STAT E-BOOK

Charting a Course for Medicine's Future

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In medical parlance, "stat" means important and urgent, and that's what we're all about — quickly and smartly delivering good stories. We take you inside science labs and hospitals, biotech boardrooms, and political backrooms. We dissect crucial discoveries. We examine controversies and puncture hype. We hold individuals and institutions accountable. We introduce you to the power brokers and personalities who are driving a revolution in human health. These are the stories that matter to us all.

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Our team includes talented writers, editors, and producers capable of the kind of explanatory journalism that complicated science issues sometimes demand. And even if you don't work in science, have never stepped foot in a hospital, or hated high school biology, we've got something for you. The world of health, science, and medicine is booming and yielding fascinating stories. We explore how they affect us all. And, with our eBook series, we regularly do deep dives into timely topics to get you the inside scoop you need.

Charting a course for medicine's future

There is a seismic shift underway in science and medicine.

Cutting-edge technologies are changing the face of clinical trials and scientific research. New therapeutics and vaccines are being developed at an unprecedented pace. Algorithms are increasingly being used to guide the care of patients around the globe.

Those breakthroughs -- and the challenges ahead for scientific institutions and health care systems -- were center stage at the 2021 STAT Summit. The event featured perspective from biotech visionaries like George Church, top executives at GlaxoSmithKline and Verily, and the minds behind the Biden administration's ARPA-H program. It also looked deeply at both the crisis of Black maternal mortality in the U.S., the future of treatment for Alzheimer's disease, and the next stage of drug pricing legislation in Congress.

These stories, taken together, underscore the important conversations happening as researchers, health care industry leaders, and policymakers navigate the future of science and medicine.


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POLITICS

Former DARPA director: Biden's new science agency should be independent, not an NIH office

By Lev Facher | **NOVEMBER 18, 2021**

WASHINGTON — The former director of DARPA, the Pentagon's high-stakes research arm, says that for an equivalent health care agency to succeed, it should be fully separated from the National Institutes of Health.

Arati Prabhakar, who led DARPA from 2012 to 2017, also warned that the Biden administration should think bigger. Instead of focusing only on new medicines and vaccines, she said, ARPA-H should consider the root causes of poor U.S. health outcomes, ranging from obesity to the overdose crisis.

"If you just think about science and cures and patients, you simply aren't going to change health outcomes in a meaningful way," Prabhakar said. "ARPA-H is a clean sheet of paper, and therefore an opportunity to actually start with the factors that determine health outcomes."

Prabhakar's warning came during a panel discussion at the 2021 STAT Summit in Boston, where she spoke virtually alongside Tara Schwetz, the White House aide tasked with crafting much of the policy behind the new research office.

President Biden has cast the agency, which is formally known as the Advanced Research Projects Agency for Health, as an opportunity to "end cancer as we know it," and pledged to train its resources on other diseases, like diabetes and Alzheimer's. The administration has requested $6.5 billion from Congress to fund the agency.

Prabhakar's comments shed light on a key point of disagreement between lawmakers as they continue to draft legislation to authorize and fund the agency. While some lawmakers' proposals explicitly place the agency within NIH, others use more ambiguous language.

Prabhakar's stance was clear.

"Everyone I know from NIH gets very excited about science, which is an input, but not the output, not the objective, of an ARPA," she said. If the agency were housed within NIH, she said, "I struggle to imagine how you build a culture you need to build an effective ARPA-H, that actually ends up triggering change."

Schwetz, however, pushed back, arguing that the new agency could be created more quickly if it relied on NIH infrastructure, and that housing ARPA-H inside the larger agency would help avoid unnecessary duplication of work.

"There are obviously going to be cultural differences between ARPA-H and NIH, especially if we set this up in the way we're talking about it and envisioning it," she said. "But I think it's actually quite important for ARPA-H to be very closely linked to NIH, so that there's mission alignment."

Schwetz stressed, also, that the new agency can achieve the disparate goals that Biden and his top science advisers have respectively outlined. Biden has pitched the agency as being explicitly aimed at disease cures.

"It would have a singular purpose: To develop breakthroughs to prevent, detect, and treat diseases like Alzheimer's, diabetes, and cancer," he said during an April address to Congress.

Yet Francis Collins, the National Institutes of Health director, and Eric Lander, Biden's science adviser, have advocated for ARPA-H to pursue "platform-level" technologies instead — for instance, a catalogue of specific genes' location within a human chromosome. Such technologies could eventually transform medicine, but in the near term, might not actively represent therapies or vaccines.

"I don't actually see those things as, necessarily, mutually exclusive," Schwetz said. "You can have some really amazing ideas come together around a platform that's broadly applicable for a variety of different things, but then also have a more focused effort to solve different problems that are arising."

Schwetz and Prabhakar did, however, agree on several key questions regarding the new agency.

Both voiced strong support for strict term limits for ARPA-H's project managers. Both also said that ARPA-H's campus should be located separately from the NIH's Bethesda, Md., headquarters.

The pair also stressed that the position of agency director should not be subject to Senate confirmation, as congressional gridlock and the Capitol Hill calendar likely "dooms the appointment to a phenomenally lengthy delay," Prabhakar said. Schwetz later added that there was "broad agreement" within the Biden administration that the position should not be Senate-confirmed.

That's already the case for a number of high-profile federal health officials, like the leaders of individual NIH institutes or the director of the Centers for Disease Control and Prevention.

Schwetz, however, was guarded when asked whether it was important for Congress to formalize the new agency's creation by the end of 2021, when Collins, who has led the NIH since 2009, is set to step down.

"Francis has been an incredible advocate," she said. "Regardless, this is a presidential priority, so we have that going for us — as well as the fact that Eric Lander … is very supportive."

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HEALTH

From scholarship to trending: How experts took to their feeds to explain hard science during Covid-19

By Maaisha Osman | NOVEMBER 24, 2021

How does one communicate the fast-moving science of a pandemic to the public? Social media, with its short messages and inflamed memes, would seem an imperfect fit.

And yet Twitter and other online platforms have become vibrant public squares for discussion about Covid-19 since the start of the pandemic.

At the 2021 STAT Summit, three social media influencers in science reflected on their experience of using social media to communicate new scientific findings — and the challenges that came with it.

Here are the highlights:

Scott Gottlieb, a former commissioner at the Food and Drug Administration, said social media has taken debates that usually play out within the scientific community and made them public for all to see.

"Scientists sometimes have strong views on data, especially early data. It's one thing when scientists are engaging in a discussion among scientists," he said. "Now scientists and public health officials are engaging in a discussion among scientists and public health officials in public and everyone is seeing it."

The broadcasting of these debates has had consequences, he noted, with ideas and public perceptions tending to get anchored to preliminary and inconclusive results.

Gottlieb pointed to monoclonal antibodies as an example. Early data on monoclonal antibodies as Covid-19 treatments were criticized as weak on social media; it was only later, after more data accrued, that it became clear the treatments were highly effective.

