and most importantly for research purposes as well. So, the data is really the underlying infrastructure upon which research will be conducted going forward. Analytics will be done to identify challenges and problems. And opportunities for solutions as well.

So, it has become an integral part and it is a core competency that makes ARHQ distinct in the whole health care complex.

Marilyn Serafini:

Can you take a minute to -- I think most of our members of our audience are familiar with ARHQ, but I think it would be helpful to just take a minute to describe what ARHQ is, what ARHQ does and how ARHQ is involved in this particular effort.

Gopal Khanna:

I think I'll go back again to our keynote speaker. He was talking about large, big disease eradication. We are the people at ARHQ who are the bridge between research and practice. We bring it to where the need is at the point of care. Where the physicians are, primary physicians, clinicians are and working with the patients. So, that, in a nutshell, is what ARHQ all about. All the research must happen. We take all of that and make quality care happen, safe care happen, and evidence-based practices get put into place at the point of care. Where the rubber meets the road, by the way.

Marilyn Serafini:

Okay. Great. So Lucinda Maine, we're going to turn now, in full force, to the opioid epidemic and talk about how this -- how prevention and chronic care management intersects with the opioid epidemic and what's being done to deal with this or what kind of progress we're making.

Ninety-one Americans die every day from an opioid overdose and health care costs for opioid substance use disorders exceed \$26 billion -- with a B -- a year in direct costs. So, with that in mind, how should we prioritize our research efforts to achieve the best return for the nation's health while also reducing costs?

Lucinda Maine:

It's a really important question. As I think about the opioid issue, every time I try to touch it, it just gets bigger and more complex. And I think that it is a great example of really great intentions -- clinical intentions, regulatory intentions -- resulting in unintended, unexpected, and really tragic consequences. And I really think there's two elements to addressing the crisis, and there's no simple answer because there's a lot of vectors in it. One is definitely research. And the other is education.

And so, on the research side, it goes everywhere from understanding pain better as a neurological phenomenon to finding some non-addictive strategies for addressing pain more effectively. From the -- all the way to other end, to your end, of really understanding the socioeconomic and behavioral issues that would help clinicians and regulators make better choices at the individual patient level and at the population level.

And from the regulatory science perspective, you just have to think about what's happening across America when the regulators with every good intention, have limited access to the opioids as, you know, safe when used properly, regulated drugs and what happens. Heroin and Fentanyl become the leading cause of death in this.

And so, we have to have more data. We have to have greater insights into genetics to understand when genetics begins to influence the use of these products and their addictive qualities. And there's so much we don't know that that goes over into the education, which I think we can come back to later, but across the board there's just a real lack of sufficient education for clinicians and patients and everybody else in the ecosystem at this point in time.

Marilyn Serafini:

So I feel super confident that the rest of our panelists want to weigh in on this, but hold on just for a minute because I want to turn to Congressman Kennedy to talk about what you see as the needs for both research and action and answers. Congressman Kennedy is serving on the White House opioid task force along with Governor Baker. And I'd like you to tell us what's going on, where we are, and then I think everyone's going to want to weight in.

Patrick Kennedy:

Thank you. Well, I'll speak for Governor Baker as well since I'm originally from Massachusetts and now I can take up both of the time for him and I both combined. But it's great to see my former colleagues Mike Castel and Bart Gordon, great friend and of course John Porter, our great champion for research in this town and thank you, Mary, for inviting me.

So, I am an opiate addict. I'm in recovery. Six and a half years as of -- just recently. And so, I used to take Suboxone in order to be able to cope with the opioid addiction while serving in Congress. I used to also choose to go on what they were called "drug holidays" and that is because I had to take the drug just daily, I could choose not to take it. And I say that because one of the big knocks against medication-assisted treatment, which is the evidence form of care for this opioid crisis is the stigma against medication-assisted treatment. Because there is so much diversion of Suboxone.

So, where are we right now? We have soon to speak the FDA Commissioner, who's promised to make this his number one priority. He could literally expedite two different forms of medication that would transform the treatment -- medication-assisted treatment -- and absolutely end diversion. Because they're long-acting Buprenorphine, once a week, once a month, they are able to intermingle based upon the personalized medicine of the person with addiction because the person with addiction, we're not all the same, like any other illness. There are different stratification of people with addiction and that ought to happen tomorrow, given the number of people dying every day. And we're going to make that recommendation in the president's report. No reason to hold back anymore. All the due diligence has been done by FDA. The only thing is the protracted, you know, dot the I's, cross the T's. All the trials have been done.

Secondarily, to the question of pain management. So, I have -- I'm now sober, let's say four years. I try to catch a falling ping pong table. I don't recommend anybody try to do that. It nearly took the top of one of my fingers off. I had to go to the ER. I told the doctors that I was allergic to penicillin and opioids. They hadn't heard that before. It was like what? Allergic to opioids? They didn't know that you could be allergic to opioids.

That's part of the medical culture that also has to change, but my point is that's all they had to treat me. In their mind. Now, if I had to risk whether there would be side effects to a non-opioid pain reliever versus and opioid pain reliever, I would say to the commissioner, I'll take my chances with the side effects for this other option other than the opioid, even if it has potential real detrimental side effects because against me getting addicted again, I'll take that. Right now, there aren't adequate number of drugs in the pipeline to treat those who have the high-risk. And by the way, we don't need to know the genetics. All you need to know is a family history. But God forbid a physician ever asks for a family history of addiction when you go to the physician, and I mean any doctor.

We're not talking primary care. Orthopedists ought to be top on the line, but it ought to go right down the list to geriatricians, pediatricians, -- everybody ought to be able to triage their patients for addiction because at some point or another they're going to need to know that if they're going to adequately treat their patient. And so, you'll hear from Governor Baker, if he gets the chance to say it, that this whole system of medical education needs to be changed top to bottom in response to this crisis.

[applause]

Marilyn Serafini:

Okay. So at this point, we heard about changes at the FDA. We heard about getting adequate drugs into the pipeline. I think there may also be an insurance question, a coverage question in there, so I'd love to hear from other panelists about -- we're now well into what we need to do about this and how we approach this. So, I'd love to hear from some of you about -- in response to the congressman's comments and also if there are other areas we need to touch on.

Anne Schuchat:

Yeah. I'd like to sort of follow up on the practice issue. When you look at opioid prescribing in America, it's really shocking. We have a six-fold variation from high prescribing counties to low-prescribing counties, and even though we've had a decrease in prescribing since 2010 in America, our rates are three-fold higher than Europe. You know, not to blame anybody. We got into this with good intentions, but clinicians like me were taught that you can't get addicted to these medicines if you're really in pain. And we thought they were safe and effective. It turns out for a lot of types of pain, opioids are not effective for chronic, long-term pain of many types as you were describing, and they have tremendous harms and you cannot always anticipate who they're going to have the harm in.

So the young athlete, high school football player who injures their back and gets started on something is just as likely to become addicted as that person that you're really expecting to become addicted. So, as clinicians, we have to do better. In March 2016, CDC issued a guideline for prescribing for chronic pain that was really about think twice before you start one of these medicines. If you do start people on opioids, have a plan. Follow up actively. Start slow. Start slow -- start low dose and go slow in increasing it. It's going to take us a long time to deal with all the people who are already addicted, but we really need to prevent more people from becoming addicted by improving prescribing.

Marilyn Serafini:

So, I'm going to Dr. Maine a minute, but first I want to ask you, Dr. Schuchat, what was the effective of those recommendations? Did it make any meaningful impact?

Anne Schuchat:

You know, we've had a huge response to the guideline. We have actually started to see some decreases in some health plans, but we've seen medical schools, residency training, nursing schools, pharmacy schools adopt them into their core curriculum. And it's, you know, just the beginning. We have a lot of tools that are going to make them easier to implement: checklists,

and apps, and things that can be baked into the medical record. But, there's a huge culture of medical practice that has to change that six-fold variation in geography tells us that there's hot spots that we really need to work on. And having better data about where the morbidity is and the mortality as well as the prescribing, can help us and can help the states really focus in on the areas that have the greatest need.

Marilyn Serafini:

Dr. Maine, I know Governor Baker's going to weigh in on this, but I'm not sure we can dance around the education issue. He'll weigh in when he gets here, but --

Lucinda Maine:

I actually had a medical education colleague recently admit, that there's approximately one hour on addiction in a classic medical education curriculum. I can't tell you what the analogous number is. I should be able to tell you what it is in pharmacy. I know it's bigger than an hour.

I also wanted to mention that there have been some structural issues associated with the insurance enterprise that I know there are very important dialogues going on right now. Some of this is influenced by other federal regulation like the DEA and we really need to invite them into the conversation about these controlled substances and how they should be managed. Things like partial fill so that I don't go home from a simple tooth-extraction, you know, with 30, 60, 90 pain pills of any kind and there's a good chance that I might need two. But there are some things about insurance and the co-pay and things that can easily be addressed once we have all of those issues on the table.

Patrick Kennedy:

There's another issue here, and that is the lack of interest amongst any of the medical professions to actually become a medication assisted treatment provider. The docs got us into this mess in the first place and yet they're refusing to get us out of it. What -- the AMA ought to have a moral responsibility to ask all of their members to write for medication assisted treatment. Right now, less than ten percent of the providers in this country write for medication assisted treatment, even though Nora Volkow from NIDA and all the other experts, ASAM, said this is the gold standard for care. Can you imagine only 10 percent of physicians in this country adhering to the gold standard of care with the size of this epidemic the way it is?

Marilyn Serafini:

Why? Why are we not seeing --

Patrick Kennedy:

Because they don't want to treat addicts. We're not a popular bunch. We're not a very sympathetic crowd. People usually don't like us, especially when especially when we're active in our illness.

Marilyn Serafini:

Does it have to do with reimbursement? They simply don't get -- it takes a lot of time?

Patrick Kennedy:

Well reimbursement's another issue, it's a function of politics. No one advocates for this crap and hence, we underpay. I'm going to go see Mark McClellan's former colleagues over at CMS tomorrow, and I'm going to read them the Riot Act. Because I want to ask how many in that room have suffered from addiction? I guarantee hardly anyone is going to put their hands up, but I'll check. Maybe you can give them a little heads up. I'm coming to ask.

[laughter]

And then, I'm going to ask them how many of them believe this is the real disease and, of course, they're all going to put their hands up because they all want to look enlightened. And I'll say, "Well, if it is a real disease, why aren't you paying for it like any other medical disease?" Because the reimbursement for substance use disorder is criminally low. It's criminally low. You would not allow this to take place if there were any other illness, period. And yet, CMS doesn't reimburse for it. Why should any of the other big insurance reimburse for it? They take their message for CMS. So, we have big problems, big time.

Marilyn Serafini:

What specifically are you going to ask them to do to change this problem?

Patrick Kennedy:

Well, I've got -- I've got very specific recommendations for them to beef up, bump up codes, particularly the collaborative care, coordinated care codes. Going to tell them they've got to reimburse for all RAISE, which is early schizophrenia episodes. They ought to be paying for that now. I'm just going to tell them all of their value will show that this makes economic sense for them to treat people, especially with Hep C growing at record amount right now.

You know, it costs over \$30, \$40,000 to treat Hep C -- not even in a perfect cure -- and the skyrocketing rate of Hep C means it's going to dwarf the cost of treating people with addiction in this country. Whether you've got 45,000 cases of Hep C at 30,000 a pop.

All I'm saying is, like, we need to have -- get out of denial. We are in collective denial as a country. The only reason we're paying attention to hurricanes is because they're on TV all the time. We see the images. We go, "Oh, my God -- it's horrible." If we saw those images every single day, people getting crated out of, you know, West Virginia or New Jersey or any other state, people would be horrified. They'd be saying what are we doing about this problem? But we kind of -- we got the eye shades on because no one likes this crowd.

Oh, it's, you know -- and here we are, and it's going to get worse. It's going to get worse. And it's -- if we don't get all hands on deck and get our docs out there, we're going to be in real trouble. And right now, hardly any docs are signing up to treat the people with this, you know, illness.

Anne Schuchat:

Yeah. I was just going to say I think -- I think we're -- I mean, I don't really want to argue with you, but just --

[laughter]

-- but why not; right? Okay. So, I actually think, as a nation, we're beyond denial now. I mean, the places that I visit, state after state, recognizes this is in so many communities and so many families. Everybody knows somebody who's been affected. I just got back from Vietnam where we had a demonstration of what they're doing about the addiction problem, and they talked about it used to be called a social evil and people were incarcerated. And we saw this, you know, room full of young people training to be addiction counselors. And you know, medication-assisted treatment is entering their lingo.

I think, in America, politically, socially, economically people recognize this as a catastrophe and we have to do more. CDC is funding 44 states to improve their prevention programs to strengthen the prescription drug monitoring modules, you know? So, that docs could know if a person got three or four other prescriptions right before they were entering a new prescription. They are tracking hot spots so they can get there for whatever the latest Fentanyl equivalent is that's on the streets. We're working closely with public safety, with DEA, with DOJ to address the high-incidence drug trafficking areas.

I just think this is touching too many families for us to be in denial, so I don't want to argue, but I think we have a turning point.

Patrick Kennedy:

The bottom line is two weeks we lost 45 tragic deaths due to Harvey. How many opioid deaths in two weeks? At twice that a day. And we just appropriated first tranche \$7.5 billion. And yet, for the best we can do in Congress if \$500 million a year and that took a lot of bargaining. And I guarantee when the other supplementals coming up, we're not going to have any problem appropriating \$100-plus billion, which is what they're calling for Harvey. And I'm just saying, you know, you make the case. It's -- this issue's not getting the attention that a true emergency requires.

Anne Schuchat:

One of the women that I met in Kentucky, which has been like the hardest hit state of the epidemic, described it in her community. What she said was we've been admiring the problem too long. You know? We've been talking about it. We've been admiring it. And we really need to do something. So, perhaps I'm not arguing with you.

Patrick Kennedy:

No, no, no. If you were in charge, it'd be all right.

[laughter]

Marilyn Serafini:

So, where are on --

Anne Schuchat:

Somebody write that down.

[laughter]

Gopal Khanna:

On the positive note, I must admit that Congressman that ARHQ, the Agency for Healthcare Research and Quality, in our humble little way, have recognized in working with our agencies to identify that we need MAT. So, we are working for states to identify how we can do medicine assisted treatment so that we can figure out what might be the best way to make that happen in rural America. Because a lot of people think that it might east coast or west coast problem. But actually, opioid is agnostic to race, age, income levels and location and we have to think about even the mid-America and the rural areas where -- and figure out how we can make that happen. So, you're right. And then we need to do that.

Patrick Kennedy:

So, specifically DEA should not be breathing down these doctor's backs. After all this crisis we're jumping on them and now they've -- why do they want to bring up any opioid treatment strategy? They're all scared to death of it, and so unwittingly in the effort to clamp down on opioids, we're clamping down on the opioid replacement therapy that is the evidence base to treat the crisis that the docs got us in the first place. So, who's going to actually train to do medication-assisted treatment when they've got DEA breathing down their back and they don't get paid for it? Ding, ding, ding. No one wants that. Don't like to treat patient, don't get reimbursed and they got DEA down their back. Pair it, three. [demonstrates] Strike out.

So all I'd say is if you had real political will, you'd say enough of this. Enough of this. Get everybody out there prescribing, save lives, people are on Fentanyl now. It's going to take so much to get them off Fentanyl. We need, you know, Commissioner Gottlieb to get going on releasing these new medications, and we need to get alternatives for other pain other than these opioids in the first place.

Marilyn Serafini:

So, how much of this is education and the medical professionals, everybody from the physicians to the pharmacists to anybody who's involved in this, not having the education, and not perhaps knowing what to do? And how much of it is the money? The reimbursements? We also talked about funding, which I think we were talking about something a little bit different there, and I want to get to that in a minute, but how much of it is the education versus the reimbursement? It's not-- they can't make it work with the time that's involved.

Anne Schuchat:

You know, I think we have to resist the urge to oversimplify and that this is a really complex epidemic. There's a culture change that we need. You know, there are lots of structural barriers that we've been hearing about with insurance and payment and, you know, those kinds of barriers, but there's a huge issue for clinical practitioners in terms of their culture change. And a huge issue for consumers or the public as well.

At CDC, we think about this similar to antimicrobial resistance where we used to think

antibiotics were like miracle drugs, lifesavers, no harm. Just try it. You know, you don't want someone to, you know, die of an infectious disease because you didn't start antibiotics. Now we realize, wait a minute, you know, there's times where we've been overdoing it and we're seeing the complications now.

So, we think the public really has thought, you know, little pain med, you know, I got it from my dentist, I'm keeping it, I'm using it for something else -- in some people can lead to long-term addiction. So, you know, in addition to this big challenge of educating or changing the practice of physicians, we also need to change that culture of consumers to, you know, now I know lots of people ask their doc, like, I don't know. Do I need an antibiotic? I'm a little worried about that to get that same idea about pain control. You know? I think I'm okay from the dentist. I don't want that, or can I just have, you know, a small prescription instead of a larger one?

So, again, we're trying to get, you know, a PSA campaign going that will be launching later this month to really have that prescription medication culture change. Lots more to do on a list of drugs, but since so many people -- I think it's two out of three right now who end up on heroin started with prescription opioids, so we think that -- I mean, I wouldn't say education or, you know, insurance, that we really need to tackle this on every front.