And yet utilization of monoclonal antibodies remains low — in part, Gottlieb suggested, because of the tepid reaction that many people initially saw on social media.

"We can change our perceptions very quickly as scientists based on a new study that comes out," he added. "But [with] the public, it doesn't happen as quickly."

Darien Sutton, an emergency medicine physician and contributor to ABC News, said he was surprised by people's discomfort with the notion that science is fluid.

"I think one of the hardest things is to help convince those who are not actively involved in science that it's an ongoing process," he said. "Maybe something that we learned to do before may not be helpful, accurate, or necessary now."

Natalie Dean, an assistant professor in biostatistics and bioinformatics at Emory University, said she and other scientists have also sometimes been challenged by the sheer speed of information on social media. "Sometimes I really want to sit with something before I can tweet about it. But if you wait more than a few hours people have already moved on," she said.

Perhaps the biggest challenge on social media is misinformation. The rapid global spread of Covid-19 created a huge demand for information on the disease. But it also ushered in a tidal wave of people looking to exploit the pandemic for their own purposes, triggering what the World Health Organization has described as "massive infodemic."

"We are clearly up against a big misinformation challenge," Dean said.

Algorithms on social media platforms are primed for engagement. Recommendation engines in these platforms create a rabbit-hole effect by pushing users who click on anti-vaccine messages toward more anti-vaccine content. Gottlieb noted that, "social media facilitates developing your own information microcosm."

Individuals and groups that spread medical misinformation are well-organized to exploit weaknesses of the engagement-driven ecosystems on social media platforms.

"The information they are seeing is very carefully curated, to portray certain facts and certain opinions," said Gottlieb. To combat this, he believes it's important to find people who can break into these tightly knit communities.

Despite the problems with misinformation, Sutton said social media platforms can be important vehicles to explain science as it evolves.

He recalled standing maskless in a busy emergency room with other colleagues and coughing patients at the beginning of the pandemic, not knowing what was about to come. Scientists have learned so much about Covid-19 since then, and have taught the public along the way.

"As we step into our new normal, and we get back to the things we used to do, I think, for me [I will continue] using these platforms to encourage people to continue to look at science and understand the beauty of science," Sutton said.

STAT

HEALTH

Virus expert Trevor Bedford on annual Covid boosters and the inevitable next pandemic

By Andrew Joseph | NOVEMBER 24, 2021

In January 2020, computational biologist Trevor Bedford told STAT's Helen Branswell about the then-new coronavirus: "If it's not contained shortly, I think we are looking at a pandemic."

Talk about a prediction.

Last week at the 2021 STAT Summit, Branswell again caught up with Bedford, a scientist at the Fred Hutchinson Cancer Research Center and an expert on viral evolution and epidemiology. They talked about the future of the coronavirus and antigenic drift (essentially, whether the virus mutates in ways that escape the protection generated by vaccines or earlier infections), as well as what's in store for flu season, and what might lie ahead with the next pandemic.

Excerpts from the conversation are below, lightly edited for clarity.

HB: With the evolution of the virus, the feeling has been that transmissibility was going to top out and future mutations were going to be about evading immunity. What do you think?

TB: The variants have felt like this 2021 thing, where suddenly there's all kinds of variants and now everything is Delta. But if you look at the actual evolutionary history, the real relevant evolution that created these variant viruses was happening in 2020 — the very first Delta virus existed in October 2020 — and it was in 2021 that they really spread and competed.

I'm pretty confident that the rate of adaptive evolution has slowed in SARS-CoV-2 since then, but whether it's leveled off or how much more is there, I'm not sure. I do expect a transition in the next, I don't know, year or so, to more of this antigenic drift rather than this continual increase in transmissibility.

In terms of antigenic drift, which is a term we often use in flu to describe the way the virus is changing to evade vaccines, do you think that given what we've seen with SARS-2, that this is a virus that is going to force us to update vaccines on a regular basis?

If you look at seasonal coronaviruses [which cause common colds], we don't have vaccines for them, but if you look at their rates of evolution, they look a lot like influenza B viruses. Flu B vaccines need to be updated every five or so years, so that would probably be my low end for expectations for SARS-CoV-2. In the last year and a half, it's been remarkably evolvable. The actual rates of adaptive evolution have been perhaps five times that of the fastest influenza A [viruses], and perhaps 10 times that of the seasonal coronaviruses, though again that has slowed down.

My median expectation is something more like H3N2, based upon what we've seen, where we update the vaccine every year or two, though I would totally buy something like flu B where the vaccine needs to be updated every five years or so.

The impact of that will depend on how long immunity lasts, the protection we get from vaccines or from infection. Given what's known so far, can we hypothesize about whether or not that means we're facing annual boosters or every five years, something more like tetanus?

You could theoretically have the situation where there is no antigenic drift, but waning is such that we still need annual boosters because that's just what our immune response looks like. On the other side, you could have little waning, rapid evolution, and still need annual boosters. In reality, it's going to be some mix of the two things.

If I had to guess, there would be a booster offered every winter season.

When is this likely to be less disruptive? When will we reach a point when SARS-2 and humans can coexist more easily?

Without the variants, we would have been to endemicity this winter, but the emergence of Delta and that wave has changed things. It's made this season a bit funny, but I would expect that next winter, 2022-2023, looks like winters are going to look.

[Going forward], if it's quite transmissible, and it evolves as fast as flu, and there's waning immunity, and even breakthrough infections do sometimes result in severe outcomes, you end up with something that looks worse than a normal flu season. Super ballpark numbers would be more like 50,000 deaths, maybe even 100,000 deaths a year. That's not so much worse than seasonal flu, which has on average 30,000 deaths a year, and occasionally 50,000 or even more. But we haven't done much with seasonal flu. We recommend that people get the vaccine, and half the population does so. It's hard for me to judge how we'll respond as a society if those are the health impacts that are happening each season.

Influenza has effectively been absent since March 2020. At a point, it will return, and then we will have two of these things.

I have some hope that we'll stabilize at less flu circulation than pre-pandemic, if we improve building ventilation, if we've slightly normalized people staying home if they're sick. Not even huge things — we're not talking about lockdowns. But I think that will have some impact on flu circulation. It's not going to eliminate it, but I could hope for less flu circulation into the future.

Last year, there were warnings about a twindemic of Covid and flu, which did not materialize. Flu activity is still pretty low, but the things that have seemingly helped keep it in check — mask wearing and the dramatic reduction in international travel — those are starting to ease. Do you think we're likely to see a true flu season this year? Or will it be next year before flu season makes its full return?

If you look circulation right now compared to a normal year, it is way low. The only flip side there is that University of Michigan has just had a very large campus outbreak of H3N2 [a type of influenza A]. That would presage that maybe we'll see something pick up as the season goes on. Based on timing, I'd expect that it couldn't ramp to be a very large season, because it takes time for that to happen. If I had to guess, it would be that yes, there will be a flu season this year, but it'll still be smaller than an average pre-pandemic season.

What do you see as the important lessons to take from this pandemic?