Lucinda Maine:

We had the opportunity to talk with Secretary Price earlier last month, and this was the focus of the conversation. And I used -- the term it feels like a whack-a-mole situation where, you know, okay, it's education. We're going to get that. It's regulation. It's -- and it's all of the above. I have thought that it would be very useful if all of the principles had a map from causation, you know, through treatment -- appropriate treatment with prevention in the middle. And we could really systematically determine where the most important touch points are.

It is absolutely core to health professions education today as it has probably not ever been in the past. We have students who are going out working on drug take-back initiatives and into the elementary schools and the high schools doing, you know, drug prevention. And so, it is -- it is on everybody's radar screen, but I think we feel a little bit inept in getting to some of the root causes of the problem so that we can get to solutions without causing other unintended consequences.

And that's the really frustrating thing is that if it's not going to be opioid it's heroin with Fentanyl and car-Fentanyl. And that's actually probably more responsible for the death experience right now than the prescription opioids.

Marilyn Serafini:

And what about the role of pharmacists? What can pharmacists currently do and what do we need for them to be able to do? Do we need for them to take a greater role in figuring -- you know, determining where there are problems and what should their role be and what is it currently?

Lucinda Maine:

They certainly are a conduit to both the problem and getting these medications out of the control

system of a pharmacy out into the community where we know they get diverted. I actually had a person who manages our health -- exercise fitness place, bring me a bag of OxyContin and related products that she had stored in her home over multiple years. Why? She didn't know if she would ever need them again, and she didn't know how to get rid of them. So pharmacists can be really important agents in helping ensure the public understands what to do when you don't need 43 of the 45, you know, capsules that you get.

They can be very important in terms of health professions, colleague education and team-based care and just yesterday a conversation about the inadequate ability of clinicians writ large to manage pain. This was in the context of veterans' health. And the fact that they -- we really need to gin up more pain specialists and make them available for some of the more difficult retractable pain situations. So there are a lot of opportunities for pharmacists to have their role to play in this larger system, but it's in collaboration with everybody else in the ecosystem.

Marilyn Serafini:

So, we already heard that the physicians are not getting -- and the, you know, the other practitioners are not getting reimbursed properly so they're not getting into this. What about the pharmacists? I mean, every time I get my prescription filled, they're just like boom, boom, boom. They can't count the pills fast enough and get on to the next --

Lucinda Maine:

Mary, can we have another 45 minutes?

[laughter]

There's no question that there are issues associated with the distribution of medications today. And how they are being reimbursed. Ninety-five-plus percent buy third party public and private payers that are paying modestly for distribution and not adequately for education for monitoring and for the kinds of services that could be available in the most accessible outlets of care across the United States, which are community pharmacies.

Marilyn Serafini:

OK. So, Congressman Kennedy, I want to get back to you because you ticked off a number of -- you've got a full agenda. You're going to CMS tomorrow. You're talking to -- you said you believe a lot needs to happen at FDA, and I was wondering if you could expand on that in terms of what you think FDA needs to be doing differently and how it can do that. How it can get there.

Patrick Kennedy:

Well, going back, everyone's recited that this is going to require a comprehensive approach. And that's what I heard just this morning when people were talking about FEMA. It was enacted because we needed a comprehensive approach to get our arms around any natural disaster. You needed housing involved, you needed to involve the schools, you needed to have all -- you know, employment. You needed to involve commerce. You needed to involve -- I mean, health care.

It was like -- and when you think about this opioid crisis, you need to involve, literally, every

facet of the government, and you need to have a strategic plan, but you start by putting out the fire. You don't start monkeying around with let's put the plan together and we need a comprehensive and this needs to include this and that -- hey, Governor.

Marilyn Serafini:

And we have Governor Baker here. Welcome.

Patrick Kennedy:

And that's what's been missing because people with addiction need supportive housing. They need supportive communities. They need, you know, this medication-assisted treatment. They need access to inpatient treatment where necessary. I mean, they need a whole array of things and that's what ideally the commission that the governor and I serve on is going to recommend and hopefully the administration is going to follow.

But the immediacy is if you're requiring docs to get eight hours more treatment to do medication-assisted treatment than to prescribe opioids: hello. You got a problem. Okay? You want to know if this is an emergency. Get rid of the additional hours required. Okay? Do more continuing education make it easy because like I said, that's a barrier. Reimbursement is a barrier. And DEA: barrier. Collaborative care: barrier. But let's just start acting. We don't have to go search this stuff. You know? Former Surgeon Generals reports lay it all out. This is not new. We need political will, not a whole lot more talking about this, in my view. Because we know what we need to do. We just haven't gotten around to giving it the political will to get it done.

Marilyn Serafini:

Fantastic. Governor Baker, welcome. Glad you could join us. We have been talking about chronic conditions, prevention and how that all ties in to the opioid crisis. And you are like Congressman Kennedy, you serve on the White House task force on opioids. And I'd love to hear what you really see as your top priority -- the top priorities of that task force. And what you are doing personally with the task force and otherwise to where you see your top priorities.

Charlie Baker:

Well, first of all, I'm really thrilled you're all here to talk about this because one of the big things that I learned when I was campaigning for governor in 2013 and 2014 is most people really didn't want to talk much about this. And almost every conversation I had with people early on happened when somebody came up to me after the event was over and said, "You're a health care guy; right?" And I said, "Yeah. I spent most of my career there." And they say, "Well, I got this friend," and then they'd tell me a story about somebody who is dealing with addiction.

And I literally heard it almost everywhere I went. And my wife, who was also out campaigning, and much better at it than me, would come home and say the same thing. And we started to wonder if we were just listening for this or if this was something big going on.

So, I did what I usually do in those situations, and I went and visited with a bunch of docs and care providers I knew who worked in emergency rooms, and I went and spent some time with some EMTs and some first responders. And I said, "I'm hearing this opioid thing kind of

everywhere I go. But I'm not sure if I'm just hearing it because I'm listening for it or if there's something big going on here." And to a person, they said, yeah, and then they used, you know, avalanche catastrophe, calamity, whatever word you like.

And then I had my folks on the team go and do a little research – and this is still campaign season –, and they came back, you know. Just dug around in the data and came back and said what I think a lot of this space already knew, which is that there was a gigantic crisis going on here. And it was completely off the radar and when I talked to some of the folks in the ERs, and I said, "You guys all know me. I mean, I've known you for years, and how come I had to go talk to you about this to find out about it and bring it up? How come you just didn't tell me?" And they said, "Well, you know, I'm busy. I'm just doing my job and I'm not really paying that much attention to sort of higher order issues."

And one of the things we tried to do with our task force and with our legislation, which I'll bore you with if you're interested in, was to elevate the conversation around this. You know, we've done public service campaigns and straight out media campaigns on stigma, and we've done a lot of work to expand our treatment and recovery capacity. We've increased it by almost 50 percent and the last waiver we got from the federal government for our Medicaid program dramatically expands our mental health and addiction coverage capability. And we're the only state in the country where you can't graduate from medical school, dental school, nursing school, or pharmacy school without taking and passing a course in opioid therapy and pain management. And we're the only state in the country where if you're licensed prescriber, when you go back to get your license renewed, you're going to have to take and pass a course in opioid therapy and pain management.

Because one of the most unbelievable elements of this whole issue, for me, has been how undereducated and underinformed the folks on the front end who do a lot of the prescribing are. And continue to be. And the fact that the pain community and the addiction community have never really had any ongoing serious conversations with one another about the role they both play in all this is bizarre. There needs to be more of that. But my view is take as much as what we've done that I've seen work in Massachusetts and as much of what we've seen that's worked in other states on this stuff and get into the national conversation and make it part of a national platform.

And the other thing I'd say, and this is the point I really wanted to make here today, we have not done anywhere near as much investigatory research around what works in addiction as we have in so many other areas. And I would love to see the feds get as serious about this issue with respect to research and protocols and best practices and all the rest as the feds are in so many other areas. If we think this is a crisis, we think this is an epidemic, well then, gosh darn it, the feds ought to be -- ought to be stepping up and playing a much bigger role in helping people understand what works and what doesn't, and why. And doing the kind of work that's made so much progress in so many other fields.

Marilyn Serafini:

So, I want to ask the panel to expand on that, as to where the research needs to be, and what kind of funding we need, and through what channels. But before we do that, Governor, I want to ask

you specifically about Medicaid. And specifically, the challenges with opioid addiction for the Medicaid population. And are there opportunities to work through the Medicaid program to deal with this issue?

Charlie Baker:

Well, certainly, the waiver, the 11-15 waiver that we got approved about a year ago significantly expanded our mental health and our addiction coverage. And that was for a reason, because we were well aware of the fact that this is a huge issue for people that are served by that program. But I also think it was a big message that we sent to the provider community and others that this was an area we wanted to invest in, and we wanted them to help us figure out how to do it, and how to be smarter about it.

But I'm one of these people who thinks that, you know, you can't – you can't solve-- you can't think about this just in terms of treatment and recovery. You have to think about it in terms of prevention and education. You know, frankly, I'm a healthcare guy, but the healthcare community created this crisis in this country because they got extraordinarily casual about something that they weren't so casual about 20 years ago. And you can't write 80 percent of the world's opioids when you represent 5 percent of the world's population, and not expect that there will be consequences to that.

And truthfully, there was a lot of information out there for a long time, if people had been able to stitch it all together, they would have started telling people that there was something really big going on. And for one reason or another, it just didn't find its way into the public bloodstream until we were way down the road. So, we're going to do a whole bunch of things on the treatment and recovery side. But we have got to be focused on the prevention and education side of this thing or you know, we're simply never going to get where we need to go.

Marilyn Serafini:

Okay. So, let's talk about research, and where we -- what we need to be focusing on in the way of research in this area. And after we do that, we're going to open it up to some questions from the audience. So, go ahead and get your questions ready. And in the meantime, where we should be focused?

Seth Ginsberg:

I'll go.

Gopal Khanna:

Go ahead.

Seth Ginsberg:

So, you know, full disclosure. First of all, I'm a co-principal investigator of a patient-powered research network funded by PCORI. Arthritis Power collects patient-reported outcomes from people living with all forms of rheumatic diseases. And to us, PRO – patient-reported outcomes is the fulcrum of addressing so many of these issues long before they become the problem that we've been discussing today. All right, we're talking about 15, 16 million people with migraines, right? How do you measure a migraine? How do you compare one's pain to another?

I can tell you, right now my wife's threshold for pain is an order of magnitude greater than mine. And yet, you know, we would still be classified as the same patient technically and same with, you know, rheumatic disease pain and so forth.

So, in our view, the emphasis can be placed on patient-reported outcomes for so many of these conditions. Because I really appreciate the conversation here, and the dialogue, and the important work that everybody is doing collectively to address the epidemic of opioid addiction. But I don't want it to come at the risk or the cost of eclipsing the genuine and incredible pain, literally, that millions of Americans are living with.

We can do better, we can do both. We can help the people in pain and we can prevent the people from getting addicted and I just want to make sure we're addressing both sides of the ledger and I believe, we believe, that patient-reported outcomes could technically sit as a fulcrum between those sides.

Charlie Baker:

How much conversation between the pain community and the addiction community takes place?

Seth Ginsberg:

Not nearly as much as it should -- as there should be.

Charlie Baker:

Yeah. That's what I think too.

Seth Ginsberg:

Pain Week is coming up next week, I think in Las Vegas. No, I think that we have a lot more. And again, it gets back to the difficulty in quantifying pain. How do you quantify a migraine? How do you quantify pain associated with a malignancy? You can't. You could look at a radiographic evidence or, you know, bone-on-bone joint degeneration and you could say, "Yeah, that's probably pretty painful," but -- or someone with a spinal cord injury, but you can't of so many of these other syndromes.

And so, the challenge there is quantifying, and clarifying, and specifying what that means. And I just -- the last -- I think the word we all should leave here thinking about when it comes to addressing so many of these issues, is technology. Literally, technology. How can tech address so many of these issues? Because today, we are finally at that intersection of medicine, science, communication, and technology and we were never there 20, 30, 50 years ago. And so, going forward, how can tech serve as the pivot point for so many of these challenges?

Marilyn Serafini:

How can it, panelists?

Seth Ginsberg:

[laughs]

Anne Schuchat:

I was going to go in a different direction.

Lucinda Maine:

So, let me just make a point about technology in this specific crisis. In a conversation that a colleague had with someone from Sweden; they were comparing the use of opioids in their country versus here. And as you alluded to, the comparison is crazy. They say, "Well we eliminated our opioid misuse problem by requiring electronic prescribing of every prescription." How does that relate to research? As I sit here and think about what we've learned in our country, yet, again, we could squeeze down and optimize the appropriate prescribing of a very challenging and difficult-to-manage substance that does address some pain well.

But what about -- what don't we know about the unintended consequences of making that portal very narrow? And are we then, igniting the other related crisis of illicit drug use and addiction. So, it is not -- there are no simple answers, obviously, to the question. And there are researchable questions that are fundamental to our progress across the entire spectrum of research.

Marilyn Serafini:

Okay, we're going to turn to Doctor Schuchat and then to questions. We're going to have two roving mics. So, if you have a question, you can already raise your hand, and a mic will start to come to you.

Anne Schuchat:

Okay. I just wanted to kind of build on the issue of measurement. You know, I'm a measurement/data kind of person, but one of the ways we got into this problem was a measurement issue where, in quality of care in hospitals, people were asked about that fifth vital sign, and, "Are you in pain, and how much?" And, we got into a vicious cycle of over-treating a quantitative, you know, self-estimate of pain that probably worsened the overprescribing that we had.

But measurement is really important going forward and we had this plea for the holistic nature of the problem and the holistic nature of the solutions. As we've been working across government in some of these research evaluations of medication assisted therapy and what works and what doesn't in cohorts, we've realized that we can't just be looking at health outcomes. We can't just be looking at overdose and hospitalizations. We need to be looking at, you know, return to work, family crises, issues of stability. And really, understanding the bigger picture so that we don't go down a road of more unintended consequences.

Seth Ginsberg:

And my point of tech, sorry, is at least we have the computing power today, to do that. At least big data is a reality that we can input all of these domains to begin to understand this.

Anne Schuchat:

And just of saying that it's not just the health data --

Gopal Khanna:

Right.

Anne Schuchat:

-- that we need to be looking at.

Gopal Khanna:

There's a lot more data in the volume, the variety and velocity with which it's hitting us creates both challenges as well as huge opportunities to have a deeper understanding for solutions. And from ARHQ's perspective, talking about research, there's a dimension that we cannot forget, which is applied research so that we can bring all the solutions that have been talked about -- MAT, et cetera, and deliver it to the point of care. And the faster we can do that, the better our solutions would be.

Patrick Kennedy:

I'm wondering on the data. Do we really have the accurate data on the number of people dying from this?

Anne Schuchat:

Yeah, so we -- thank you. We don't, but we're making progress. So, we -- you know, CDC's vital statistics program tracks deaths, and those come from medical examiners and coroners. There's a lot of missing data. There's a lot of slow data. Lots of times, unknown cause is probably overdose. Lots of the overdoses, we don't know what the overdose is due to. Delays in toxicology testing -- you know, one of the big secrets that is out there is how fragile our medical examiner and coroner system is in this country. CDC's started to issue a monthly report. So, instead of having three years old data, we only have eight months old data. But we just reported, you know, the 2016 data, which is, unfortunately, 64,000 deaths due to drug overdoses in 2016. A 21 percent increase from the year before.

Patrick Kennedy:

But just for everyone -- you check out at CVS. You have bar code that they know what you bought and when you bought it. The notion that we have to wait eight months while we're having a pandemic cross this country in this day and age -- I mean, does anyone strike -- doesn't that strike you as odd, that it would take that long? And that we would be relying on all of these elected coroners. I mean, a lot of this country elects the person that decides what your death certificate looks like. I'm not kidding you. So, we don't have a real hand on the size and scope, is my point, and I thank you for -- doctor, for confirming.

Marilyn Serafini:

All right. Thank you. So, let's go to our first question right here. If you could identify yourself, please?

Victor Dzau:

Sure, this is Victor -- I should stand up? Okay. This is Victor Dzau from the National Academy of Medicine. Thank you very much for this great discussion. You emphasize research education, but I haven't heard anything about educating the younger people who actually are the ones who are more prone to addiction, nor the research of biology of pain, and biology of

addiction. That's where I believe where the investment should be. Because once you have a much better handle of different types of pain, and also the biology of the addiction, as you see. For example, if you look at the age-dependent addiction, the last surgeon general told me that when he looked at the data, if a 13-year-old's exposed to an opioid, 75 percent chance of being addicted, whereas if you are about 20 years old, the number drops to about 25 percent, right? So, there's a really important biology, and ultimately education, in that particular population.

The other thing that we didn't discuss was somewhat touched on are the social issues -- the root cause issues. We can blame all the medical profession, but we're dealing with a fundamental issue in this country with some social economic determinants which makes you more prone to seeking out these things. So, I would appreciate someone talk about those.

Gopal Khanna:

I just would like to add one little clarification that I used to think that it's a young people problem, opioid crisis. But actually, our data shows that it really is age agnostic. We have young people problem. We've got middle age problem, and we've got aging population problem, when it comes to addiction. And actually, one thing I taught was that it's more likely men problem, but it's really not. Women have caught up, and they're now equal to the number of men addicted to opioids. And this crisis has many dimensions and nuances to it. So, I just want to be sure that we realize that it's --

Patrick Kennedy:

Excellent. I think, Victor, the point about how we could do an opioid recommendation and neglect the fact that we have a suicide crisis as well is a terrific point, and that this is indicative of a broader systemic challenge. And hopefully, in our commission report, whatever we recommend for the opioid challenge could also be helpful in impacting the terrible, you know, rise in suicides.