Maybe super broadly, that for early pandemic warnings, you want to be identifying the new spillover event early on. I do think that that will has improved — you can think, globally, of how much capacity and sequencing exists that didn't exist two years ago. We will be more poised to detect something than we were before the Covid pandemic.

How that translates into actual response, that's trickier. In terms of the actual public health response, that seems like it's been tricky in so many places in the world.

Do you feel we're better prepared for the next pandemic? Please keep in mind I'm not just asking you about the science foundation for responding, but also the human foundation.

If I had to guess that, globally, we're better off. In the U.S., I'm not quite as sure, given political divisions, etc., if something were to emerge in 2022. But that's hard to speculate on.

STAT

HEALTH TECH

‘We all have to come together’: Experts lay out how to keep AI in health care in check

By Maddie Bender | NOVEMBER 23, 2021

The reach of artificial intelligence in health care settings has expanded to touch everything from cancer care to appointment no-shows. But as AI algorithms transition from exciting proofs-of-concept to a routine part of care, regulators, researchers, and hospital leaders must determine how to keep the technology in check to prevent bias.

“There are gaps in our datasets that don’t adequately represent our population at large,” Maia Hightower, chief medical information officer at University of Utah Health, said last week at the 2021 STAT Summit. “I think one of the big challenges for data scientists and health care systems is, as we’re curating the data … that we’re closing the gap and not widening the disparities gap when it comes to digital AI.”

Part of that work hinges on knowing exactly how well an algorithm performs for a given patient population — as well as how it will ultimately be used. If an algorithm will only serve patients in Palo Alto, it should be trained on data from patients in the area, and prove accurate and useful for that pool of people. But if it’s meant to be used far more broadly, an AI algorithm must be trained on data from multiple regions and a wide range of patients.

Now is the time to navigate those critical questions about oversight and performance, said Nigam Shah, professor of medicine at Stanford University and associate chief information officer for data science for Stanford Health Care.

Shah compared the hype around AI today to that of genetics at the completion of the Human Genome Project in 2003, when there were projections that all cancers could be cured by 2010.

"We're pretty much at that stage in AI, where there are a lot of great possibilities," he said. "But if you ask how many individuals' care is guided by an algorithm, the answer is going to be shockingly small."

To train and test models thoroughly, researchers must have access to representative data — a step which requires online infrastructure that smaller, underfunded health systems do not always have, Hightower said. Implementing cloud capabilities at these health systems will go a long way in collecting data on diverse populations.

Once an algorithm has been developed, there's still a need for transparency, said John Halamka, president of the Mayo Clinic Platform. There's no one-size-fits-all way to examine and judge algorithms, but there could be certain criteria set by the industry to help measure performance.

"When you buy a can of soup, the soup says, '1000 milligrams of sodium, 50 grams of fat, 500 calories a serving'— I won't eat that soup. But yet on an AI algorithm, there is no such label," Halamka said.

Current reporting standards for clinical trials — which require drug makers to publicly disclose the demographic makeup of study participants — could offer a model for algorithmic transparency, Hightower said. That, however, would require buy-in from developers who may not wish to disclose details about proprietary algorithms.

Even if developers fully disclosed the details about how AI algorithms work and perform in different patient populations, there is still a question of how they will be regulated going forward, and by which agency. Both the Food and Drug Administration and the National Institute of Standards and Technology could play evolving roles in that oversight, Shah said.

And for AI models to be rolled out successfully in clinical settings, the developers behind them — and the clinicians tasked with using them — will need a firm handle on how they fit into the full picture of a patient's care.

"My wife was diagnosed with stage 3 breast cancer in December of 2011, and an AI algorithm could certainly help understand her care plan — her care path — but equality is not equity," Halamka said. Someone facing the same cancer under different circumstances might have needed transportation to appointments and a care manager to help with medical decision-making, he said.

All three experts were hopeful that in the future, AI will be able to solve problems in health care, rather than contribute to them. Halamka said that ongoing conversations about AI regulation demonstrate a willingness to collaborate on regulatory solutions.

"We have all come together to create guardrails and guidelines as a community," Halamka said, "and that gets me very optimistic."

STAT

BIOTECH

‘Growing a chair is easy’ and other words of wisdom from the audacious George Church

By Megan Molteni | NOVEMBER 18, 2021

George Church, the larger-than-life Harvard biologist who pioneered both DNA sequencing and gene editing, is known for making bold bets. He’s founded more than three dozen companies, including ones promising to curb climate change with cold-tolerant elephants, end inherited disease with a dating app, and keep your DNA out of the hands of hackers through, what else, the blockchain.

What’s behind his audacity? An “open mind,” Church said in a conversation with STAT senior medical writer Matthew Herper during the 2021 STAT Summit. “One of the reasons people misestimate is because of exponentials.”

The tendency, he said, is for people to think that exponential technologies — those that double in capacity while halving costs, a la Moore’s Law — are limited to the realm of semiconductors and computing. But that would be a mistake. “Now biotech has exponentials that are even faster than electrons and computers and people just constantly neglect that.”

It was one of many provocative things Church said at the event Wednesday afternoon. Here are a few more:

Enhanced organ engineering

On eGenesis, a company he co-founded to produce human-compatible organs inside the bodies of gene-edited pigs, Church said he expects them to be able to donate not just kidneys, but any organ currently transplanted between humans. "And they could actually be better," he said. "Because a lot of human organs are rejected because of infections or not being healthy enough because of the transport and also pigs are resistant to certain human viruses as well. So there are a lot of opportunities for actually making enhanced organs."

Church added that non-human primate studies with donated CRISPR'd pig organs have been going on for more than a year and are going well. As to when the company could apply to the FDA to start trying them in humans? "It could be any day."

How Covid vaccines will bring down the costs of gene therapies

Early on in the pandemic, Church made the decision to take an experimental, DIY vaccine brewed up by one of his former students. He said it was an educational opportunity to demystify the process of vaccine development. He later got the FDA-approved Moderna shots, which he described as another teachable moment, but from the point of gene therapies.

"Most people don't think of these as gene therapies, but even the ancient vaccines are in a certain sense introducing genes. In this case, they were literally gene therapies," Church said, referring to the vaccines made by Pfizer, Moderna, J&J, and AstraZeneca.

"They took the common way we thought of gene therapies, which was $2 million a dose down to $4 a dose for the AstraZeneca vaccine, so it really made me feel better about gene therapy knowing there's a path to a more equitable price."

When Herper pointed out that calling these mRNA and DNA vaccines "gene therapies" could make some people nervous, Church brushed those concerns aside. "By every criteria, they're gene therapies," he said. "I don't see it as my task to reassure people. It's to try to present things as accurately as I can. And when you've got a piece of double-stranded recombinant DNA going into adenoviral capsids, that looks and quacks like a gene therapy."

The next revolutionary breakthrough?

"I would probably pick using developmental biology not just for providing organs but for 3D printing in general," said Church. Biology, unlike 3D printing, he went on, easily scales up or down — from an ecosystem down to atomic resolution. And it can be harnessed to make things like fiber optic materials and the component parts of semiconductors. "There's no obvious limit, and because proteins and nucleic acids are sensitive down to the sub-nanometer scale, that's very attractive," said Church.

When reminded that this choice had echoes of engineering trees to grow chairs, something the founders of Ginkgo Bioworks talked about doing more than a decade ago, Church scoffed."Growing a chair is easy," he said. "It'd be a waste of this atomic precision."

The next revolutionary breakthrough?

When reminded that this choice had echoes of engineering trees to grow chairs, something the founders of Ginkgo Bioworks talked about doing more than a decade ago, Church scoffed.

"Growing a chair is easy," he said. "It'd be a waste of this atomic precision."

Pigs, mammoths, and whales, oh my!

So what's next for Church, after he conquers pig-to-human organ transplants and rewilding the Arctic with tree-toppling neo-mammoths? Are there any other animals he hopes to add to his CRISPR menagerie? "This is probably enough for me for now," he said.

But he did express hopes that other groups who are advancing efforts to use some of the CRISPR techniques developed in the Church lab to bring endangered species back from the brink of extinction will take up the cause of one marine megafauna in particular. "I have an affection for the blue whale," Church said. "I'd love to see that be more common."

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BIOTECH

Set to retire, Alnylam's Maraganore reflects on his successor and his next steps

By Kate Sheridan | NOVEMBER 17, 2021

John Maraganore's decision to step down as Alnylam Pharmaceuticals' CEO after almost 20 years came as a shock to people outside of the company — enough to send the company's stock tumbling by more than 16% that day.

But it was a shock, too, to people within Alnylam, Maraganore recalled at the 2021 STAT Summit in Boston on Tuesday. Including, even, his successor as CEO, Yvonne Greenstreet.

Greenstreet, who will take over as CEO in January, was "excited," "nervous," and "a little bit angry," when he broke the news over dinner at Sorellina, Maraganore said.

"She immediately said, 'No, you cannot do this,'" he said, noting that Greenstreet's anger was not a unique reaction.

"She felt I was leaving her behind," Maraganore said. "I got that same reaction from some of my other colleagues — which, you know, they've forgiven me for that," he added.

Greenstreet joined Alnylam, which is behind the first FDA-approved drug based on a scientific technique called RNA interference, in 2016. Maraganore recruited her with the idea that she could be the next CEO.

When an Alnylam Phase 3 clinical trial failed later that year, he said, Greenstreet showed that she could lead a biotech company.

"We worked all weekend together," Maraganore said. "She was writing press releases, she was helping on communication documents. I mean, it was clear that she could roll up her sleeves and do the hard work that was needed."

"That distinguishes, I think, a leader in our industry from a leader in pharma," he said.

Maraganore also discussed what his approach will be to mentorship after he leaves Alnylam on Dec. 31. He reported speaking with venture groups, with individuals who reached out to him, and with Nucleate, a student-led biotech entrepreneurship program — though his precise moves are still to be determined.

"I think for me, success would be if the plurality of the people I mentor are really diverse," he said.

"We have a huge gap in the diversity of our leadership as an industry across all aspects of the industry," he said. "We need to do more on that front, and I will make that part of the commitment."

STAT

BIOTECH

Watch: Experts challenge Eli Lilly exec on effectiveness of Alzheimer's drug

By Theresa Gaffney | NOVEMBER 19, 2021

Months after the Food and Drug Administration approved Biogen's Alzheimer's drug Aduhelm, Eli Lilly hopes to secure approval for its own similar landmark treatment. But the company's data came under question by experts in a spirited back-and-forth with Mark Mintun, Lilly's senior vice-president of neuroscience research and development, at the STAT Summit Thursday.

The pharma giant started filing for accelerated approval from the FDA for its drug, called donanemab, based on a mid-stage study which achieved its primary goal of slowing the rate of cognitive decline compared to a placebo, Mintun said. Like Aduhelm, donanemab works by reducing amyloid plaques in the brain, a biomarker which the FDA established as a new but highly controversial standard for accelerated approval.

But panelists Panelists Maria Glymour, professor of epidemiology and biostatistics at the University of California San Francisco, and Rob Howard, professor of old age psychiatry at University College London, raised concerns that the benefit observed in the Lilly study was too small to be clinically meaningful for patients with Alzheimer's.

Howard acknowledged donanemab reduces amyloid plaques in the brain, but noted that this didn't necessarily translate into a clinical benefit for patients. Glymour was critical of Lilly's reliance on biomarkers and the lack of diversity in the company's study, pointing out that only a handful of patients were people of color.

"When people invoke the biomarkers as their best evidence, it makes me feel like that's active hand-waving at this point," Glymour said.

In response, Mintun said, "We agree it's a really complicated place, but we're not wavering in the concept that donanemab can provide some benefit, and we're moving forward."

Watch the full session, moderated by STAT's Adam Feuerstein, here:

STAT

POLITICS

Moderate Democrats are still seeking changes to the party's drug pricing package

By Nicholas Florko | NOVEMBER 17, 2021

WASHINGTON — Rep. Kurt Schrader, the Oregon Democrat who has played an outsized role in shaping his party's new drug pricing compromise, is still pushing for changes to the proposal ahead of a key vote on the legislation expected as soon as this week.

Schrader and a number of other Democrats are meeting Wednesday to discuss their proposed changes to the ultimate package, he said, hinting that moderates like Reps. Scott Peters (D-Calif.) and Kathleen Rice (D-N.Y.) could be in attendance. He declined to lay out the full list of meeting attendees.

"[We are] trying to nail down a number of key elements," Schrader said Wednesday during the STAT Summit.

Schrader, who sits on the powerful House Energy and Commerce Committee, was one of three Democrats on that committee to vote against House Speaker Nancy Pelosi's earlier drug pricing plan in September. That revolt prompted Pelosi to negotiate with Schrader and other moderate Democrats to find a compromise drug pricing plan.

It's not clear if Schrader is pushing major changes or smaller tweaks, though he described moderates' efforts to rework the bill as an effort to "make sure [the bill] is what we think it is."

Some changes Schrader outlined, like requiring additional transparency for drug middlemen, are straightforward. But he was more cryptic about certain changes he wants to see. He said, for example, that he wants to "make sure that there's a true negotiation that goes on between the secretary of Health and Human Services and the companies when it comes to the pricing."

Schrader also added that he wants to make sure that the bill's language outlining when the federal health secretary can negotiate with drug makers is actually in line with what lawmakers agreed to when they announced a drug pricing deal earlier this month.

Despite his proposed changes, Schrader signaled that he will vote for the bill unless serious changes that he disagrees with are made.

"I'm anticipating voting yes," Schrader said. "Until I'm proven differently, I'm thinking we are in a good, good spot right now."

The House of Representatives is expected to hold a vote on its social spending package, which includes the drug pricing reforms, as early as Thursday.

Schrader took multiple shots at Pelosi Wednesday. He claimed that activists' backlash against his decision to vote down Democrats' more ambitious drug pricing bill "shows me that Pelosi's propaganda machine is alive and well, and misinformation can rule the day."