Victor Dzau:

Gopal, I realize that in the age group would be, you know, prone to addiction. But I think the biology shows you that you're more prone to addiction when you're younger. And if you look at the surge, they affect more of the people in the teens to 30's. So, I just to point that out as a fundamental issue, a crisis.

Gopal Khanna:

I understand.

Charlie Baker:

One of the things we did was -- in Massachusetts, if you play a sport at the middle school or the high school level, you have to participate in a pre-meeting before the season begins. It involves your parents, your coaches, and somebody from the medical community. And it was always set up as sort of a health and safety conversation about hydration and concussions, and stuff like that. Well, opioids are now part of that conversation, because the more we can do to make sure people early on -- not just the kids, but the parents and the coaches and folks in the schools know about this and talk about it, the less likely we are that somebody's going to get surprised by some of the downside consequences of this stuff.

I also think the -- I'm not kidding when I say I'm glad you're having this conversation. A huge part of why this became the kind of issue it became, in my opinion, was because no one would talk about it. I can't tell you how many parents I've talked to over the past few years who said "I never told my neighbors. I never told my friends. I never told anybody what killed my son or killed my daughter, because I was embarrassed." And the more we can do to get people to the point where they're willing to speak openly about this, the faster we're going to be able to get people to get serious about spreading the word, and engaging in the conversation about the prevention and the education stuff on the front end, and the fact that there are treatment methodologies that can work for people.

And for folks not to literally shy away from this in a way has just been extraordinary for me to watch. I mean, people love to talk about illness, but they don't love to talk about addiction. And it's a big problem. So, the fact that you're here talking about it, and the fact that the issue's being raised is good. That we should do more of this.

Marilyn Serafini:

Thank you. We're going to --

Patrick Kennedy:

If I could, one last --

Marilyn Serafini:

Go ahead.

Patrick Kennedy:

-- because this is another elephant in the room, down the road -- is marijuana. So, we got inundated at the commission by people proposing that all we do is expand marijuana availability in order to deal with the opioid crisis as kind of a substitution drug because it -- but to your point, Victor, you know, the exposure of marijuana on the young brain, to your point, whether it's opioids, marijuana or alcohol, it's the judgment of Nora Volkow at NIDA that that puts you at extreme risk for later addiction. And I only wanted to use that as an opportunity to throw that in the mix.

Marilyn Serafini:

Thank you. I think we could talk about this for hours and hours, but unfortunately, we only have time for one more question, and here it is.

Jay Gershen:

Thank you. Jay Gershen. I have the pleasure of serving as president of Northeast Ohio Medical University. And I also have the pleasure of serving on the board of the Ohio Chamber of Commerce. And last week, I was at a board meeting, and they had just completed a survey of the state's businesses. And not shockingly, the number one problem that businesses are having are people not passing the drug test.

Female Speaker:

Right.

Jay Gershen:

And therefore, there's economic impact to these businesses -- they can't find enough employees because there's not enough people who are drug-free. So, getting back to the Congressman's point about, you know, a 100 billion versus a half a billion. How do we -- how can we leverage the business community to begin to take this on from a national policy perspective, to make it more impactful, and to get a more of a multiplier effect?

Anne Schuchat:

I just want to say one thing. I think the business community is a key issue. I think the Department of Defense as well, if you look at, you know, how you can fill the ranks of what you need to fill. So, our nation's defense is really threatened by this epidemic. So, I think your points are fantastic.

Seth Ginsberg:

And the business community needs to be acutely sensitive, not just to the opioid addiction issue. But again, to the precursor to it, to the absenteeism and presenteeism issue, with pain, chronic pain, migraines, and so forth, so that they can address that in -- within the ecosystems of their companies as well.

Patrick Kennedy:

It's an opportunity for Tom Donahue and Rich Trumka to come together. I mean, this is a -- Janet Yellen said it, and this isn't to you, Jay, so you're in good company. The fed said, "this is a drag on our economy."

Female Speaker:

It is.

Patrick Kennedy:

The President cannot initiate his whole infrastructure bill if he repatriates those hundreds of billions of dollars in overseas corporate profits. There's nothing to pay for. We can't get enough workers. Walmart can't open enough stores. There're not enough workers to build them. I mean, this is like a real crisis, why business has not come out, like, in a stronger way, to your point, Jay, is pretty shocking. Thank you for bringing that up.

Charlie Baker:

Let me bring that up with some of the ones in Massachusetts, and see what they say.

[laughter]

Marilyn Serafini:

There you go. So, please join me in thanking this panel --

[applause]

-- for addressing this very tough issue, not only today, but every day. And with that, I'm going to turn it back over to Mary, to give us instructions, moving forward.

Michael Castle:

To keep things moving, I'm going to start talking, even though some people are busy doing other things right now. My name is Mike Castle. Mary's going to get --

Mary Woolley:

Hello. Hello, everybody. Would you please hold down your conversation? We want to keep the program going, please.

Michael Castle:

Okay, thank you, Mary. My name is Mike Castle, and I am the chairman of the board of Research!America. And a lot of you are probably looking at this and saying, "I thought that John Porter was the chairman for life." He should be the chairman for life. He was that effective and that good, and I have no illusions about being able to follow in his footsteps. But nonetheless, I'm in that position now, and we'll do the best we can.

I would like to thank our distinguished panelists, in the first panel and those who are to come, for joining us here today. And thank them for sharing their thoughts about the opioid epidemic and other escalating health threats that will inform our thoughts and actions on these issues, going forward. From one who is a recovering governor myself, as well as recovering Congressman, I might add, I'd just like to thank Governor Baker for making the time to get here for the discussion. Obviously, he had to go through a difficult transition to be here, and we appreciate that -- his leadership as an advocate for medical and health research in Massachusetts and nationwide is commendable, and we are proud to be your partner.

I'd also like to thank Congressman Kennedy, whom I served for his obviously -- zeal that he has for dealing with this problem, and for being very candid about his own problems that existed before. I think it makes a big difference, that we have two of the five commissioners on the President's commission on combating drug addiction in the opioid crisis with us today is remarkable. Governor Baker and Congressman Kennedy, you are helping our nation overcome a crisis that is wreaking havoc on individuals, families, and communities across the nation. Thank you for your commitment and leadership.

It is now my pleasure to introduce the commissioner for the Food and Drug Administration, Dr. Scott Gottlieb. Dr. Gottlieb was sworn in as the 23rd FDA commissioner in May. As a physician, policy expert, and public health advocate, Dr. Gottlieb was extraordinarily well-equipped to lead an agency that oversees products that account for about 20 cents of every dollar consumers spend each other. And in a few short months as commissioner, Dr. Gottlieb has laid out clear goals, and has been knocking them out one by one.

And like his predecessors, one of whom, Mark McClellan, is joining us on the next panel, Dr. Gottlieb is demonstrating the caliber of leadership that it takes to ensure that products seeking the agency's stamp of approval are safe and effective, all while putting patients at the heart of his work. We at Research!America are proud and privileged to be advocates for the FDA.

Welcome, Dr. Gottlieb.

[applause]

Scott Gottlieb:

Thanks a lot. Thanks for the opportunity to be here. It's actually -- it's almost 25 cents of every dollar, and it's not because the economy is shrinking. I should -- I probably shouldn't say it's because the regulatory state's growing, but it's because Congress has given us a lot of new responsibilities in recent years. So, the scope of the FDA's mission has expanded dramatically in the number of years. And in particular, the time period since I was last at the agency, about a decade ago, as a Deputy Commissioner.

I wanted to talk about pre-clinical research today. Last week, FDA approved, as many of you might know, the first gene therapy product of the United States. The new treatment was targeted toward a rare form of pediatric blood cancer. It will initially be indicated for just a few hundred patients a year. Those numbers shouldn't taper the enormous milestone that was crossed in the approval of this product, nor the meaningful benefit that some patients are going to derive -- some very young patients and very sick patients are going to derive from the hopeful therapy.

For many decades, we've grappled with the science to enable us to alter the gene sequences underlying disease as a way to treat human illness. Using the tools of gene therapy, and there have been many scientific and human setbacks along the way, as many of us are familiar with. But the technology to do these things continue to advance, owing to the perseverance of scientists, the persistence of sponsors that were dedicated to these endeavors, and most of all, the patients who continue to brave the uncertainty of clinical trials that were key to evaluating these new methods.

A long series of small breakthroughs along the way all consolidated into advances that enabled these new platforms to progress, not least of which, in the case of gene therapy, was the advent of reliable vectors for delivering the gene sequences. And so, we've now reached a momentous inflection point in science. FDA currently has more than 550 active investigational new drug applications related to gene therapy products, and we have 76 investigational new drug applications, active investigational new drug applications related to CAR T cell products. And we have hundreds more that aren't active at this time.

Gene therapy is just one of a number of new platforms that are coming to fruition as a novel means to treat disease. Two decades ago, we made some fundamental advances in life sciences with the firming of the science and the tools around genomics and proteomics. Now, that basic science is being fully translated into therapeutic products that may radically alter the course of medicine and arrest the progress of some retractable diseases.

But a lot of policies -- and yes, our regulatory framework, are fashioned to a much different paradigm of science and drug development. And so, we are challenged to see how we adapt those policies to make sure that we have the right framework to properly evaluate the safety and effectiveness of these new technology platforms. The recently passed CARERS Act gave us certain tools and resources to address these challenges, but we know much work remains. And

our ability to fully capitalize on this science and maintain FDA's gold standard for product review means that FDA also needs to modernize itself along with the new platforms that we're evaluating.

This modernization process has been under way for many years; it was crystallized with the formation of the critical path initiative when I was last at FDA under the leadership of Dr. Mark McClellan, who is here with us today and will be on the next panel. And now, at FDA, we're going to be taking some fresh steps to continue to advance similar ambitions as it relates to the development challenges associated with these very novel platforms that we're seeing now. We need to be able to make sure that our policies match the complexity of the novel science that's being harnessed to attack disease. And to accomplish this, we need to ask ourselves some new questions.

For one matter, how do we adjust our approach when the primary complexity and uncertainty inherent in a new product isn't the clinical question related to whether it works, but the features of the delivery platform, or how it's being manufactured? And what do we do, for example, when the most complicated risks aren't acute toxicities that can be observed up front? Instead, they're long term and more theoretical risks as -- and uncertainties, such as the potential for off-target effects of gene therapy interventions.

These questions challenge us to adjust our regulatory policies, and think differently about our overall mission, especially when it comes to complex products that are part of intricate delivery systems. These are situations where the products are delivered transiently, and sometimes, with just a single administration, but they have sustained effects. In these situations, determining safety and effectiveness doesn't boil down to a judgment made at a single point in time. It's not a binary measure; a single discreet threshold. The proper evaluation of safety is an ongoing process, and it crosses over the threshold of initial approval.

This means more emphasis needs to be placed on how new technologies perform in clinical use during routine care. Long-term risks and benefits need to be carefully monitored, and this is similar to the way we evaluate many medical devices. Our questions related to these platforms would increasingly relate to their long term performance. More of our emphasis will naturally shift to our post-market tools. Over the coming months, I'm going to be talking about some of the steps we're taking, and steps we plan to take to adapt our regulatory principles to the new challenges we face, and properly evaluating a very different set of scientific opportunities.

At a speech I'll be giving Monday at RAPS [Regulatory Affairs Professionals Society], I plan to talk about the steps we're taking during the clinical stages of development to make that process more efficient and more effective. And then, at the end of the month, I'm speaking at the National Press Club, and I plan to address how FDA approaches its broader role as a medical staff, and the post-market obligations that accompany our stewardship over the evolution of the full life cycle of a product.

But today, I want to start that conversation by talking about FDA approaches the early pre-clinical stages of development. I want to highlight some of the new efforts we're undertaking as part of our overall approach to this new technology under a new strategic policy road map that

we'll unveil soon, and I'll outline more of our policies very shortly.

First, we're adopting new policies for earlier engagement product developers. These are especially relevant when it comes to those working in very novel areas of science. Our evidence shows that earlier and more frequent engagement can help make the initial stages of development more efficient and increase the odds of success. And we know that academic and individual medical sponsors, as well as startups, and some small biotechnology companies, sometimes don't have a full understanding of what it will take to get an IND [Investigational New Drug], where to get a BLA [Biologics License Applications] filed with the FDA for their product. It's often the smaller companies of the individual researchers who are working with the most novel technology platforms as well.

And so, at FDA, therefore, we're encouraging very early meetings to give more early feedback to product developers. These efforts are particularly prominent in the Office of Tissues and Advanced Therapies and our Center for Biologics Evaluation and Research. Increasingly, these meetings occur very early, during the non-clinical or pre-clinical work for the IND. It's been our experience and our observation that some sponsors sometimes overestimate the amount of information needed to file an IND, and that too many times, the cost of development, therefore, get front-loaded, increasing the cost of initiating new science.

Ideally, it would be easier to get products into development with more of the cost pushed further out after some of the initial pre-clinical work is already done, and there's a better understanding of whether the new product has clinical promise. Toward these goals, the FDA review staff is sometimes able help significantly streamline early development processes by eliminating unnecessary pre-clinical tests. Or by suggesting optimal pre-clinical or clinical designs, such as more adaptive trials for early stage research or Bayesian approaches to the statistical evaluation of results, where randomization is not possible in early stage clinical trials.

Our Center for Biologics Evaluation and Research under the leadership of Peter Marks will be further clarifying to academic and industrial developers how we will foster the development of innovative products to the kinds of early substantive interactions that I described earlier. These new approaches to clinical -- pre-clinical scientific engagement will also be featured in education material that we'll be making available to sponsors. Our drug center has been implementing similar approaches to these pre-clinical processes.

We're going to be taking our new steps to make sure that our policies governing early, pre-clinical science are more closely matched to the complexion of modern technologies. One is evidenced in how clinical trials are initially designed. In certain cases, there are a lot of common features across the same platform, even if it's used to target different genes or proteins. There may be plausible reasons to recognize how a product or platform can work across multiple disease states, and leverage the learning from one setting into other opportunities.

So, how do we make sure we're efficiently taking advantage of these opportunities? For example, we may be able to take a more adaptive approach in our pre-clinical evaluation of different therapies that share a lot of common characteristics in the overall platform used to deliver a gene product. Consider two gene therapy vectors that contain CRISPR constructs,

differing only by one base pair. These two products might not need the same early amount of pre-clinical data for the second variant, as was required for the first one. If we can borrow what we learn across different clinical applications of the same basic construct, by comparison, if the CRISPR inserts were different at five or more base pairs that might require more data.

The bottom line is this: we need to carefully but efficiently evolve our pre-clinical regulatory models to adjust to what we need as the science evolves and indicates what is critically necessary for the safe application of the new technology. These are just some of the new steps we're taking to modernize the pre-clinical aspects of drug development. I'll have more to say on these issues, as well as steps we're taking to address the other stages of drug development very soon, and we'll make sure we stay firm to FDA's gold standard for product review while embracing these new technology platforms. These new platforms are the practical outgrowth of gene and protein based science that was firmly established just a few decades ago.

And we're at a point in the history of medicine, similar to other great inflections in science, where fundamental principles of science and medicine became firmly established as part of a great leap in public health. Our aim is to make sure our policies match the sophistication of the science we're asked to evaluate, and help enable this new paradigm of beneficial innovation. That's going to be a big focus of my medical innovation access plan, parts of which we've already announced, and our forthcoming strategic policy road map. This road map will serve as an organizing framework, a strategic plan for unveiling and advancing the major policy efforts we plan to undertake across all our centers.

Today, I focus just on some of the steps we're taking with respect to the pre-clinical aspects of drug review. In the coming weeks, I will discuss how these same policy goals will be made evident in how we approach the clinical portion of the drug development process, and our life cycle approach to medical product stewardship. I want to thank you for having me here today. I hope I left time for questions, and I appreciate the opportunity. Thanks a lot.

[applause]

Female Speaker:

Hi, Scott. Thank you. That was really helpful. I wonder if you could talk a little bit about the role of the patient, as you begin to take a look at the changes that you want to make in the direct development process.

Scott Gottlieb:

We're going to look for ways to make the patient participation in clinical development more transparent, more systematic. So, we're going to be announcing soon we're going to standing up a new office inside the Office of Commissioner under the leadership of the principal deputy, Rachel Sherman. They'll be focused on coordinating patient engagement across all the medical product centers. And so, that's something we'll probably do either in the next three or four weeks.

This will be a policy coordinating function to try to make sure we have consistent practices across different aspects of medical product review. It's not going to dislodge the relationships

that patient groups and patients currently have with medical product centers. But if there are best practices that we think we should be democratizing across the agency, or barring some of the things CDRH [Center for Devices and Radiological Health] may be doing well into the drug development process inside CDER [Center for Drug Evaluation and Research], those are the kinds of opportunities we want to pursue. And so, this new policy-making function, which is going to be a small office -- we're not looking to build a very large office, but we do feel we need to have some kind of central policy-making function inside an office of medical policy that will report to the principal deputy.

Susan Dentzer:

Scott, Susan Dentzer, a member of the Research!America board. Thank you so much for your talk. And as you mentioned, the approval of Kymriah represents just a major, exciting new development for all of us who've experienced cancer at our own families.

I have a question about post-market surveillance in particular, and real-world evidence accumulation. And as you mentioned, as we look at the long term effects of these therapies, the unknowns are obviously vast in number. I presume you're going to make some comments on this when you unveil the strategic plan and road map for the FDA, but what kinds of investments do you think we need to make as a country in the data infrastructure to continue to harvest the benefits of real-world evidence? Particularly in the face of these dramatic advances in gene therapy and related therapies?