He also got in a dig against the Biden administration, which he accused of trying to "buy off" moderate Democrats who had raised concerns with the earlier drug pricing proposals.

STAT

BIOTECH

Flagship Pioneering's Noubar Afeyan on the crazy idea behind Moderna and professional entrepreneurs

By Kate Sheridan | NOVEMBER 21, 2021

On his desk — placed so its visible on his Zoom calls — Flagship Pioneering founder and CEO Noubar Afeyan has a plaque imploring those who see it to "trust your crazy ideas."

It's effectively a slogan for Flagship Pioneering, the brazen venture capital firm behind Moderna.

Moderna itself was something of a "crazy idea" — using mRNA as a therapeutic wasn't mainstream when the venture firm spun out the startup in 2010.

And although "Moderna" is now used as a shorthand for a Covid-19 vaccine, developing vaccines was not originally in Moderna's game plan.

"We were not — as has been well-covered — initially considering vaccines as among the top things to do," Afeyan recently recalled during the 2021 STAT Summit. "There was a precedent company called CureVac that was making vaccines with mRNA, except they weren't modifying them and they weren't delivering them with [lipid nanoparticles]."

"And but for those two things, it was a good idea," he quipped.

The road to Moderna's Covid-19 vaccine triumph was a rocky one. Employees told reporters in 2016 they were disappointed the company had pivoted away from other types of drugs to vaccines as the company faced broad criticism for a "caustic work environment" and rapid turnover.

But vaccines just made sense for mRNA, Afeyan explained.

"Once we had developed the platform, we went back to vaccines and realized, actually, it's the easiest thing to do with this technology," he said.

Afeyan often describes the process that Flagship follows to develop companies as a new approach to entrepreneurship. Like many other early-stage biotech investors, Flagship Pioneering tends to spin off companies with its own employees as critical parts of the founding team.

But unlike other firms, Flagship tends to also own the intellectual property that its companies are built around. And an organizing idea for Flagship has been that the people who create companies should create companies professionally, following a repeatable and predictable process.

"The notion that you could professionalize entrepreneurship — which to this day, by the way, I believe is inevitable and is happening — but 20 years ago, it was considered […] very, very offensive."

"People really celebrate entrepreneurship because of its amateurism, because of its romanticism," he added. "That's what they said to doctors 300 years ago — they said, 'if you can just save one out of these 50 people who are dying, you're a hero.' And now they go, 'if one of them dies, you know you're in trouble.' Well, what happened? The thing became a profession."

Afeyan acknowledged that Flagship's model is still a work in progress, estimating that they probably understand only "10% of what it takes to do this professionally."

"But boy, I'll take 10% 'professional and on the way to learning' over 'every one of these [companies] is bespoke.'"

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Asking the big questions to drive health equity

By Genentech

Increasingly, leaders in healthcare and life sciences have been focusing on inequities in the healthcare system. Yet data show that disparities in care and patient distrust continue to deepen. Why, for instance, do Black women who suffer from breast cancer have an approximately 40% higher mortality rate compared to White women with breast cancer – yet represent only 6% of women in clinical trials studying the disease?

At Genentech, we are challenging ourselves to ask bigger questions to understand the systemic barriers at the root of health disparities, so that we can create holistic solutions to overcome them. For the second consecutive year, we conducted a national online survey, including 2,200 patients—more than half identifying as medically disenfranchised and as Black, Hispanic/Latinx, LGBTQ+, or of low socioeconomic status—as well as roughly 400 physicians, nurses, pharmacists, or physician assistants. We found that:

* A majority of medically disenfranchised patients (54 percent) feel that the healthcare system is rigged against them and overwhelmingly agree that healthcare inequities have worsened over the course of the pandemic.

* Almost half of medically disenfranchised patients (47 percent) have stopped seeking care because they either did not believe that their healthcare provider understood them, or did not believe that their provider would genuinely help them.

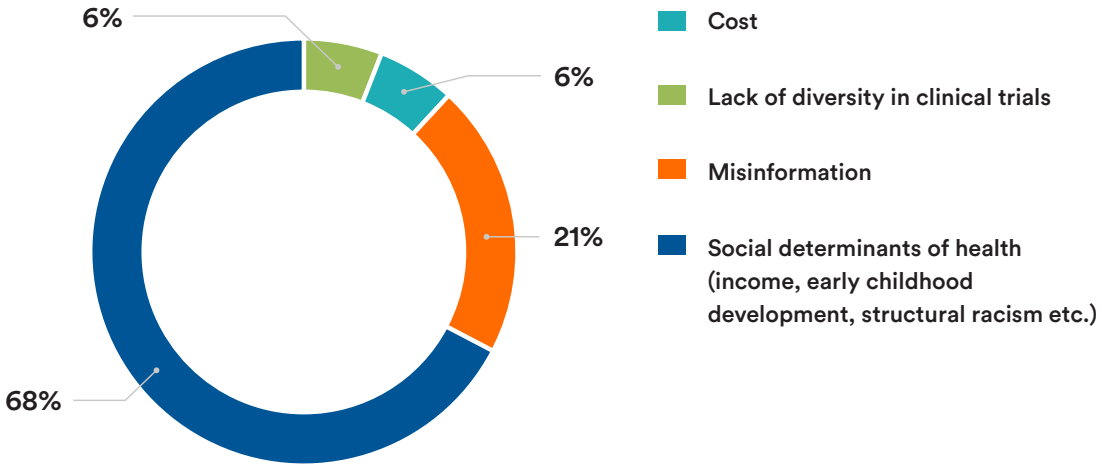
* Only half of providers (50 percent) believe that the current healthcare system acts in the best interest of society.

* Large majorities of providers say that health misinformation is a serious threat to the system (82 percent), that it is a greater threat to medically disenfranchised patients in particular (75 percent), and that patients have a more negative view of the system as a whole because of misinformation (72 percent).