Scott Gottlieb:

Yeah. You know, it's been a little bit of a frustration because we've been talking about the ability to do more real-time surveillance using databases and real-time collection of information, the ability to access electronic medical records for a very long time. This is something I remember Dr. McClellan talking about 12, 13 years ago at the FDA, when I was there with him. We've made a lot of progress, obviously, but we're still not quite at the point where we can certainly do very reliable real-time active surveillance. We're still dependent upon doing retrospective analytical work, often times on paired databases with Sentinel -- in the drug context and the device context is more difficult because the pair debate -- databases often times don't track the individual medical devices, just the procedure that was done.

So, in that realm, you're more dependent upon systematic registries and prospective registries where you can collect data, and also trying to work -- trying to align more closely with EMRs that might have data on what the medical devices we use, and not just in a particular procedure.

And we are certainly working on this inside the FDA, trying to look at what we need to do from a policy stand point to continue to advance this. We just put out some -- a guidance document from CDRH on a definition of real-world evidence. We'll try to come up with standard definition, and talk about the different clinical circumstances where RWE can become a more meaningful component of both the pre-clinical, pre-approval, as well as the post-approval process. So, where can we use RWE as an important component of the pre-market review of a product? And what -- how should the RWE be collected? What standards does it need to be meet, in order to fit into certain places in the pre-market approval process where it might supplant other kinds of data collection? So, that was an important articulation from CDRH, and

you know, we're looking to try to develop a more consistent policy across the entire medical product center.

But I don't think -- to answer your question, I'm not sure there's one sort of silver bullet that's going to make this sort of vision come into full fruition. I think it's a slow evolution. It is going to become more important, as we have these products come to market that have theoretical risks associated with them around off-target effects, when you're talking about things like gene technology, CRISPR gene therapy. You might want to follow patients for a very long period of time, but you're going to want to do it in a way that isn't overly intrusive into the patient's life, if you follow them for a decade or longer. And so, we're going to need to figure out new constructs to do that. And we are -- we've developed some. We've already operationalized some of these.

But we need to look differently at it. And one of the other things I'm going to be talking about later on is just how we think about the drug -- the pre-market drug review process more generally. And think of the mission and the role of the review staff more broadly as not just individuals who are focused on the review metrics and the PDUFA goals -- and those are extremely important because they help us discipline our process, and they help us impose good management on the review process.

But the drug review process is more than just being a deadline. It's about taking a holistic approach to the life cycle of a product, and making sure that the people who work on drug reviews are also very closely integrated to how we think about the post-market safety of those products. And I think that's going to become more important, especially with some of these new platforms, where the complexity isn't necessarily "does it work clinically?" It might be very obvious that it's providing a clinical benefit, but the complexity relates to all these other issues: the product features and the post-market considerations.

Female Speaker:

Do we have time for one more question?

Scott Gottlieb:

Sure.

Patrick Kennedy:

Commissioner, you've spoken very eloquently about the opioid crisis being a top priority for you. And having also worked within CMS, and what I understand is you're a key adviser to those trying to come up with a good, coherent healthcare policy for our country. Could you just talk about the more coherent strategy that you see the Administration pulling together to address this opioid epidemic?

Scott Gottlieb:

Well, I can talk about how I'm thinking about it, from the FDA standpoint. That's not to skirt the question. I think it's most important that I think about it from the perspective of the FDA. We obviously have an important role to play across the entire continuum. We look at things like, you know, [unintelligible] formulations, medically assisted therapy. There's ways that we could

help advance non-addictive pain products. And we're looking at all of those opportunities. But I think the -- perhaps, the biggest role that FDA can play in trying to address this crisis is in reducing overall exposure, and helping solve the new addiction crisis. And it's going to take a very concerted effort by a lot of people to address the current addiction crisis. And we are certainly part of that, in trying to do our part.

But I think where FDA has a out-sized influences on a new addiction crisis because we know most people who become addicted to opioids become medically addicted. Their first exposure's going to be through a legitimate clinical prescription, or at least a clinical prescription because we might sometimes question the appropriateness of certain prescriptions. And so -- and we also know a certain percentage of people who are exposed in a clinical setting will inevitably become addicted to opioids. And so, in order to reduce addiction, we need to reduce exposure.

And the ways we're going to do that is to make sure that fewer prescriptions are written, so that prescriptions, when they are written, they're medically appropriate, and physicians have considered other alternatives. And when they do get written, they're written for dosages that comport with the clinical circumstance for which the prescription was indicated in the first place. So, you know, no more 30-day supplies for a tooth extraction. The only circumstance in which you might require 30 days of opioid therapy for a dental procedure is if you've developed a horrible complication in which you should be going back to your doctor.

And so, we think that there are things we can do within our regulatory toolbox, thinking differently about those tools to affect those two goals, whether it's how we require education of physicians, or what steps we could take to actually encourage more controlled dispensing so that, you know, you might see more three- or five- or seven-day doses dispensed rather than 30-day supplies. We actually think that there are things that we can do -- we're going to be putting out a federal register notice very soon that's going to articulate some of our thinking here.

But you know, to give you one example, we can build into -- if we can work with provider groups to build into the labeling of these products, what the appropriate dispensing should be for different indications. So, for example, work with the Dental Association to build into labeling a recommendation that any dental procedure really shouldn't be more than a five- or a seven-day supply of opioids. We could put that into current labeling. That could be used as a way to help regulate dispensing at the pharmacy counters.

So, there are ways to achieve these goals through our regulatory tools and working with the provider community, and we're going to look at how we can use our existing regulatory toolbox more creatively to try to address these goals. Because the reality is, I think the only we're really going to solve this crisis, and the enormity of it, it's going to be very hard to solve, is if we also bend the rate of new addiction. And so, we have to focus on addressing that aspect of the crisis as well. Thanks a lot.

[applause]

Mary Woolley:

Dr. Gottlieb has one of the most daunting jobs in this nation, if not the world. Thank you so

much for spending some time with us.

We're going to move on to our second panel now, and the moderator for this panel is Byron Pitts, the co-anchor of ABC News "Nightline," and the chief national correspondent. He has covered national new stories and in-depth features for the network, reporting across the news division, including "Good Morning America," "World News Tonight with David Muir," "This Week," and "20/20." Pitts is a multiple Emmy award-winning journalist, and news veteran with over 20 years of experience known for his thoughtful storytelling, on the ground reporting, and in-depth interviews.

And our panelists are Dr. Joe Selby, the executive director of the Patient Centered Outcomes Research Institute, or PCORI. Dr. Mark McClellan, the Robert J. Margolis professor of business medicine and policy and director of the Duke Margolis Center for Health Policy at Duke University, and as has been mentioned, former commissioner of the FDA. Nancy Brown, the CEO of the American Heart Association. Dr. Victor Dzau, the president of the National Academy of Medicine. Dr. Joel Beetsch, vice president of Global Patient Advocacy at Celgene, and Scott Whitaker, president and CEO of AdvaMed. Thank you. Over to you, Byron.

Byron Pitts:

Great, thank you. Well, hello, everyone. Our ground rules -- we're going to talk amongst ourselves for about 20 minutes or so, and we'll open up sooner to questions. My primary job this afternoon is keeper of the time. So, no sermons, please. Just quick Bible verses and your questions, so we can get as many questions as possible.

And so, Joe, I'd like to start with you. We just heard from the previous panel challenges and potential solutions to the opioid crisis. Tell us how your organization is addressing this epidemic with research. And how would you describe the type of research the institution funds?

Joe Selby:

Sure. Well, if I might just say thank you to Research!America for the invitation to participate in the panel, and that was a fabulous panel, I thought. So, happy to respond.

PCORI was set up to do the kind of research the governor was talking about, about research on what works. And particularly, comparative -- a comparative approach, what works for whom? And particularly, in real-world settings. So, we ask and answer practical questions in a comparative fashion in real-world settings. So -- and we do it -- we do it because we're set up to serve the information needs of patients and clinicians, policymakers, health plans.

So, we start by listening to stakeholders. And about two and a half years ago, it became very clear that patients and clinicians in particular -- payers as well, were asking us to support research on what works in the management of both chronic pain and opioids. So, we now have a portfolio of 11 major projects -- it's a targeted topic; 11 major projects, about \$65 million in investment. We have more awards being made later this month, and we have two open announcements -- one about medication assisted therapy in pregnancy, and a second one, a re-opening of an initiative.

Our research covers this spectrum -- we take a pretty holistic approach, from preventing the initiation of opioid use in the emergency room, or dental office, or other places. To managing patients with chronic pain who are using opioids to particularly reducing the use of high dose and risky dose opioids to managing addiction. So --

Byron Pitts:

Please, sir.

Joe Selby:

Just -- we do the research in settings from the VA to Medicaid programs to federally qualified health centers to prisons to integrated delivery systems because the research has to be done in the real-world. And I would say that we're examining everything from medication-assisted therapy to non-pharmacologic therapies to decision support -- for patient's decision support, for clinicians. Yeah.

Byron Pitts:

We're going to look at our conversation in three areas. Landscape, the -- challenges, the future, and then we'll open up. So, this next question is for Joel and Scott. You guys can tackle this one. And the other panelists, please feel free to weigh in, if you choose in. Now, gentlemen, how do you integrate the patient voice into the research and development? And what is on your wish list to R&D process? Sir?

Joel Beetsch:

So, from the biopharmaceutical sector, I think I speak for many of my colleagues in the room. Many of us have several different approaches to how we include that patient voice. I have the pleasure of leading the patient-focused efforts at my company, but we work very closely with the sort of ecosystem on all of this.

And I'll talk about three different ways, and maybe I'll let my colleague talk, and we'll talk about wishes as well. So, the first way we do this at my company, and many others is continuing to look across the entire life cycle of a particular product to -- or a therapy in development to determine where there are places to put that patient voice into the R&D process. Everywhere from natural history evaluation, all the way out to post-marketing data evaluation. So, the entire spectrum. That's number one.

Number two is we've started at Celgene -- and many other companies have this as well, is a patient-focused center of excellence within our R&D organization, of which I'm a strong contributor to, where we're looking at all kinds of analytics to evaluate the clinical trial patient burden index for the complexity of a particular clinical trial. How much regulatory input do we need? What does it mean for a patient to be in a clinical trial? Well, they stay in that clinical trial. So, lots of data -- and we talked about data in the first panel. Lots of data and data analytics.

And the third way, and many of my colleagues are here in the room as we work together as a stakeholders group with industry -- other study sponsors in academia with patients and patient advocates to build infrastructure around how we can incorporate that patient voice into trials that

-- clinical trials transformation initiative finally got their paper published. But we just put out kind of a guide book on how to do it.

Scott Whitaker:

Very similar from the device perspective, and I won't repeat what was already said, but the one thing I would add -- one of the things we're trying to do is have patients begin to tell the story for us about how devices and new technologies have changed their lives. I think of the previous panel and the opioid addiction conversation we were having.

I told a story recently about a young veteran who served in Afghanistan, hurt his back terribly badly. Was on opioids for two or three years. Debilitated, sort of ruined his life. And then, he found a new technology that one of our companies produced, which eliminated the pain. It was a device. It eliminated the pain, and it allowed him to get back to living a normal life. Having him tell that story is more powerful, many times, than us telling that story for him. Opioids almost destroyed his life. A device changed his life. And as we tell that to both regulators, to payers, and also to members of Congress, it changes the way you think about the patient perspective, not just from a company's perspective, but the impact it has on an individual's life. And that's been a very important part of what we do.

Byron Pitts:

Thank you, gentlemen. And Nancy, how does the American Heart Association leverage patient data and technology in cardiovascular disease research to improve prevention and treatment?

Nancy Brown:

Thank so you much. And first of all, thank you again to Research!America for this wonderful and inspirational afternoon. You know, we've been very focused for about 15 years -- very methodically collecting patient data, back when we created and launched our program called Get with the Guidelines that now is in 2,300 U.S. hospitals. And the purpose of that program at the time it was launched was to improve adherence to guidelines. So, the AHA and our colleagues at the American College of Cardiology, for decades, have created evidence based clinical guidelines that were not being implemented in a robust fashion at the point of care.

And so, we created this decision support tool that captured patient data, allowed us to look at trends in hospitals. And we've used that data, actually, in whole, to look at improvements in healthcare -- improvement in healthcare disparities in over 400 published manuscripts. And so, that's been an important aspect in using patient data.

But more recently, we've been focused on individual patients who want to contribute all kinds of data, from genetic data, to lifestyle data, to sensor data. Through our institute for precision medicine, where we've created this robust data platform to allow this data to be captured in use for scientific research. And for value to be given back to patients who donate data.

Byron Pitts:

Victor, to you -- thank you, ma'am. Victor, to you, sir. Is medical discovery itself able to speed up medical process? And tell us about gene editing, and how it -- how does it fit into the future of medical progress?

Victor Dzau:

You heard earlier -- by the way, thank you, [laughs] Mary, for putting this together. And Patrick, you were just terrific. And it does say one thing, from my perspective. We're moving too slowly. We're talking about clinical research; we're moving too slowly.

If you look at the time -- average time taken to get a new pain medication that's non-addictive, the clinical trial is needed. We know that the huge amount of dollars is needed for a clinical trial. I think the top center for drug evaluation development is about \$2.6 billion just for the development piece at home. Clinical trials is \$1.6 billion per drug. And so, you can imagine that unless we overcome these issues, it's not going to be -- you know, so I'm really glad to hear Scott Gottlieb talking about modernizing of FDA, moving things -- and you and all of us talking about how to use data at adaptive trials, et cetera.

So, my feeling is when you heard earlier speaker, Mike talked about how all these technologies now close -- yes, I think so. Gene editing is a great example. CRISPR/Cas9 being one of them, being able to precisely change a gene, and, you know, certainly is already now used in so many therapy in a big way. Therapeutically, still experimental. And of course, germline therapy, we struggle mightily at the National Academy to say should we move forward or not?

So, I think technology, in terms of science discovery, is moving really quickly. Where we're falling behind is, in fact, the taking from the pre-clinical all the way to adoption and practice. That's where I think we need a lot of push, a lot of change. We're moving way too slowly.

You heard earlier about maybe we need to think about different way of using data. First, different trial design. Adaptive trial, right? Bayesian methodology to look at new ways to look at taking data together from different early trial to a pivotal trial move faster. You heard about the idea of maybe using technology. And you know, we've been talking for a long time -- how to integrate clinical database with recent clinical research so that we don't have to rediscover every time you enroll a patient.

And I'll tell you a little bit later, perhaps, about some of the innovation that's been going on elsewhere that shows that you can actually quickly accelerate trials at a much lower cost, and we can really get integration of data, sharing data, data infrastructure, and new design -- ways of doing this. And certainly, ways by which we reduce the administration. Being at Duke, I remember how long it takes to get a contract done, right?

[laughter]

And how long it takes, in fact, to get the first patient enrolled. And so, I think there's so -- my answer your question is I think science and technology are moving at a rapid pace. We got to apply them to the last mile which, in fact, is right now, the clinical research development, which is slowing everything down, and is costly as hell.

Byron Pitts:

Thank you, sir. And Mark, what health system reforms do you recommend to help get

treatments to patients in a safe and timely fashion?

Mark McClellan:

Well, I think that solution's there, in the same direction you've just been hearing from the rest of the panel. And I, too, am very glad to be part of Research!America's efforts in this area. To say it's much easier being on the afternoon panel than the FDA commissioner's squad.

[laughter]

One of the things that Research!America has been emphasizing in the format for this meeting, and the work going forward is the need to think about research broadly. So, it's not just that the basic clinical research and kinds of things that kind of go on with NIH funding -- important and critical as that is. Important as that part of Research!America's mission is -- but really, you know, as Victor was saying, taking it kind of the last mile. And boy, it seems like a lot more than a mile to get these discoveries turned into products that can be produced reliably, used effectively.

And you heard a lot today about changes in delivery systems that are needed. There is more going on to try to shift the focus from the pain and use of individual products to really meeting particular patients' needs. You know, a patient is not just someone with pain, or someone who gets a procedure, but a whole constellation of genetic predispositions, behavioral and environmental influences, preferences that influence, increasingly, what their treatment should involve. And we are not doing a very good job of aligning all these discoveries that are coming through the process, either in the development process of knowing which treatment is going to work best in which patients, where real-world evidence and like can help, or in the utilization process.

So, still a lot of work to do there, and a big need for research on what works in getting the right treatment to the right patient. Having a discovery that is not accessible and is not affordable is not really going to have an impact on public health. And more attention to research to figure out how new healthcare delivery models can work with medical product developers that are trying to solve these problems, as we -- as you just heard, can work with payers, and there are many represented in this room who don't want to just pay for stuff but want to pay for better care and lower costs. We need a lot more research there. Joe's group is helping with that, but we've got - - we've got a lot of unanswered questions.

Byron Pitts:

You talked about -- thank you, sir -- about problems. So, let's move on to some of the challenges. And I open this up to the panel, so feel free to jump in and to follow up on your colleagues. What are the most daunting challenges in research, drug development, device development?

Scott Whitaker:

So, I'll start down at this end. I put device development into three buckets. In many ways, it's public policy, right? The first is tax policy. The tax environment has to be right to incentivize companies to invest in research. And I could go into the details of the device tax and the structure of that and how it's taking money away from our companies that we were spending on

research before, but that's probably for another conversation.

The second is around the regulatory environment. And it's less about having a quick and speedy pathway and more about having a clear and transparent pathway through the FDA to get to approval. And that's what we've spent so much time working on. Mark, when he was the FDA Commissioner, led a lot of that effort to improve it. Jeff Shuren, who's at CDRH now, for us has done a great job in both speeding up that process and making it clearer for us so we know exactly what we're into when we start down the path. And then Scott, under his leadership, I think is going to add to that and do an even better job.

The third piece is really payment policy, and that's one that many people don't really think about. Mark touched on it a little bit earlier. But clarity and transparency in the payment space, there's a lot to be gained there, right? We're not doing a great job in helping companies understand how to get the product through the FDA and then have Medicare, Medicaid, public payers, and even private payers reimburse for that. And it's not that we just want to get paid a lot of money for that. We just want to know how to get paid and what that price is so we can begin down that pathway.

Byron Pitts:

But you don't mind getting paid a lot of money.

Scott Whitaker:

We'll take that, too.

[laughter]

Byron Pitts:

Okay.

Scott Whitaker:

But what you hear from investors more than anything else is we understand the FDA process now. We have no idea what's going to happen once you get through FDA, and that's the piece I think we really need to figure out. Yes, sir?

Joe Selby:

And that's the piece that Mark was talking about and that PCORI operates in is that space -- once things become available, or at least arguably available because they've been improved, there are some hurdles. And one of them is how do these new therapies compare with older therapies that were already there? How do they work in real-world populations? Are some patients going to respond differently than others? And that's what comparative effectiveness research, the kind of research that we fund, looks at.

Most people in the room know that a good portion of our revenue set up in the Affordable Care Act actually comes from a fee on payers. No one else pays into supporting it. We see the payers' dilemma, oftentimes, that something gets approved, and then it gets -- that's predictably fairly costly. And they don't really know how it compares to what they've been paying for before. They know it maybe costs two or three times more. They do not know who's going to

benefit. They know that not everybody's going to benefit. So, as Mark said, there is a tremendous amount of research needed, and it's shocking. And we need to learn it in real-world practices. That's why we set up PCORnet, so that you can study in real-world practice how new therapies are working.

We need closer partnerships with, I think, manufacturers, probably with the FDA and with payers -- with CMS, for example -- to do it as effectively as possible. But a lot of questions need to be answered once approval has happened.

Byron Pitts:

Please.

Joel Beetsch:

Let me just jump in here. Mr. Joe, thank you for your comments about comparative effectiveness. I think we need to be really clear and transparent about how that's done. I think PCORnet does a wonderful job of putting that into the practice. But also, there are organizations looking at, you know, development of value principles that don't necessarily take the patient perspective in mind. So, I think, as Scott was saying, you know, the big issues about access -- the drugs, the devices, the therapies, the technology can be as great as it can possibly be, but without access to it, it doesn't help for anyone. So, I think, you know, that the working together with PCORI and PCORnet, with all of the stakeholders, I think will help define that a little better.

Victor Dzau:

I would -- I would agree with Scott's framework about those three big challenges. But I would like us to spend a little time talking about how we can overcome them, right? So, if you look at the first piece, to me, as I said earlier, the cost and time is extraordinary to the extent that, you know, it's taken too long for a discovery or drug to be eventually approved or get through the clinical trial. And there really are many things that we can be doing now to make it faster, and we can talk about that perhaps later.

But I also think that the issue of payers -- I think we also have to understand the elephant in the room, which is how to actually look at the price of drugs. So, how do you actually transparently figure out what you're likely to be paid and why you're likely to be paid? These things have to be really addressed. Otherwise, I think we can't afford all those therapies that's coming down this way. So, I do think that these are the fundamental issues, and each one of them can be addressed in one way or the other.

So, for example, on the first one, certainly, I was going to tell you that if you look at the ability to integrate a clinical research project into a clinical practice database and have an exchangeable, harmonized information system across different research sites, you move a lot faster. In Sweden, you may or may not have heard of this study called TASTE published in the New England Journal in 2015. They have a national electronic record. They have a standard way of collecting the information. And so, their question was, for the acute MI, patient comes in, does removal of thrombus before [unintelligible] make any difference?

Well, you know, in a 14-month period, they were able to enroll -- they found 10,000 eligible

patients because the database is all coming in common ways. 7,000 they were able to enroll. Our record? Five percent of -- in U.S. -- of eligible patients are enrolled. Huge difference, because you have an efficient system. Then those patients will get a standard of care they can randomize so at the end, the cost of that study was \$350,000. \$50 a patient. Incremental. In our country, it would be a three- to five-year study, \$15 million, \$20 million. I think there are some fundamental things we got to change. That's what I'm trying to make for this first point.

Nancy Brown:

And can I add onto that, Victor? It's such an important point. And that's why at the American Heart Association, two years ago, we formed a strategic relationship with Amazon. And we actually have created what I would say is a state-of-the-art data discovery marketplace. And since the moment we announced it in November until -- my microphone is not working -- okay -- until it was, you know, tested this Spring, and launched officially in July, we have 39 million patient records in this data infrastructure in about a six-month time period. And these are data from observational studies, they're the data from worldwide stroke and atrial fibrillation consortia, they're health system data, and we're continuing to get additional data in.

We've created 84 analytical tools. Well, we haven't. Amazon has created 84 analytical tools, and there's sandboxes off to the side that will allow this collaboration to happen with custom clinical studies just like that. And so, this infrastructure has been developed. We are, at the AHA, giving robust research grants to utilize the data, and we look forward to this data infrastructure contributing to answering a lot of these questions and speeding time to market.

Mark McClellan:

Development of these kinds of infrastructure are critical, and it highlights the two sides -- the need to change. Scott appropriately emphasized predictability and, hopefully, rationality [laughs] in the -- in the public policies that affect the development and use of new treatments. I would also like to emphasize the need for companies and the people on the private side to do things differently. There are a lot of product developers in this room, health plans, consumer groups, that are working with us in our program at Duke on implementing some of these new, much more person-focused models for paying for treatments. And a step in that direction is things like drug or device payments being tied to the results that matter for patients.

As you heard, we're just in very early stages of those kinds of arrangements now where, you know, lots of times, what really matters to patients isn't captured. I think that's not only because of, maybe, obstacles to understanding and wanting to focus on what matters to the patients. It's also because of practical obstacles. Without infrastructure like what Nancy was just describing, it is not possible to know, reliably, whether a drug or device is really affecting the outcomes that matter to patients over time. And there's not going to be a company-by-company specific solution for that. We've seen that not work on the provider side in payment reform efforts. It won't work on the medical innovation side either. So, that means, going along with the steps on the public policy side, is much more of a need for collaborative research and collaborative infrastructure that's shared.

You know, if we're trying to solve a problem with heart disease or any other condition, that is not a company-specific problem. That is a society-wide problem where we ought to find more common-ground steps we can take to reduce the cost and make it easier to really learn what's

working. PCORnet, your efforts, these are all first steps in that direction, but we have a long way to go to make these products much more widely available at a lower cost.

Joe Selby:

If I could --

Byron Pitts:

Yes.

Joe Selby:

-- just add one thing. Building on what Mark and others have said, the simple suggestion that I'd have is that we find ways to get started earlier in the process, so that if one knows that a product is going to be approved, it's looking good, you are sitting down with payers -- hopefully, you've sat down with them even before then. But manufacturers are sitting down with payers and with funders of comparative effectiveness research and planning the studies. Hopefully short, rapid in PCORnet and other infrastructures, so that you -- it does become more transparent what it takes. And what it takes is this matters for patients, this works differently than others, and these are the patients who benefit.

Those kinds of questions, if answered on the day of approval -- and they aren't, because that's not part of FDA's mandate in terms of approval -- but if we're beginning to answer those questions earlier on, we'll get to a solution to the coverage question much sooner.

Byron Pitts:

All of you care deeply about healthcare. It's your life's work, as for people in our audience. But many of you represent different lanes. What are your tensions, and how do you -- what are -- what are your strategies for managing those tensions, right? Because sometimes, I would imagine, your interests are different.

Nancy Brown:

One tension I would just mention -- I don't know that it's a tension, but it's another elephant in the room. You know, I haven't heard anyone yet today talk about people who aren't in a system. And, you know, if we look at -- for example, it was referenced earlier by our colleague from CDC, the unfortunate uptick in death from stroke. And you peel back that data, it is African-Americans and Hispanic-Americans who have driven that number up, and it looks like the entire population has -- you know, has increased in terms of deaths from stroke.

The same thing is happening with heart disease deaths. For 40 consecutive years, deaths from heart disease declined until two years ago. And now, there's this uptick related to type II diabetes, related to obesity, related to all of these things that are impacting lifestyle, but there is a disproportionate effect in certain populations. And we have to be willing to step up to solve those problems, too.

Victor Dzau:

I think it's along incentives. And by this, I'm not being critical of anybody except different entities have different incentives. And until we can get together and really understand common incentives, becomes a problem, right? So, I think that's a fundamental issue that needs to be

addressed.

The other one, sort of coupling with what Joe said, is very early, we ought to talk about an economic analysis. You know? So, many of the studies don't bother to talk about how much savings -- in terms of comparative effectiveness, how much would it cost to develop this, and how do we arrive at a rational way of payment, right?

Male Speaker:

Right.

Victor Dzau:

So, both in terms of drug pricing and payment needs to be addressed as part of a clinical trial. Whether you collect that data in terms of economic data or use an economic modeling, at least to make the case, and you can follow that in post-market surveillance follow-up to see whether you realize those kind of economic and cost-effective savings. To me, I think development -- any new device or drug has to be cost effective. The same idea what Joe is saying.

Male Speaker:

But if you --

Victor Dzau:

It's just not it can do the job. It's got to be doing better than what we have. And it's got to be -- even could be more expensive, but it's better. It's cost effectiveness that's really important.

Joe Selby:

So, the value discussion is a place where folks are trying to find common ground. Everybody can agree that something should be valuable patients. Now, it's absolutely true that in order to calculate value, you have to understand what patients value and how these different treatments affect that. So, that's a part of the -- of the mix there, that we need these kinds of studies that look at a wide range of outcomes.

We had met with a group of people with multiple sclerosis about three years ago. It was a very dramatic meeting. They are not suffering from a shortage of medications right now. They say, "We have 14 medications that will treat our disease -- 14 expensive biologics that will treat our disease." We all know -- because the FDA requires that they show, to get approved, that they change the findings on CT scans.

So, the CT scans or the MRIs look better. Great. That the frequency of recurrences is shortened by the drug. So you know, they have relapses at a certain point in multiple sclerosis for years, and so got to shorten the frequency of those relapses. And that some measure of global functioning is improved by these agents. And then, you get approved. But they say, "We've got pain. We've got fatigue. We've got a fuzzy mind. We're not thinking well. We've got imbalance." There is no evidence, because it wasn't collected -- it wasn't part of the approval process -- there's nothing that tells us whether one of these drugs is better than another in terms of fatigue or fuzzy mindedness or imbalance.

So, we're now funding a very large portfolio that gets at how do these drugs do, and how do

different treatment regimens do in terms of, guess what, patient-reported outcomes? Same in the pain -- in the pain arena. All of those studies have patient-reported outcomes, but capturing those is part of calculating value. Sometimes, when you actually get those outcomes, you really don't even need to go through the formality of the value calculation any longer.

Scott Whitaker:

I have a comment. Just using --

Byron Pitts:

Please, sir.

Joel Beetsch:

-- your swim lane analogy, or lane analogy, I think that one of the challenges is that those that swim in those lanes go into the pool, that water's circulating all around, and we swim for the day and we go back to our lane at the end of the day, right? So, we have shareholders, we've got other things that we need to pay attention to. I think what you need to do is take the lanes out and free swim it, and let --

[laughter]

-- you know, let people, you know, continue the engagement. I think there's progress being made. I think Dr. Gottlieb spoke about some of the things that were going on between the FDA and CMS and private payers and what Novartis just launched in a CAR-T therapy. There's interesting new things where there's relationships with commercial payers to pass valuable savings along to patients so they don't have out-of-pocket expenses. We have challenges, and those are things that I think we can do as a -- you know, in a free swim situation is to try to get that applied to, you know, government insurance as well.

Scott Whitaker:

So, I was going to add, there are a lot of tensions that exist in the healthcare system. Clearly, an innovator and a payer, there's a natural tension that exists there. An innovator and a regulator, a natural tension that exists there. And a healthy one, I would add. But there's one thing at the center of all those that pulls us all together, and that's the patient.

Male Speaker:

Patient. That's right.

Scott Whitaker:

And oftentimes -- and I'll speak from the government's perspective -- oftentimes, it feels like the government policy is budget-centric and not patient-centric. And I think if you think about it that way -- I know that's a broad statement, but it's an important statement. And you think about policies that might be more patient-focused than budget-focused, you might get the better solution.

So let me give you an example. Victor said, "Let's not complain. Let's look for ways to improve the system." And I think that's exactly right. There's a proposal that went through, 21st Century Cures, that was breakthrough pathways at FDA for, in our case, devices to get more

quickly through with more transparency through the FDA. Right? But the roadblock you still hit is at CMS.

So, we had a proposal that we're working on right now which is breakthrough pathway on the payment side, which would be if you meet the test for a breakthrough product at FDA, once you clear the FDA hurdle, then have CMS give you a temporary code. At that point, you can begin the process, as Mark talked about, of building the evidence, right? We're not asking for a specific dollar amount. We're asking for access to the market so that we can build the evidence as to whether it works and what's cost effective. Been met with crickets so far, but I think it's a good idea. It's ideas like that that are a little more patient-centric that might help incentivize less tension and more patient focus to what we do.

Victor Dzau:

I agree with that.

Byron Pitts:

I'd like to open up to the question from the audience. If you could please raise your hand, we have mics in the room. If you can give us -- please stand and give us your name and organization please.

Joe Hedrick:

Sure. Hi. I'm Joe Hedrick with -- I'm Joe Hedrick with Janssen Research and Development. And as we've talked about what the patient values, often, as we all know, that's very difficult to assign an economic value to -- or sometimes that economic value is not realized in the near term. So, if I'm a private insurer and I know that this person is only likely to be in my plan for three years, what's my incentive to pay for a medicine that the economic value occurs 20 or 30 years down the line?

And I'd just like to hear from the panel, are there ideas to solve that as a problem? Because the patient perceives the value. There's economic value that could be years down the line, but nobody's willing to pay for that right now. So they wait until they get there, and then they pay for expensive secondary complications of diabetes or something like that. That seems like a pretty crazy way to be operating.

Byron Pitts:

Please.

Joe Selby:

I'll just say to the extent that that's still an argument that is given, I think it's really sad. I mean, there's a cynicism about it that is just unavoidable. I think a lot of payers have gotten beyond that, and they understand that they're -- you know, that they're in a society, they're in a -- in a -- in a -- in a population, in a country, and they have a responsibility. But I can't disagree with you that it has been said many times, and it may take -- sometimes it takes policy to change that attitude.

Mark McClellan:

Yeah, I want to say something about this, too. But let me first back up a second and talk about

patients and costs. And I think in terms of another elephant in the room, it is going to be very hard to continue making progress, building on the 21st Century Cures opportunities, the pre-clinical announcements that Scott just made, if we don't do a much better job of using these and all other medical treatments efficiently in practice.

If you think about what really concerns patients these days, it's not just getting access to the treatment if you have MS, but, you know, you pretty much know you're going to be out thousands of dollars each year, even if you get the treatments that are covered. Why? Not necessarily because payers don't want to pay for anything, but just look at the cost numbers now.

So, my former agency, CMS, has an expected budget this coming -- this year of over \$1 trillion. Compared to the debate that we're having about a couple of billion dollars increases in funding for NIH and 500 million or a few billion for the opioid crisis, I mean, CMS spends that kind of money in less than a day. So, if we don't do a better job of addressing the use of these technologies in practice, it's going to be really hard to pay attention and put appropriate effort into some of these things that really matter for patients. Just to put that in perspective, too.

And I agree, this argument shouldn't really hold weight. And again, I don't think it really does. If you look outside the U.S. at countries like Sweden and elsewhere where, you know, the same people are in the same government-run programs for their entire lives, the prices [laughs] are actually much lower than they are in the U.S. because there are these real concerns about overall budget constraints.

So, I think if we want to have real innovation in this country, the kinds of things that we're talking about here, it's going to take a much better effort to change the way that we deliver medical care. So, we're spending, hopefully, more on these breakthrough therapies, but to make that sustainable, we got to spend less on the -- Victor and I did a -- write a report recently that the National Academy of Medicine put out on vital directions, which remind us again, 30, 40 percent of healthcare spending is probably not contributing much, if anything, to outcomes that patients value, and some -- a lot of it is actually harmful.

That may be viewed as something that's kind of outside the purview of people who are developing these new treatments, but again, you're going right in. We're talking about alignment, about what matters for patients. Alignment, what matters for patients is not just their outcomes, but the total cost of what they're having to pay. So that's got to be part of this solution, too.

Male Speaker:

Mark?

Male Speaker:

[unintelligible] Mark?

Byron Pitts:

Mark, you mentioned the 21st Century Cures Act. Where does that stand now from you all's perspective? I mean, it was -- it was presented by one administration. Some see it being viewed differently by the current administration.

Mark McClellan:

Bipartisanship is alive and well, right?

[laughter]

No, this is -- I don't have a long answer to that, but I think FDA is doing a great job of starting to implement that program. And it does two things, two main things, I think. One is it gives FDA a lot more authority and needed resources to develop new kinds of treatments, precision medicine, data from patients, these kind of new clinical trial models and real-world evidence systems that Scott talked about earlier. But the second thing it does, it really encourages a lot more of a collaborative -- I don't know if I want to use free swimming, but --

[laughter]

But, you know, swimming --

Nancy Brown:

Synchronized.