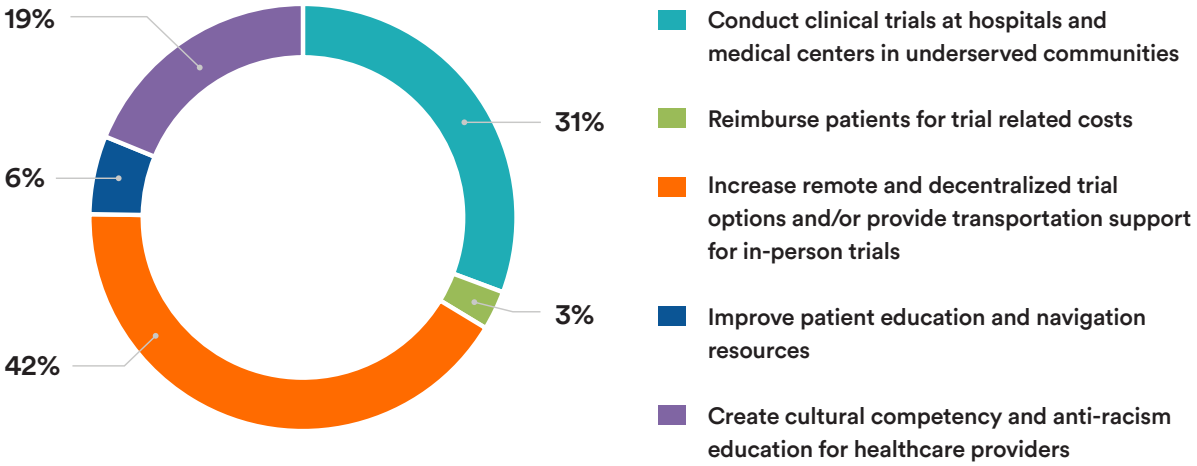
We polled attendees of the STAT Breakthrough Science Summit to get their perceptions on how we can begin to address these deeply-rooted iniquities. We wanted to know which interventions participants believed would have the most meaningful impact in diversifying clinical trials and decreasing inequities within them; and what policies or practices could reduce health inequities in historically marginalized communities. We also asked how the healthcare industry can partner with those communities to advance health equity, and at what point we will know we have achieved success in these efforts.

At Genentech, we believe that addressing health inequities starts with asking the boldest and biggest question: How can we eliminate disparities in access and improve health outcomes for ALL patients? We know that advancing diversity and inclusion requires broad societal transformation, and that we must work to identify and dismantle systemic barriers and replace them with pathways to equitable healthcare access, education and career opportunities and advancement. To learn more about Genentech and our work, please visit gene.com/askbiggerquestions.

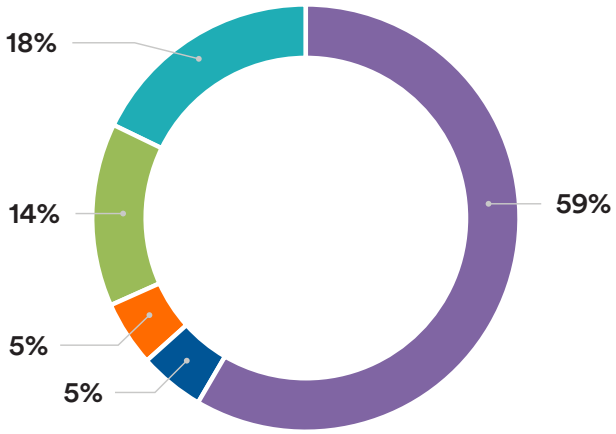
We know that inequities in healthcare are deeply rooted and systemic in nature. What piece of the system needs to be addressed first?



Which of the following interventions will have the most meaningful impact on diversifying clinical trials and decreasing inequities within them?

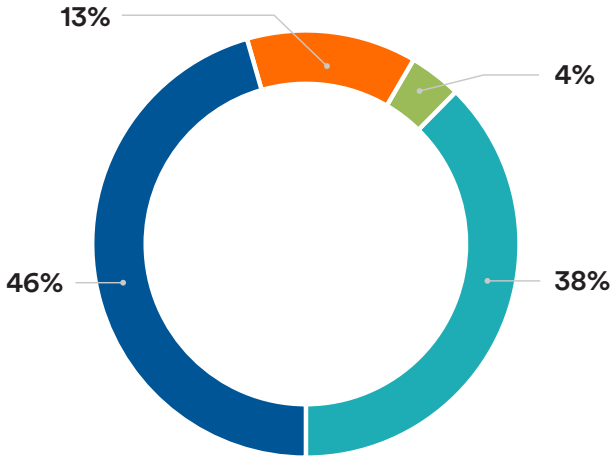


What policies or practices do you believe could have the greatest impact on reducing health inequities for patients from historically marginalized communities?



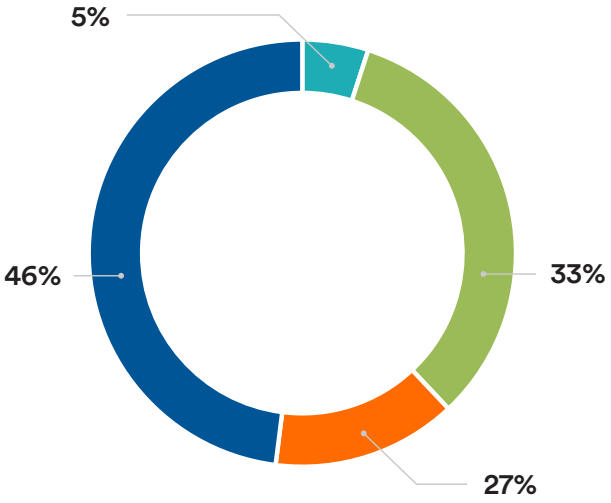
- Increase diversity in clinical trials and biomedical research
- Mandate diversity requirements for clinical research studies to ensure they reflect the epidemiology of the disease being studied
- Dedicate resources to supporting innovative care models
- Build coalitions between industry, regulators and providers
- Create new solutions together with the patients and communities most impacted by inequities

How can the healthcare industry partner with historically marginalized communities in meaningful ways to address health equity?



- Fund grassroots and community-based health equity organizations
- Collaborate to produce health education initiatives and materials
- Facilitate open conversations about the impacts of structural racism, historical health injustice, and building a path forward
- Fund STEM-education efforts to build a pipeline of diverse future scientists and health care practitioners

At what point, as a society, will we know that we have achieved health equity?



- When the demographics of all clinical trials reflect the population of the disease being studied
- When everyone has reliable and equal access to care
- When all patients can say that they trust the healthcare system to act in their best interest and in the best interest of their communities
- When health outcomes do not vary based on demographic group or zip code

STAT

HEALTH

From medical gaslighting to death threats, long Covid tests patients

By Elizabeth Cooney | NOVEMBER 22, 2021

The nightmare that is long Covid unfolds in many stages.

Long Covid collectively means symptoms that persist after Covid-19 infections have cleared, spanning both mental and physical health, the neurologic and psychiatric, cardiovascular and pulmonary, gastrointestinal and musculoskeletal. Within each organ system, severity spans a spectrum. In neurology, for example, that ranges from headache to encephalopathy to muscle weakness to "brain fog" that looks like dementia: memory gaps, trouble finding words, inability to do simple math, such as calculating a tip, or worse.

People can suffer months-long impairment even if their infection was never serious enough to require hospitalization. They're short of breath, unable to sleep, to return to work, to live what used to be their normal life. We know all this thanks in large part to patient groups raising their voices, on social media and elsewhere, to draw attention to symptoms that would not go away.

Lauren Nichols, vice president of Body Politic, a group formed to destigmatize issues facing people with long Covid and other chronic illnesses, recently recounted her 20 months as a patient and patient advocate at the 2021 STAT Summit.

First, there's the infection itself, which for her meant not only dealing with illness but also fighting to be tested in March 2020. Previously a healthy, active 32-year-old who walked 6 miles to and from work each day, she was denied once, but then after her second attempt, she tested positive for acute Covid-19 infection.

Then came the medical gaslighting, when her catalog of symptoms was not taken seriously by a series of clinicians: debilitating fatigue, painful lower esophagus burning, chest pain, shortness of breath, fever, night sweats, loss of taste, loss of appetite, and headaches and migraines.

"It was incredibly difficult because we were not believed. It's one thing to have the physical pain, but it's another to have those pains dismissed because someone has made up their mind that that's not real, that that's not attributed to Covid," she said. "That hurt worse."

During the first four months of her illness, frightening neurological symptoms also emerged. "I forgot how to use a toothbrush," she said. "There were times where I looked at my hands and I couldn't tell you what they were, I didn't know what these things were called."

She began posting her concerns on Instagram in March 2020, frustrated by how little recognition of long Covid existed in health care systems or government institutions.

Then came the death threats.

"As a result of that advocacy I began getting death threats. I was told that I was a paid actor by the government. I was told that I was an attention-seeking you-know-what and I was told that everything I was saying was made up and that I couldn't be that ill if I was able to speak to the news," she said.

"You're trying to help these very people that are wishing you ill at a time when you are just trying to survive and using the very little energy you have to help others not be in your shoes."

The vitriol hurled her way sent her into a period of suicidality that she has battled throughout her illness. Now, while recognition has grown and research into long Covid is gathering steam, she said patients are not as central as they should be to the discussion.

"We're still prioritizing the medical voice over the patient voice. And you have to have both," she said. "That's where medical innovation can occur. But right now, it's not happening that way and that's been a bit of a challenge for us."

STAT

HEALTH TECH

Verily's Amy Abernethy hints at clinical trial blueprint for 2022

By Mario Aguilar | NOVEMBER 19, 2021

Verily's quest to become a major player in the life sciences has resulted in a scattershot string of efforts, but as the company plans for 2022, charging forward with its clinical trial strategy will be the Alphabet spinout's priority.

Speaking at the 2021 STAT Summit, Amy Abernethy, president of Verily's clinical trials platform, said that company is gearing up to release a new "blueprint" for its future in the space, and spelled out some of the pillars of the approach. The company's strategy includes making it easier for a diverse pool of people to participate in trials, enabling more robust data collection, and preparing for more complex study designs that the first two pillars enable.

"Practically speaking, we are going to focus on building longitudinal datasets that can be put to use for understanding the contours of illness that can be put to use to test multiple different treatments simultaneously," said Abernethy, adding that it's important to be able to reach participants wherever they are to collect patient-reported measures. She added that the company hopes to create a vast repository combining real-world data, medical records, and traditional clinical trial data.

When Verily hired Abernethy, a former FDA principal deputy commissioner, it signaled the company's intention of becoming a significant player in the competitive field of clinical trials tech that has already minted a handful of billion-dollar companies on its potential to enable faster development of lifesaving treatments. The big question is what Verily has to offer that other companies do not — many of Abernethy's talking points about making "clinical research to be more inclusive of all people" could have easily come from a competitor.

Abernethy said that the company's advantage will come from its focus on data quality and its plan to partner with other decentralized clinical trials providers to create vast datasets. She said that in some ways, Verily's role will be to act as an enabler of such an ecosystem.

In 2022, Abernethy said the company will build on its existing efforts with the Project Baseline to "reduce the burden of participation" in clinical trials with a streamlined e-consent solution and simplified tools for collecting trial data. She said the company's recent acquisition of SignalPath will allow the company to also reduce the burden on study sites.

Abernethy said that it's critical to get things like electronic consent right, so that people trust the process and so that Verily can properly manage the long-term usage of data so that the company has a "detailed understanding about what permissions a person has given for their information at any moment in time."

Ultimately, the company's success will be a balance between its tech roots and its life sciences focus.

"We recognize that we're an Alphabet company and we have to make sure that when appropriate, we leverage our Google roots and heritage in really smart ways, like building really exceptional patient experience," she said. "But we also leverage the focus that we have at Verily on, for example, quality management systems and regulatory grade systems — and on basically building the evidence to document with confidence for safety and effectiveness of our products."

STAT

BIOTECH

Nancy Hopkins, pioneering biologist and advocate for gender equity in science, wins STAT Biomedical Innovation Award

By Isabella Cueto | **NOVEMBER 16, 2021**

Nancy Hopkins, an MIT professor who has made significant strides in molecular biology and a tireless advocate for gender equity in science, was named the recipient of STAT's 2021 Biomedical Innovation Award on Tuesday.

"It's very easy to forget how much progress there has been because we haven't arrived where we'd like to be. So we see the problems that still lie ahead. But you periodically have to pause and say, 'Oh, my gosh, look how far we came,'" said Hopkins at the 2021 STAT Summit, where she was honored for her work. The STAT award, now in its third year, honors biology and medicine researchers whose work has helped define their field. Hopkins was selected by STAT editors with input from outside experts, and received the award during the annual STAT Summit, a three-day event focused on health care. She is the second woman to receive the award, which was given last year to CRISPR researcher Jennifer Doudna.

"We're in a period of dramatic advances and daunting problems," said Matthew Herper, STAT's senior medicine writer and editorial director of events. "Society needs every great scientist we can train. And that means that we need women every bit as much as men. Hopkins' advocacy in this area has been instrumental in starting to create a more level playing field — a project on which there is still much to do."

By the mid-1990s, Hopkins had worked at MIT for 20 years, but still found herself one of a small proportion of women faculty in science at MIT. She had seen no woman professor become head of an MIT science department, center, or lab. There were no women administrators in science or engineering.

"I thought it was a choice, once the door opened," Hopkins said. "And I think we were all surprised to discover that behind the door that had opened were a whole series of obstacles that we really hadn't thought about."

Over time, her illusions faded so all she could see was a perplexing problem. So she did what any good scientist does: She studied it. She surveyed female colleagues about their experiences at MIT and then went big, chairing a committee that produced landmark reports exposing gender-based discrimination, structural sexism, and pay disparities across MIT departments.

STAT

Fauci on the next phase of the Covid-19 pandemic and the 'insanity' of the threats he faces for pushing masks, vaccines

By Andrew Joseph | **NOVEMBER 16, 2021**

Anthony Fauci, the country's top infectious disease expert who himself has become a something of a Rorschach test for people's views on the pandemic, warned that the politicization of the Covid-19 response threatens the country's ability to withstand future health emergencies, even at a time of great scientific progress.

"How do you change a mindset in a country that is completely antithetical to a response to an outbreak?" Fauci said Tuesday at the STAT Summit. "If ever there was any phenomenon that required people pulling together in a society, it's an outbreak that's killing hundreds of thousands of people. I don't know how we're going to get that divisiveness behind us."

Fauci noted that there are scientific preparations for a pandemic, as well as public health ones. The country's years of work on improving vaccine platforms allowed scientists to develop Covid-19 shot in record time — a demonstration of the value of that scientific preparedness.