Mark McClellan:

Synchronized, maybe. But the public and private sectors working together to solve some of the problems we've been talking about today. So, I think those are -- those are really good -- really good steps.

Byron Pitts:

Question. Yes, sir?

Albert Reece:

My name is Albert Reece. I'm Vice President of the University of Maryland and Dean of the School of Medicine. I felt a little sensitive -- from the last panel regarding the responsibility of physicians for the opioid crisis, so I just want to make one comment and then ask a question. One is that, at least at the University of Maryland School of Medicine, we make sure that we -- every year in medical school, every year, the students are educated on opioid addiction, prevention, and the biological complications. So, let me get it off my chest.

[laughter]

I want to say, first of all, terrific panel just now, we had all morning. But there's one thing that I want to comment, and Victor made the comment regarding the expensive nature of producing a drug, and also the time it takes from bench discovery to actual patient care. And that is certainly well acknowledged, and when I give the talk, I use the -- from Brown and Goldstein's Nobel Prize to the formulation of statin and how many years it took. And that was one of the faster drugs to be produced.

But one thing that we haven't covered yet so far that I'd like to ask you to make a comment on, and that is the whole idea of recognizing that there are many, many drugs that have been

approved by FDA. And those drugs have -- some of them have failed in clinical trials. And it would be worthwhile -- in fact, I think it's a great idea -- to repurpose those drugs. Because in that case, you actually circumvent going through the whole process. At my institution, I really encourage, once a discovery's made, try to find molecular characterization of the molecule and try to find a drug that resembles that molecule. As opposed to creating a new drug, a drug is already on the market, is already approved by the FDA. You're simply going to have to repurpose the drug.

My question to you is, how do you see that fitting into the landscape, Victor, and being able to at least shorten the time frame from a discovery to patient use?

Victor Dzau:

Well, as you know, Al, there's a lot of interest and activity in repurposing drugs. I thought you were also going to mention precision medicine, because really, when drugs fail and you don't pay attention to the specific -- whether it's genotype or phenotype of that particular patient, the well-known drug in terms of lung cancer, EGF receptor. Well, you can really re-look at the genetic profile and then find that it actually works in smaller population ineffectively. So, I think there's a huge possibility for repurposing. Point's well-taken.

Nancy Brown:

I might add to that, as well. We have a really great research program at the American Heart Association -- Google's life science company, Verily, and AstraZeneca have funded to the tune of \$75 million -- one investigator and a team of people. And part of the work that that group is doing, based out of the Brigham and Women's Hospital in Boston, is exactly looking at this topic of drug repurposing and using the high computing capabilities that are available to us through this collaboration, the available, you know -- the molecular library, but as well as the drug library. So, we're working on that as well.

Albert Reece:

I wish it were much more promoted and much more -- it's available, but somehow, our investigators, or even the public, it's just not highly promoted and highly visible and highly recognized. It's certainly a way to go --

Joel Beetsch:

Yeah.

Albert Reece:

-- but it's really underappreciated.

Joel Beetsch:

I mean, from the biopharmaceutical sector, this is happening daily, and it's not well-publicized. I think the -- I think the biologic sciences and the genomic sciences are catching up to the pharmaceutical sciences in that you won't be treating diseases any longer, it would be treating genetic and other molecular pathways. And it's happening. There are examples where there's drugs on the market for oncology that immediately go into multiple sclerosis. And so, there's examples there. I think we need to look closer.

Byron Pitts:

We have time for a few more questions. If we can make the questions as tight as possible so we can get as many questions as we can. Yes, ma'am?

Nancy Buck:

Hi. Yeah, I appreciated Joe's -- oh, Nancy Buck, Avalere. I appreciated Joe's comment about sitting down with payers earlier in the process, but I wondered how constrained drug and device developers feel by rules around pre-approval communications, FDAMA 114, and how do you communicate -- how do you balance communicating value and cost effectiveness when you have some of those rules in place?

Scott Whitaker:

So, it is really tricky. I'll tell you what we're doing right now on the federal level is we've been engaged with the HHS Office of Inspector General to try to get a better understanding of how that process should work. There may be some safe harbor rules and regulations that you can put in place to allow that communication to go forward. If it's done under the best intentions, which it would be, I think, speaking from device and drug companies both, it can work really well, but it is an impediment right now. And honestly, it's hard to get over that without some changes into either federal statute or regulation.

Byron Pitts:

Question from this side of the room. Please, sir.

Male Speaker:

Speak up louder.

Male Speaker:

Go ahead, speak loudly. I never have a problem --

Male Speaker:

Your name --

Male Speaker:

A little softer.

[laughter]

Jay Siegel:

I'm Jay Siegel, Johnson & Johnson. I wanted to follow up on repurposing because I agree that the opportunities are extensive, and I certainly agree that when you look at drugs as influencing pathways, you know, as we did, for example, with Remicade. We found 16 different indications for that, for that drug. There are limitations, though, especially in the IP space. And what we find on a regular basis is that we have a drug that we realize a new use for, for an important disease, and we can explore that use simply by investing \$250 million at the end of which time, there will be generic competitions and we will never recoup anything close to the investment, or by a similar competition.

So, I know that some work has been done in terms of IP in that space, but -- and yet, still, there is so much more in terms of innovation that could be done. So, the question is should we, as a group supporting innovative research, be looking to better IP protection for that sort of repurposing?

Scott Whitaker:

The answer is yes. The question is the people who have to make that decision and have that debate usually do it in a public forum. And all of the sudden, it gets away from an actual conversation about IP protection for the patient that your trying to serve into a political conversation about the cost of drugs and its impact on society. Now, once you get into that conversation, it kind of ends, right?

So -- but if somehow you can have public dialogue where people are having honest conversations about the value of intellectual property to our system, then maybe you can get there. Until then, it's going to be, just frankly, really hard, Jay, to have an honest conversation about it.

Byron Pitts:

As we run out of time, if we could have closing thoughts from each of you and, Mark, I wanted - - I'm sorry. Victor, I wanted to start with you. You mentioned the word "innovation" earlier. So, in your closing remarks, if you could talk about something that you're excited about that you see as part of the future that will -- that could potentially be a game changer.

Victor Dzau:

Well, I think there is certainly a lot of discussion on the use of data that we can collect now through different ways, wearables, electronic health record, many others. And I'm excited about that because I think it gives you a lot more data that's useful, hopefully, and that if you can share it, it would be very powerful. And that, if one can develop analytics, as we said earlier, then I think we can really transform the way by which we can do our clinical research and move things much faster.

You know, I'm thinking that even if you use innovation technology as a way to look at patient recruitment -- in Scotland, there's a program called "Share" where they are actually looking at every patient that comes to the system is registered. And automatically, they consent to being searched online anonymously for any condition that they have. And if there's a match with a potential trial, they will be de-identified, contacted, and they can opt out. So, now you can save a lot more time.

So, I think if you look at technology innovation, innovative way of doing things, I'm on the bandwagon that we've got to think about these kind of things in order to move things forward. If not, then you'll be coming to the same-old, same-old, you know. Clinical sites, protocol at a time, each group [unintelligible] at a time and, you know -- and trying to look at data analytics at a time, and it's just not good. So, I'm excited about the data and innovative ways of using it.

Byron Pitts:

Scott, we'll go with you and then down the line, about 30 seconds.

Scott Whitaker:

My industry is on the front edge of cutting innovation. I've got on my watch, which just happen to remind me. A sensor that connects to my daughter's blood glucose monitor. It's a continuous glucose monitor. We used to prick her fingers eight to 10 times a day to draw blood so she could check her blood sugar. She's type I diabetic. Today, she wears this monitor. It sends a signal via Bluetooth to my phone to let me know if she's high or low. That's innovation.

It changes the way patients live and it has a positive impact on long term outcomes. And if we embrace that technology and aren't afraid of it, it will be much better in the long term. I'd go on about 10 more items of amazing innovations in our space but that's just one.

Byron Pitts:

Thank you, sir. Please. Thirty seconds, if you would.

Joel Beetsch:

I think the data world -- we're creating data lakes and data oceans and I think, Victor, you said it nicely, is that we need better analytics tools or better fishing poles -- since we seem to be going down the path here.

Male Speaker:

Like swimming. Yeah, exactly.

[laughter]

Joel Beetsch:

But I do think that data is an important piece, but I think the patient-focused element is a critical one. I think there's a lot of focus on including that patient voice. I think the patient-focused drug development efforts that the FDA has underway. I think the European regulations that are being put into place in 2018 to make sure that that patient voice is included. I think we can make innovative trials that are friendly to patients to encourage them to join in a clinical trial and stay in it.

Byron Pitts:

Nancy? Thank you, sir.

Nancy Brown:

I would just add to all of the discussion on technology, I think it's inspiring, all of the companies that are not traditional healthcare companies that care a lot about helping to solve these problems. Everyone in this room needs to help those companies understand what the problems are, understand the basics of the -- you know, how clinical care happens, how patient prevention happens and how science happens. And I think we can see magical things in the years to come.

Mark McClellan:

Yeah, not even magical, but reality of healthcare and health that's really focused on intervening or intercepting diseases or preventing them before they happen. Care that's much more

prevention focused and that people can get at home, like Scott was just describing. I don't want to underestimate the hard work, though, to get from here to there. It means everybody not just talking the talk but really walking the walk of getting to value and putting patients at the center. And it means letting go and trying hard with new kinds of research on how to do this. We have long way to go to get there and this group can make a big difference in making it happen.

Byron Pitts:

Thirty seconds, please, sir.

Joe Selby:

Number one, patients. Patients have blown my mind, all of our minds, I think, in the last five, 10 years, the ways that they refocused us on the right outcomes and the right research questions, making for research that I think will move faster through the pipeline because everybody agrees that it's needed.

Number two, big clinical research networks like Coronet, Sentinel, the Convergence, a single national resource that brings the systems, the clinicians, the patients, the payors -- very importantly, the payors -- and ultimately, the sponsors of research, including industry, together to discuss what's worth doing.

Byron Pitts:

Please thank our panelists and thank all of you.

Mary Woolley:

That was super. Expect you to swim out in synchronous ways. Just terrific. Thank you all, so much.

And we've got another fabulous panel for you this afternoon, and the moderator will be Jeanne Cummings, the Deputy Bureau Chief for the *Wall Street Journal* in Washington, D.C. She was previously the *Journal's* political editor. Before joining the *Journal*, Jeanne served as the Deputy Managing Editor at Bloomberg, where she covered the White House, Congress, and the 2012 and 2014 elections. She also developed enterprise and analysis pieces that gave readers new insights, more context, and a better understanding of today's fast-paced news events.

And our panelists today are Dr. Francis Collins, the Director of the National Institutes of Health; Dr. Mikael Dolsten, President, Worldwide Research and Development of Pfizer; Dr. William Hait, Global Head, Janssen Research and Development, the Global Research and Development arm of Janssen Pharmaceutical Companies of Johnson and Johnson; Dr. Ann Cary, Dean of the School of Nursing and Health Studies at the University of Missouri, Kansas City; Gary Reedy, CEO of the American Cancer Society; Dr. Iris Loew-Friedrich, Chief Medical Officer for UCB; and Dr. David Neal, Senior Vice President for Global Research at Elsevier. Over to you, Jeanne.

Jeanne Cummings:

Good afternoon, everyone. That's a tough act to follow. That was a really interesting panel that you all just had, but you now have an array of brilliant minds again in front of you, myself not included. As she noted, I cover politics, so --

[laughter]

-- we don't cure anything. We don't heal anything. We pray for fights. So -- and injuries, blood works. It all works.

Male Speaker:

Your prayers are answered very regularly, too.

[laughter]

Jeanne Cummings:

Indeed. We call that "job security."

[laughter]

So, I wanted to start us off with a question here for Dr. Collins. When we talk about ending disease, there are all kinds of ramifications but there's an awfully long road to that particular goal. And for a long time, we have been hearing a lot about research into genes and other different types of research work that initially held such promise. Can you bring us up to date on whether expectations were too high, how well is it going, what is the status?

Francis Collins:

So, yeah, absolutely, delighted to be part of the panel. I'll try to make what could be a two-hour presentation very quick here in terms of what's the promise, where are we. I do think we have some unprecedented opportunities in medical research and accelerating that pace is highly justifiable. And I'm glad to be on the panel here with other people who are part of that important ecosystem that has made America such a successful story in this regard.

Let's talk about first prevention because if you want to reduce illness, it's better not to have it happen in the first place. In that regard, I'm happy to highlight, for instance, the Lasker Award going to Doug Lowy and John Schiller for HPV vaccine. There is a prevention strategy just this week being recognized in that way. That kind of approach we should be pushing forward.

Coming up with a universal influenza vaccine, which is a big effort right now on the part of NIH, working with industry, is going to be critical if we're going to avoid what could be the greatest threat to human life on the planet in the next five or 10 years, which would be a worldwide pandemic of influenza a la 1918. And we're overdue for that. So, if we're going to talk about trying to save lives that's a great place to put our investments.

But in terms of the regular process of prevention and treatment of chronic disease, I have to highlight where we're going with precision medicine and particularly, the "All of Us" program, which is in the process of beta testing what is going to be the largest prospective follow-up study ever conducted in the United States. Enrolling one million Americans with great diversity in geography and socioeconomic status, ethnicity, age, and gender, and which is going to give us a database accessible to all qualified researchers of unprecedented depth in terms of both environmental exposures, genetic factors, health behaviors, opportunity to get information from

wearable sensors and electronic health records, this should be and it will be transformative.

But it doesn't happen overnight. It gets better and better as such a thing goes forward. Certainly, something to watch. The full launch of that is expected late this year or early next year after we learn everything we can from the beta test, which has already enrolled several thousand people, but in this test mode.

And then, when it comes to treatment, there are so many things I could say, I'm sure. Cancer, immunotherapy would be one of the things people first wanted to point to considering what a revolutionary development seems to be happening there, but it doesn't work for everybody and we need to figure out why. And there are good ideas about how to take the success stories and make them happen more often.

And maybe I would say one final thing, in terms of a development in research that I think has only just now begun to be anticipated in terms of what it could mean, and that is the whole process of gene editing with CRISPR-Cas, the opportunity to be able to go in and change a single letter in the genome without leaving other footprints.

When you think of those 7,000 genetic diseases for which we know the molecular cause. 7,000, and affecting millions of people. We don't have treatments for any more than about 500 of those. But if we could come up with a strategy, and something the NIH is very interested now in investigating of CRISPR-Cas, not just ex-vivo but in-vivo to somatic cells to be able to correct those genetic glitches in a wide variety of those conditions. That would be phenomenal and it's the sort of thing that could be done not just as a series of one-off's for 7,000 diseases; it needs 7,000 approaches. This would be something more generalizable. So, watch that space. I could go on but I'll stop.

Jeanne Cummings:

Well, Gary, why don't you pick it up from there and talk about cancer and what progress is being made there.

Gary Reedy:

Thank you very much. And I also want to thank Mary and Research!America, and the organizers for getting this panel together. I was just mentioning backstage how it's really great that all three panels are building on each other as we look at what we're going to do to end disease.

From a cancer standpoint, you know, as Dr. Collins said, I mean, we're very excited with what's going on with cancer immunotherapy right now with precision medicine. You know, we're excited from a research perspective. We help fund a lot of basic research as being the largest not-for-profit funder of cancer research in the U.S. So, we feel like that we're all -- that we're finally making progress. And, you know, today, obviously, we're focused not only on the research aspect of it, but also on the patient support aspect of it, and making sure that, you know, that the patients have access, you know, to the research and what's coming out of the laboratory now.

So, you know, from where I see it today, we're very optimistic. We're very optimistic that in the cancer arena, you know, in the next 15, 20 years a lot of the common cancers that we see today will be either cured or managed as more like a chronic disease.

Jeanne Cummings:

Such as? Which ones?

Gary Reedy:

Well, breast, prostate, colon. You know, a lot of the more common ones. And maybe -- I'd like to hear from some of the researchers on the panel. I mean, maybe I'm being a little bit too conservative. You know, maybe we'll be -- have some of the more aggressive ones as well.

But I think -- one of the things we're still -- we're challenged with and this has been mentioned several times today, and that's kind of why we put an exclamation mark on it, is, you know, with all the great research that's going on, until we really address the social determinants of health, you know, a lot of people are not going to be able to have access to that research and if we can -- and I agree with Dr. Collins. You know, the primary goal is to stay well and to not get cancer or any other disease, you know, to begin with. So, if we can address, you know, some of these socioeconomic issues, educational issues, access issues, that's going to help a lot, as the research train, you know, starts to pick up speed and move faster.

So, we're very optimistic from, you know, what going on in the cancer space, but it's multifaceted. So, we have to make sure we're addressing the other issues at the same time we're advancing the research.

Jeanne Cummings:

And, Ann, that's very important to you. Do you want to --

Ann Cary:

I'd like to add to that because we know that about 80 percent of healthcare outcomes are due to nonclinical interventions. And so, if we think about that space and we think about where the research needs to focus, we need to think about redirecting or expanding our research dollars into those areas that we know do impact, such as health behaviors, such as the social and economic determinants of health, and the physical environments that are patients are in. So, the precision medicine is important because it studies people where they are and we can tailor and mediate some of the interventions based on genetics. Because zip code is an important as genetic code in this country in terms of healing and prevention.