The pandemic, however, exposed the country's cracks in public health: problems like how limited resources are for contact tracing and isolation, and issues like the scarcity of diagnostic tests or issues with lab capacity. Public health officials have been relentlessly undercut by politicians and attacked by people they're trying to serve, and countless public health or health care workers have departed their fields.

Still, Fauci said, the country can invest in improving its public health infrastructure.

But Fauci cautioned that the "much more nebulous" factor that could undermine the country's response to the next pandemic is some people's staunch opposition to measures meant to protect their communities. Fauci said he's received threats for urging people to wear masks indoors and get vaccinated — the results of a divide that has been cited as the "new normal."

"It's the normalization of insanity, I think," he told STAT's Helen Branswell in the video interview, which was prerecorded Friday.

Fauci noted the association between partisan divisions and vaccination rates as evidence of how politics is shaping the U.S. epidemic, with more conservative areas seeing drastically lower immunization coverage. Fauci says he tries to stay out of politics — he has, as the director of the National Institute of Allergy and Infectious Diseases, served under presidents of both parties — and that "the thing that matters is the common enemy, which is the virus. And it just doesn't make any sense to be essentially fighting with each other when we should be fighting with the common enemy."

Fauci also spoke about what the country could face in its second pandemic winter as Thanksgiving and other holidays approach. The U.S. case count that had been falling earlier this fall stalled out at around 70,000 to 75,000 daily infections — and has started to tick up again.

But Fauci said that "it is within our power to influence that greatly." If the country can reach more unprotected people with vaccines, get boosters to people whose waning immunity has left them susceptible to infection again, and keep up with some precautions like masking in public indoor spaces, "we can get through the winter reasonably well. If we don't do that, I think we're in for some trouble."

Branswell noted that the country has tallied about 85,000 deaths from Covid-19 in the past two months, even with a surfeit of vaccines. If that level of death wasn't enough to sway the tens of millions of people who remain unvaccinated, what would?

"It is painful and frustrating to me as a public health person, as a physician who takes care of people and sees firsthand what disease and death is, repetitively," Fauci responded. "As you said, it just doesn't make any sense, it's almost inexplicable. But it is what we are dealing with."

But Fauci said that a portion of the remaining people aren't hardcore holdouts. Some will still get vaccinated if they get the right information from people they trust.

Beyond that, Fauci said he was supportive of vaccine mandates for adults because people who remain unimmunized aren't just putting their own health at risk, but posing a risk to others as potential transmitters of the virus. The Biden administration's vaccine mandate for large employers is tied up in court battles.

Fauci said it's a different situation for mandates for schoolchildren to get Covid-19 vaccines, at least right now. He said authorities could wait for more safety data and noted that pediatric shots have emergency authorization at this point, while the Pfizer-BioNTech vaccine for people 16 years and up has full Food and Drug Administration approval.

But he said he could potentially see mandates in the future, noting that schoolchildren are already required to get vaccines for pathogens less dangerous than the SARS-CoV-2 coronavirus.

Because data indicating vaccine-elicited immunity starts waning some six months after the shots, there are questions about whether booster doses will be required regularly into the future — that perhaps there's something about the mRNA vaccines that most immunized Americans have received or the immune response we generate against the coronavirus that will require a regular jolt.

But Fauci said there was a "reasonable possibility" that a booster dose will provide a "durability of protection that goes well beyond" what's been seen after the first round of shots — though he stressed that scientists will have to keep watching to see if that is indeed the case. He said that extra dose after six months will allow the immune system's memory to mature to the point that the resulting protection could last longer, and argued that third doses of the mRNA vaccines from Pfizer-BioNTech and Moderna should be considered an extension of the primary series.

"A booster isn't a luxury, a booster isn't an add-on, and a booster is part of what the original regimen should be," he said.

Boosters are currently authorized for seniors, adults at high risk of contracting Covid-19 or developing serious disease, and anyone who received the one-dose Johnson & Johnson vaccine as their primary shot. But some states, trying to dampen any potential winter surges, have called on everyone to get boosters — even as many scientists continue to argue that boosters aren't necessary for many younger adults at this point.

The interview ended on a bright spot, with Fauci saying that his daughters are coming home this year over Christmas.

STAT

PHARMALOT

Pfizer to file for emergency authorization Tuesday for its Covid-19 pill

By Ed Silverman | NOVEMBER 16, 2021

In an anticipated move, Pfizer (PFE) chief executive officer Albert Bourla said the company plans to ask the U.S. Food and Drug Administration on Tuesday to authorize emergency use of its antiviral pill for combating Covid-19.

Bourla announced the company's intention to file at the 2021 STAT Summit, and the company formally made its request later on Tuesday. The step comes shortly after the company reported its pill, called Paxlovid, reduced hospitalizations by 89% among patients who started within three days of symptoms and also prevented deaths in a large, randomized study. The disclosure followed news from Merck (MRK) that its own pill reduced hospitalizations by 50%, although data was not shared on patients treated within three days of symptoms.

While neither drug maker has released complete study data, the one-two punch of top-line announcements generated considerable enthusiasm that helpful tools may finally become available to tame the coronavirus, which has claimed more than 760,000 lives in the U.S., according to the Centers for Disease Control and Prevention.

The Pfizer pill is given as a five-day course, and must be combined with a second medicine called ritonavir, which is made by AbbVie (ABBV). The Pfizer regimen involves taking 30 pills over a five-day period. For now, the cost is unclear, although Pfizer has signaled it will sell its treatment directly at a price comparable to what Merck charges for its own pill, which sells for as much as $750 in Japan.

The Biden administration is expected to announce this week that it is purchasing 10 million courses of the Pfizer pill, according to The Washington Post. The price struck between the administration and Pfizer for its drug is less than for the Merck pill — closer to $500 per treatment, although administration officials say the final details are not done.

The agreement has the potential to generate anywhere from $15 billion to $25 billion in sales in 2022, if the pricing holds between $300 and $500 a treatment course – and 90% of those are distributed, according to Barclays analyst Danielle Popper.

Elsewhere, Pfizer has signed a licensing agreement with the Medicines Patent Pool, which in turn can now strike deals with other manufacturers to provide generic versions of the drug to 95 low and middle-income countries. The pricing will be determined by the generic companies, but the move comes amid mounting on pressure on drug makers to widen global access to Covid-19 medical products.

Meanwhile, Pfizer has suggested its pill may eventually be prescribed more broadly as an at-home treatment to help reduce illness severity, hospitalizations, and deaths, as well as reduce the probability of infection following exposure, among adults. However, it is worth noting that ritonavir can cause serious interactions when combined with other medicines.

The Merck pill drew scrutiny after the company signed a $1.2 billion deal to supply the U.S. government with 1.7 million doses, which works out to a $712 unit cost for a five-day treatment course, according to the contract. But the actual manufacturing cost for a five-day treatment course is estimated to be $20.

However, the Merck pill was developed with support from the federal government before it was licensed to Emory University, which later licensed it to Ridgeback Biotherapeutics, Merck's development partner. This opens the door to debate over the price the U.S. government should pay for a badly needed treatment developed, in part, with taxpayer dollars.