So, again, I think looking at where research dollars are being spent, looking at the impact -- the true impact -- of the clinical care paradigm by flipping the paradigm, and reinvesting in some of these understandings of social determinants of health are going to be very important to that ultimate success for our patients.

Jeanne Cummings:

If I can jump all the way down to the end, Dr. Neal. In Washington, there's a lot of debate about delivering care. There's very little debate about curing illnesses. There was a time in the 1990s

when there was more discussion along these lines, where even with a Republican Congress, Speaker Gingrich wanted to expand NIH. He wanted to expand funding for science and study. We've moved to a different place now. Why do you think we have moved there and how -- you know, as Ann said, where we put our research dollars matter. What's the role of government in that environment, in today's political environment?

David Neal:

Thank you very much. I mean, you've asked the one -- perhaps nearly one -- looks like two -- non-U.S. people on the panel, so I can only give you a perspective from across the pond, from the UK. And clearly, there's a debate on balances between spending money on health and research, and I would simply -- one of the things we're thinking a lot of at the moment is really unintended variation in healthcare. So, if you think of horizon one, you know, how could we improve healthcare right now? Whichever country you look in there is enormous variation in the quality of care given. And I think there's a lot that could be done in terms of providing support to nurses and doctors in the workplace to give guideline driven care. It's something our colleague from the Heart Foundation was commenting on before.

So, I think in terms of research, I mean, one of the things I would point out again is as a practicing physician, an academic physician before I joined Elsevier, there's a huge increase in knowledge. It's growing at 4 percent a year, and for any expert it's becoming increasingly difficult to keep up to date. So, I think one of the things we could do is to try and provide better tools to inform researchers of things that are going on, and getting that practice into care more quickly.

I probably can't give you any advice about how the government should respond from a UK perspective because we're suffering the same attrition in both dollars for clinical care and for research.

Ann Cary:

I don't think it's up to the federal government to be the only investment in research. And I actually think that if we can expand to the other stakeholders of the outcomes of research, for instance, our corporations and our foundations. The Robert Wood Johnson Foundation in their Evidence for Action initiative is very much interested in looking at what constitutes a culture of health in this country and what are the dynamics involved in understanding how these multi-sectorial partners are making a difference in our research outcomes and in our healthcare of our cultures.

So, I think that we have to step back from relying just on the federal government as the only partner and the only one with moral courage to conduct the nature of the research that is needed in this country.

Francis Collins:

Although we are a partner and we do have moral courage, thank you.

[laughter]

Jeanne Cummings:

Dr. Hait, it looked like you wanted to get in there.

William Hait:

Yeah, thinking about the whole topic of ending disease, my -- last year, my 15-year-old came home from boarding school and she said, "Dad, what are you working on?". I said, "A world without disease." And she said, "Well, that's impossible." And I said, "Well, difficult perhaps." But I never met anyone who said, "Boy, I'd really like to get a disease." Maybe a show of hands -- would anyone in the audience like to get a disease?

[laughter]

Almost never. But the facts of the matter are that as you age, and around 50 you begin accumulating diseases. And by the time you're 60, 70, 80, you have four or five of these things, and they're pretty miserable. And if you -- if lifespan is increasing somewhat and you're getting these diseases at 50, you're going to live a longer period of time carrying along these unwanted accompaniments through life. So, we're all incubating some disease, whether we like it or not, and our approach has been soon we'll understand susceptibilities to most diseases, and by putting in real data, we'll understand risk.

And what if we could then understand -- have more knowledge to understand how we could intervene to either prevent a disease from ever happening or intercept the disease-causing process. And I think if we move in that direction, as Francis was pointing out, prevention, how critically important it is, then I think we'll make real progress.

And just one area about research I'll bring up and then shut up is we ask questions like lung cancer -- horrible, horrible problem. Ask, what causes lung cancer? Everyone in the room would probably say cigarette smoking. If you then say, what causes cigarette smoking, there's silence for a long period of time. And the whole area of behavioral research which always seemed to me a little soft around the edges, which I think an investment in perhaps psychobiology, whatever it actually is, to understand why people do certain things, why people make choices could go a long way to helping us prevent disease.

Jeanne Cummings:

Dr. Dolsten?

Mikael Dolsten:

I think it's a great discussion here and, you know, the balance between prevention and intervention is a key part of both public and medical policy, and I think we heard earlier today that unfortunately the U.S. has not been the most active country in having enough preventive program. Whether it's for preventing the use of painkillers of the opiate nature, or we spoke about the rise of the obesity epidemics. When it comes to infections we, in contrast, have a proud tradition here to be among the leaders in developing vaccines.

And at Pfizer, we have had for almost two decades a tremendous experience, starting with pneumococcal vaccines. We are able to immunize infants and now also adults, and actually

prevent thousands and thousands of deaths and tens and tens of thousands of hospitalizations every year, and more over a million days of antibiotic use.

So, you know, there are so many more of these bacterial and viral threats, and we see a tremendous opportunity to broaden vaccines as a real pillar in our healthcare system. And it just makes me more enthusiastic to think about how you can probably rebalance between intervention and prevention.

I heard from the colleagues in the cancer space, they're also about some breakthrough findings in certain type of tumors. I think we heard the new Commissioner Gottlieb speak about the recent approval in certain blood cancers of gene editing cells. We have seen in immune oncology initially flourish in certain tumors, like melanoma and in kidney cancer, but some of the larger tumors have been less responsive. I think, like many breakthroughs, it's the tip of the iceberg. We are making some initial progress and the key is to look upon this as a journey with a tremendous outcome but it may take longer than we expect. But the rewards will be really rich if we can bring together these efforts for the big challenges like lung cancer, colon cancer, prostate, and breast.

Jeanne Cummings:

Iris, let's get you in here. Here's a question I have. When we want to end disease, it's -- I guess a question that I wonder about is, are we talking first world or third world? I mean, we have lots of medications now that can handle malaria and things like that, and yet we have outbreaks of these diseases that still occur. So, how do you have a world without disease when some parts of the world aren't -- don't have access to all of the things that they need?

Iris Loew-Friedrich:

I fully agree. I think we cannot talk about a world free of disease if we are leaving out certain geographies. I think we have to be very clear in understanding what are the patient needs in these geographies, and they might be very different from first world patient needs. But I think we have an obligation as a world community to really look into what are ways to provide adequate treatment and care to patients in the third world.

From a UCB perspective, we are trying to address this by working with physicians in the field of epilepsy in Africa, in rural areas in China and other geographies because we have a longstanding leadership in the care for epilepsy patients and we feel a very strong obligation and commitment to ensure that we bring our medicines also to patients in the developing world.

We painfully recognize that this is only a drip in the ocean and that it's difficult, even in collaboration with the World Health Organization, to really provide a complete and comprehensive care approach. So, there is definitely opportunity for us, but I feel very strongly that as a world healthcare community we have an obligation there.

William Hait:

You know, I think it's also the responsibility of great corporations to take on the issues of global public health. You go back to what Merck did with ivermectin and river blindness, what J&J recently did with an Ebola vaccine with drug-resistant tuberculosis making a chewable version of

Mebendazole to de-worm kids around the world. These are responsibilities for corporations, very profitable corporations to do the right thing in the world. And I think it's our responsibility to step up and bear our part of the effort.

Francis Collins:

I'm glad we're talking about the fact that when we say a "world free of disease" we're talking about the whole world, because if this is just a target for the developed countries then we have basically failed to live up to our responsibilities. And I think what Bill is saying is very true. There's a tradition here of that kind of outreach that we need to expand. We also need to work harder to help the low and middle income countries develop their own capacity for doing research, and developing, therefore, research projects that are targeted at the needs that they see, as opposed to something that somebody outside their area has decided is the need.

We have -- I'm afraid -- a need to switch the kind of concept for research in a place like Africa from what might be called donor ship to ownership, where basically African governments -- African institutions develop their own capabilities and strengths. Working with The Gates Foundation, and with The Wellcome Trust, and with AESA, which is the Alliance for Accelerating Excellence in Science in Africa located in Nairobi.

And now, in a partnership -- in a discussion phase with multiple companies and philanthropies, there's momentum behind an idea building -- something called CARI, the Coalition for African Research and Innovation to try to see what could be done over, maybe, a 10-year period to get us into a position where African research institutions have increasing strength and infrastructure. And that, in turn, keeps the brain drain from continuing to deprive Africa of its best and brightest.

This is something we all ought to get on board with. Africa does have in many places now some more economic growth opportunities. African governments are beginning to see they could make these investments, and they are in fact good investments just in terms of economics. But, unless we all kind of rally around this and figure out how to make it happen, it's going to take a very long time. So, I just want to put that out there as a current initiative that needs everybody's support.

Jeanne Cummings:

Dr. Neal, did you want to get in?

David Neal:

Yeah, I do. I mean, it's very interesting point, and you start looking at the causes of early death in some African countries. You know, The Gambia for instance, maternal mortality is a huge problem, and it's really a delivery of basic care to people. So, it's a thing about getting things we know, right, how to deliver, really high-quality care into different environments. And I think your point about local ownership is absolutely key. I mean, I've been interacting with The Gambia, and it's actually critical that they're taking that forward. It's a completely valid point. Thank you.

Gary Reedy:

I just want to add, I think as the research advances, that we have a great opportunity to apply

what we already know. Not only here in the United States, but around the world. You know, to Dr. Collins' point of certainly helping other countries get sustainable research programs, or initiatives, or sustainable prevention programs.

But, going back to Bill's comment about lung cancer and about cigarette smoking. You know, we know for a fact that tobacco causes 80 percent of all lung cancers, and 30 percent of all cancers. So, and we also know today -- I would say there's probably not a lot of people in this room that use tobacco, so we're kind of like talking to ourselves. But, we know the groups that are using tobaccos, and we can use our knowledge, and our technology, and our behavioral learnings to help hopefully: one, help them stop. But, something that can -- up in the previous panels that was really important is, you know, where are we putting the effort today around education?

So, it's, you know, as Dr. Collins says, "It's a lot better, you know, to not have a disease versus trying to cure a disease." Well, it's a lot better to make sure that we're educating people early-on, you know, how to lead a healthy lifestyle, you know. So, what are we doing in the schools? What are we doing in communities? What are we doing here in the United States? And then, how can we transport that or share that outside the U.S.? Because, until people -- until we look at -- all of us look at health care as an investment versus a cost, I mean all parties, and we all get serious about it, and apply what we know, and make sure that the young generations are embracing that. Even with all the research that's going on we're not going to get where we need to be, and that's true for cancer, heart disease, diabetes, you know, anything that's out there.

So, I think there's a huge opportunity as this research train accelerates that we start applying a lot of things that we already know work to make sure that we're trying to move somewhat in sequence with it.

Mikael Dolsten:

I was just thinking of two things trying to make an impact also in the less privileged parts of the world. And educating and training like African and also heard about maternal health from the other side.

So, one experience we are getting at this moment that I think is very exciting: working together with the Gates Foundation, we are developing simultaneously a vaccine for maternal immunization to protect the newborn infant from Group B streptococci, which is a vulnerable part early in life that can cause both fatality and a lot of sequelae for life. And through Gates Foundations, of course, experiencing Africa, we are in parallel doing studies in the developed world -- in the developing world. And, you could just think about one of the few products that actually would be available almost at the same time in these two very continents that are so different, because many of our earliest experiences have been on treatments that have been available decades here. We're trying to make them available in Africa, but for me, it would be a dream to come true if there were more things that instantly would become available in both continents.

Jeanne Cummings:

So, Dr. Cary, let's say you all achieve your goal. What does that world look like? And in every story of utopia, of some sort of utopia, the story or the movie, the spine of it is the unintended

consequence. So, what is, you know, he [William Hait] was mentioning that you could live longer while you're harboring a disease?

William Hait:

You don't want to do that.

[laughter]

Jeanne Cummings:

That sounds like a really good time. But, really, I mean if -- what is a world without disease?

Ann Cary:

Well, if we could get rid of the sagging, I'd be really happy.

[laughter]

Other than that, [laughs].

Jeanne Cummings:

Will our researchers please take note? [laughter]

Ann Cary:

One of the things I've been thinking about related to that question has to do with productivity. So, imagine the economic impact if people were healthier longer in terms of economic productivity. And how that might translate, then, into the opportunity to have even more investment in further research once you get that economics reinvested in whatever the country decides. So, one would be an economic engine from increased productivity. We already talked about the sagging.

[laughter]

And then, I think, the third thing might have to do with the fact that, you know, in many of our disciplines we are seeing retirements in terms of numbers when, in fact, we need to see those in terms of lost intellectual capacity in this country and especially for innovation. And so, I'm thinking that if we were a world without disease, we would have much more innovation. People would be innovating longer, and there would be much more payoff for that. The downside to that, in my opinion, is what about the overpopulation? How do we gather the resources then on the non-health side to be able to support people living longer? And that would be a much more expensive proposition.

William Hait:

We actually developed a term for a world without disease. We called it, as opposed to immortality, immorbidity so that's living a life free of disease and enjoying it. The question that came up was, well then, what do you die from?

Jeanne Cummings:

Exactly.

[laughter]

William Hait:

We said, “Well, we’ll worry about that when we get there.”

[laughter]

David Neal:

One of the interesting things was the unintended consequences, and partly what we regard as disease. And some of the most passionate people I’ve come across are people who’ve been designated as having a disability, and whether that should or could have been edited out. And you then -- really exposing, really, quite significant ethical problems, and the unintended consequences of evolution, if you’d like.

So, my grandson, for instance, has got quite bad Asperger’s syndrome, and you know this is one of a spectrum, where if you said, “Well, we should get rid of that.” What effect would that have for future generations? So, I think we’ve got to be quite humble in the face of natural selection and evolution as to what we interfere with. I think it’s quite an incredibly complex business once you start designating those sorts of things as disease.

Mikael Dolsten:

So, I was thinking on, you know, what does it mean ending disease? And, clearly, ending some disease in the near future is very compelling, and ending fear of disease. And Francis spoke a little bit about tremendous technologies for rewriting the code of life DNA that are now appearing. So, I do think that some of the disease that are hereditary and dependent on a miswritten gene will be soon examples of disease that will be ended.

In other cases, it’s a longer journey, but if we can end the fear of disease, and the fear is often that you don’t feel trust that there will be new treatment options that are tolerable and that give you life quality, and I think that’s a mission that we have been very active on as we get into success with a treatment option we start to think about how long will it last and what can we then offer that continues to make patients live with disease, but without of disease. And that’s at least one significant battle and, meanwhile, it gives us time to end that disease.

Iris Loew-Friedrich:

At the risk of taking us down from the utopia, I think we should underestimate and -- just to build on your comments, we should not underestimate what it really means, right? And it would mean that we completely and fully, in all of its dimensions, understand human biology and that we understand in every nuance the operations of biology that make the reason for disease and that’s a huge undertaking. And we’re far away from it. I’m with Dr. Collins that, you know, in neurodegenerative diseases like Huntington’s we will probably see CRISPR becoming an available therapy at some point in time. We will see probably in just putting stem cells together with CRISPR having a value in neurodegenerative diseases like Parkinson’s disease.

But, if I’m just looking at the topic of Parkinson’s disease, it means that we much better understand than we do now what causes the degeneration of the dopamine-producing neurons.

We have to diagnose much earlier, and we have to find the pathogenic mechanisms in all these patients and they're not the same we know some but they are not the same. And then, we have to agree on how do we bring these medicines forward that will be disease more defining but maybe not symptom controlling. So, I'm just talking about relatively small patient population that we need to dissect in some populations to make sure that we maximize the treatment effect.

Jeanne Cummings:

Well that was one other question I had, and, Dr. Collins, I'll throw this onto you first and that you know I'm a layperson, right. I read it, I see it, and you know it seems like these things become priorities in waves, you know, people have been on the hunt to cure cancer for decades. And from everything you're saying, we're starting to like really make some serious progress there. It seems like now the emphasis is turning to diseases of the brain: Parkinson's, Alzheimer's. I could be wrong, anybody could correct me, and I will say, "You're right, I was wrong." But, I'm wondering, like -- so for moving now to really emphasize to really make some progress with diseases of the brain, what's next? What are the next big targets?

Francis Collins:

So, it may seem as if there's sort of a fashion of the day that medical research is kind of moving all of the resources over here and then, "Oh, let's move them over here." That actually isn't the way it is carried out and certainly there's a complicated calculus that goes into a decision about where medical research resources ought to be spent certainly NIH and an industry and other countries as well.

And it's a mix of what's the public health need, which is certainly huge when it comes to something like Alzheimer's disease. But it's also a part of it is scientific opportunity. Do you actually at the moment actually see a path forward that, supplied with resources, could make more rapid progress? That's the thing we're always trying to balance, is to figure out where are the places that are ripe for a push that would have the maximum impact on people's lives.

And I think much of this is driven, the conversation we're having, maybe we're not focusing so much on lifespan as we're focusing on health span. The span of your period of life where you are essentially with somebody asks you "are you doing okay?" and you're able to say, "yeah, I'm pretty good, I'm healthy," which all too often cannot be said by people throughout the course of life but especially in the older age categories and we would like to figure out how to give that health span a greater measure even as we admit. And let's admit even though we're having a wonderful utopia here, the death rate folks is going to be one per person. I'm sorry.

[laughter]

Unless you're going to come up with something really amazing,

[laughter]

I think the utopia will still be guided by that. But you'd want to have that health span prolonged as long as possible before that one per person kind of kicks in. In terms of what you asked about brain diseases, it is true that we see an opportunity now, scientifically, and it's pretty bold and audacious to say this, that we may actually be able to understand the human brain, which is the

most complicated biological structure in the known universe maybe the most complicated structure of any sort, when you have 86 billion neurons between your ears and each one of them has maybe 1,000 connections, and it does amazing things with very little power requirements that we really don't understand, and we are on the brink here with a lot of new technologies of beginning to unravel those mysteries, and figuring out how circuits in the brain, not just the individual neurons, do what they do in real time.

If we had that foundational information about normal function, then we'd be a lot further along understanding epilepsy and Alzheimer's and schizophrenia and traumatic brain injury, and Parkinson's, and all the other things that we desperately need a better handle on. And I think that community is revved up about this and a lot of the young talent in biological science is migrating into neuroscience because they have that same sense, "Hey, we could be part of something really dramatic here in terms of understanding."

And, of course, if you want to ask, "Okay, economically and in terms of human tragedy, where are the places that we still don't do very well?" Well, start with Alzheimer's disease, where already more than five million people affected, expected to rise substantially as our population ages. Economic costs already over \$200 billion a year, going towards a trillion. We have to come up with something here, or it is going to break our bank and break our hearts. And, so, the public health urgency there is incredibly compelling.

So, there is a reason why you might have sort of seen that shift, but it's not as if we're walking away from cancer because just at the moment cancer's getting exciting. Nor are we walking away from diabetes because, you know, maybe we'll figure out, with stem cells, how to come up with an alternative to kidney transplants, which is costing our nation a huge amount of money for all those people on dialysis. Maybe that's also in the works. Kind of put all of these things together, and it's an amazingly broad menu.

But oftentimes a sort of public discourse tends to want to focus on one or two of those things, rightly so, because of a pressing need or a scientific opportunity. That's why it sort of seems like maybe we're being inconsistent in our view of the future.

Jeanne Cummings:

Well, actually, I think you answered my question, and it was --

Francis Collins:

Phew! That's good.

[laughter]

Jeanne Cummings:

But, indeed, if, you know, there's quiet work that is maintained all the time behind the scenes, but when you see that there's almost a eureka moment close, then resources go in that direction.

Francis Collins:

And one more thing. A lot of what's going on behind the scenes is basic science. It's not the sort of thing that people write articles about because we don't oftentimes even know where it's

going, but it is a foundation of everything. The biggest mistake we could make right now is to move all of our scientific effort if very disease-focused ways, and forget the basic science foundation because then we'd have no future.

Gary Reedy:

Yeah, I'd like to just to add to that. I mean we are making -- great progresses being made in cancer today. But we still have a long way to go, you know, so but I think what's happening in cancer maybe today is -- you know, what my colleague from Pfizer said earlier is that, you know, when I was growing up, people lived in the fear of having cancer because it was basically a death sentence. You know if you got it, you were going to die. It's just a matter of when.

I think today with the advances that's gone on in cancer, you know, people are starting to say, "Maybe if I have a cancer diagnosis it's not a death sentence, you know, maybe I can live a somewhat normal life. And now, even today with the immunotherapy maybe I won't have to be subjected you know to chemotherapy and go through all the side effects and all that." So, I think that -- and that's part of the story too, is helping the public understand what's going on.

Because one of the challenges we still have today in the cancer arena is people who are living in fear of it are afraid to go their doctor's, because they're afraid they might have it. And they need to do just the opposite, because the sooner we can catch, the greater the likelihood we can do something about it. And, this whole conversation about utopia reminds me of -- first time, I guess 20 years ago, when I met Doctor Lasalle Leffall. He told me, he said, "Gary," he said, "I want tell what you what the secret to life is." And I said, "Awesome, let me have it. I'm all ears."

[laughter]

He said, "The secret to life is to die young at the oldest possible age."

[laughter]

So, I think it's what we're talking about now 20 years later.

David Neal:

Yes --

David Neal:

-- similar to that, Archie Cochrane, who was -- critical person in designing Phase III randomized trials decided when he was 65 to start smoking and riding a motorcycle.

[laughter]

On the grounds that, you know. It's the same thing.

William Hait:

I think this idea that it's very critical point that Gary was making, and it raises some systemic issues, and that's getting to a disease at the earliest possible point including when it's not a

disease. So, for example, this morning -- or at least not defined as a disease. This morning, it was mentioned before we got into the opioid epidemic -- pre-diabetes. And pre-diabetes is a definition of an A1C that's not quite diabetic or fasting glucose, not quite in the range. But on the other hand, these people as you follow them over time go on to develop all the complications of diabetes.

And if you take that to its logical conclusion, once you get the complications of diabetes, you have a horrible life to live from kidney failure to eye problems to heart attacks to all the things we heard about. But, yet, when you start talking about intervening in pre-diabetics, there are a million roadblocks that people raise and throughout the whole system including the regulators and the people in my own company, who I say to, "we have to stop worrying about decreasing glucose, we have to get to prediabetes and figure out what's going on."

And there are people in this room who know very well that goes over like a lead balloon because someone says, "Well, the trials will take 100 years. There's no regulatory endpoint. I'm not even sure there's a market for these drugs." And I say, "Well, that doesn't sound right to me. If we could take someone who was on their way to getting a disease as bad as diabetes and intercept that process, I would think that there'd be a very good market if that's the end result."

Mikael Dolsten:

I was thinking as Bill brought up getting in early into diseases, and some diseases like the metabolic, diabetes, you can measure markers, and you can see, of course, gaining body weight and risk factors. Often, in brain diseases the challenge has been they developed over many decades whether psychiatrics, schizophrenia, or neurological, and we have great difficulty to find a way to stay close to millions and millions of patients in order to be able to intervene early.

There is an interesting technological revolution in the internet of all things, and the use of all kind of devices that measure your steps, or your internet behavior, that will increasingly allow us to see change in behavior. So, for example, multitasking, and that, most of us do, changes when you have more of neurological impact on your behavior. And you can actually influence and train it, that allow you to perform like 10 to 20 years younger in life. Similar, we know that motor functions like very early Parkinson's is very difficult to detect, but now with everyone wearing these bands to measure your steps, you can soon learn how you take your steps.

You can monitor language, what sites you visit on internet. So, I think we'll see in the future that everyone will be able to see if there are changes. And if the results are hopes for interventions, this will allow us to look at brain diseases at completely different, maybe like you described, pre-diabetes.

William Hait:

And those are reasons to --

Jeanne Cummings:

Can we just --

William Hait:

-- suspect that these diseases are easier to treat. I'm not sure about this, but there are some

examples the earlier you get to them. So, for example, aspirin is a pretty good treatment for colonic polyps, the precursor of colon cancer. But if you treat colon cancer with an aspirin, the probably only thing that'll happen is you'll bleed. And same with perhaps other diseases that become more and more complex, certainly malignancies become more and more complex over time. So, the earlier you can push back the diagnosis, and this points to the critical importance of more sensitive more powerful diagnostics, I think the better the outcomes will be.

Iris Loew-Friedrich:

My key concern around this, and just to build on what has been said, is in the light of the dimensions of the issues to address, and the opportunities likewise. Do we have enough cooperation all across to really tackle these issues? Because for example, whether we look at, and I say with my Parkinson's disease example, whether we look at neurodegenerative diseases, and the efforts that are required to find biomarkers, to diagnose them early, to follow patients properly. Do we maximize the opportunity that we have in a pre-competitive space to work together to understand these problems they address?

Francis Collins:

I would love to have -- address that exact point because on the stage here some of us that have been trying to figure out how can we identify models that allow the pre-competitive space to be richly populated with ideas and resources? The Accelerating Medicines Partnership, which involves 10 pharmaceutical companies including two represented here. And it has as co-chairs of its executive committee, Mikael Dolsten and myself has in fact initiated efforts for Alzheimer's disease, for diabetes, for rheumatoid arthritis, and lupus, and very recently for Parkinson's disease, and with a serious discussion now about doing something similar for cancer, immunotherapy, and for opioids.

It has emerged, I think, as a very compelling model of how to put public and private sectors around the same table, figure out what fits into that precompetitive space, then design an actual work plan with very specific goals, milestones, deliverables, budgets, and then everybody's got skin in the game, because it's not just an intellectual experience, it's also one that requires resources. And then, we all hold ourselves accountable.

That kind of model I think we could do even more of for efforts of this sort. It's a little exhausting. It takes a lot of time, it takes a lot of commitment at the right level. But, I'm glad you brought it up, because it's one thing to say, "We got scientific opportunity." It's another to say, "Are we taking advantage of that scientific opportunity by getting all hands-on deck from all sectors including advocates, including philanthropy, to make sure that we're pushing this forward, that we've got our foot really down on the accelerator."

William Hait:

We talked about commitment. I just want call out when we first started doing this I was so impressed Francis was on all the calls. Now that's commitment. That was impressive.

Francis Collins:

Still am.

[laughter]

Jeanne Cummings:

As a daily journalist, a pre-competitive environment is like --

[laughter]

Francis Collins:

Sorry for you.

Jeanne Cummings:

I'm going to open it up here, if you guys have questions. Do you all have mics that you're walking? Okay.

Male Speaker:

Yes, well, I'm kind of curious, I mean, we and we've heard this alluded to throughout the conversation. So, we've talked a lot about prevention, right? So, stopping something before it even starts and, you know, today we do a lot of disease care, we don't really do really much health care, really. And this idea that Bill mentioned earlier: intervening at the earliest point. And that brings up this issue of biomarkers, making a diagnosis on the basis of biomarkers, rather than what the patient experiences or the doctor recognizes as symptoms.

What's the role for the NIH, for example, in pushing that from research into practice? Or, to get that data great research programs into the hands of regulators that they can evaluate the use of those tools for trials or ultimately for making these diagnoses at a point much earlier in the disease. And how can that process be streamlined? Because I think it's a real challenge. I've read thousands of papers about biomarkers, very few of which are in use today.

Francis Collins:

That's a great question, and it's part of this whole ecosystem that needs to work together. Certainly, NIH and our partners in industry are very invested in this whole effort of trying to identify reliable biomarkers.

I'll take Alzheimer's disease. Will it turn out that we actually figure out how you can prevent the symptoms of that disease if you use amyloid or tau PET scans to identify the people who are at high risk that have not yet developed symptoms? And then, you apply the appropriate therapies to slow or stop the process. That would be a great biomarker story. It's a hard one to come up with the evidence that will convince people who are skeptical, and we should all be skeptical until the evidence is there. So, that means industry, NIH working together with FDA to figure out how do you qualify such a biomarker? And ultimately it means you've got to convince CMS and all of the reimbursement systems that this is ready to be compensated for in the practice of medicine and you can't lose that one as well.

One of the things I've tried really hard to do as an NIH director is to be sure that the lines of communication between NIH, FDA, and CMS are wide open, and I think they are, but oftentimes it's tough to get the science to the point where you're absolutely able to make the case. That's the big push. I think we're all committed to getting there.

Jeanne Cummings:

Yeah. One up here, and one back there.

Lucinda Maine:

Right here. I have the next mic. Lucinda Maine, Colleges of Pharmacy, and as a 13-year stage zero breast cancer survivor, I am all about early screening and effective treatment.

[applause]

But, that has nothing to do with my question.

[laughter]

For the higher education people, here and watching, what are your thoughts about preparing the next generation of scientists? What are the critical areas, competencies, et cetera, that we should be thinking about driving into our graduate programs?

Jeanne Cummings:

Go ahead.

Ann Cary:

So, I'll start. Well, first of all, I do believe that if we flip the lens through which we view health and disease that we need to train them to do adequate assessments in terms of social determinants of health. And where patients live. And then, secondly, we need to look at health behaviors. Health behaviors are critical. I mean, we just heard where we've got an HPV winner for the Lasker Award and yet we know that we're not meeting the Healthy People 2020 goals for HPV uptake, okay, because people are afraid of the vaccine and they're in very specific communities so something is going on there. So, I think those two things for sure.

And the third area I would recommend is looking at the population health as a perspective on the disease, in addition to the individual. In some countries, they really start with the big picture, they start with public health and population health in their work force development, and then through that they begin to narrow and define the focus in terms of disease. So, they start with health and the infrastructure in what works on the research, and then they began to look very specifically. So, we might look to other countries in what they are doing well.

And then, finally, I have to say, it needs to be in a professional in terms of work force development, because no science is an n-of-1 anymore.

Iris Loew-Friedrich:

I would call that, I would say curiosity, the willingness to collaborate and the humility to accept that in today's world nobody knows and understands everything at all. And I hope that we will also be in a position to provide decision support to our young physicians. That all of the data that are available will be used to help the young physicians to say, "You know, this patient that I have in front of me, how does he cluster with other patients where we know what the best therapy is?"

Again, if I talk about epilepsy, patients often have a year-long journey to get to the right medicine that provides seizure-freedom to them because they are very much dependent on the individual knowledge of their physician and the physician preferences. If you would have a tumor, that based on everything that is available in terms of real world data, say a patient with these characteristics is predicted to respond best to this combination of therapies. Year-long journeys to get to a good treatment could be replaced by one push of the button.

Jeanne Cummings:

Dr. Dolsten wants to respond.

Mikael Dolsten:

Yeah, so you know, I want to make a plea for the funding of science in United States and the funding of NIH. We used to rise-up and be proud of the nation believing in the willingness to put science for the long-term and to be looking at physicians and the medical practice as an occupation that would do good because you were made for not only life, but for [unintelligible].

My son is in college, 19 years old, he is really talented in science, he loves science, he's spent summers at some of the best labs in cancer research, and do you know what the postdocs tell him? "This is not the place if you are as talented as you are," they tell him. The funding is dwindling, we are lucky if we can get a postdoc and we may need five postdocs because there are no prominent positions. And it's so sad to have him come home and say "You know, should I take on the challenges? All of my friends are saying we hear such a bad sentiment about the willingness to fund science."

So, I think unless we turn this around we will see a lot of the most passionate talents not going to science and distorts all with having sufficient NIH funding which is to source for all the labs across the nation as well as Bethesda. And willingness for all of us to say that, you know, we are here to make sure we can live a rich life. It's not just about that décor, so there are a lot of other distractions in life.

William Hait:

I wonder also, what's going on in the medical schools. I know where Francis and I trained two of the highest calling, the role models, and the faculty and those people who are trying to understand the disease of the patients we were seeing. We admired the master clinicians but even the pinnacle with those who were digging in and understanding the causation of the disease and, you know, I think that's what motivated so many of us to go into research who might not have thought about it before.

Jeanne Cummings:

So, we only have 2 minutes left so let's try to get 2 quick questions in. So, right there, he's been waiting.

John Dwyer:

I'm John Dwyer from the Global Alzheimer's Platform, I'm one of those pre-competitive things you didn't know about.

Jeanne Cummings:

Nor understand.

[laughter]

John Dwyer:

I'll let you know when I do. So, in our work, what's become clear as we watch the development process for drugs, we want to get more runway especially in Alzheimer's, for a therapy to get developed and the community, and Dr. Collins, you talking about -- you spoke to it a little bit. What can we do more effectively to marry science and nutrition and fitness in a way where you are actually saying that these are steps to, both deterring disease, it's actually got very profound effects on changing your risk factors and creating curiosity about further exploration of medical research.

Because it is, in Kansas City, where you are from, there is wonderful research funded by NIH on fitness and nutrition in deferring Alzheimer's disease. They even have a kitchen in the darn research center, but this is unusual in the extreme. And so, you get a lot of equivocation out of the scientists about what works, what doesn't work across all. So, what can we do to give laymen the ability to say there is something I can do right now that may lead us into a positive slippery slope of interest in research more profoundly?

Francis Collins:

Well certainly you make a great point that the number of opportunities are wide in terms of interventions for conditions like Alzheimer's. It is encouraging that the Congress sees this now as such an important compelling research need. Just today, the Senate committee that oversees appropriations has increased the funding for Alzheimer's disease for the fourth or fifth year in a row. So, Alzheimer's funding in NIH is now almost three times what it was a half-decade ago, growing faster than anything that people can remember. That makes it possible, then, to conduct more research where you consider more kinds of interventions as opposed to having to limit it a smaller set.

As you know, those kinds of studies are incredibly complicated and expensive, but I think we have opportunities now to do that, and believe me, NIH would agree with you completely. If we could identify interventions that people who are concerned about Alzheimer's could undertake that they knew were going to reduce the risk- that would be a huge contribution. Right now, the data is still a little hard to get your fingers on and say exactly what works and a lot of the time you can't be sure that it does. We need more data.

Jeanne Cummings:

Well that's the end of our time, our panels I'm sure would be happy to take your questions if you catch them after. I want to thank all of you for staying for the final panel. And I want to thank all of the panelists for their --

[applause]

-- excellent observations.

Mary Woolley:

I certainly add my thanks and that of Research!America, to this panel and to all of our panelists and speakers today. I'd say that we heard some "straight talk," right? But what we need now is, indeed, walking that talk. We need action, and Research!America looks forward to working with everyone in this room, with your colleagues, to those who are joining us by webcast, to get to the action point, and there's lots of different kinds of action, more research, and where we live and breathe, more advocacy.

So, I really encourage you to think about what you're doing as an advocate, to let us know how we can help you be an effective advocate and how you can join in. Lots of voices demanding faster medical progress will be heard, and we have the capacity, if we all are swimming synchronously -- I love that metaphor -- we have the capacity to actually achieve a decade's worth of progress in five years or less. That's a worthy goal. We're really happy to be part of that.

I thank you all for being here today, and I thank our sponsors and, in particular, our lead sponsor, Pfizer. I wish you a great afternoon and good evening.

[Applause]

[Music playing]

[End of transcript]