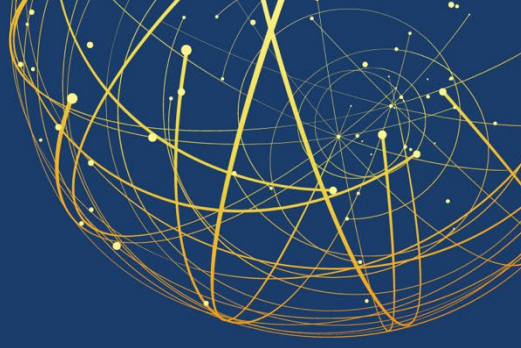

THE NEXT WAVE OF HEALTH BINNOVATION

[Video plays]

Alice Park 01:01

Good afternoon, everyone, and welcome to this afternoon session. I am Alice Park, senior health correspondent at *Time*, and it is really my pleasure to be moderating this discussion about a topic that always generates pretty heated and very passionate discussion, and that is the issue of health innovation. I think it's fair to say that we are now in an unprecedented era of breakthroughs in innovation. We've seen amazing accomplishments in technology with imaging, able to see inside the body as we've never seen before, genetics with gene therapies and gene editing that can actually cure diseases now, stem cell therapies, regenerative medicine that can replace ailing organs, and even advances in transplant with xenotransplant. So, we're going to blue-sky it a little bit over the next few minutes, but always maintaining and grounding ourselves in the reality of what it takes to make exciting innovations happen. So, I'd like to start by asking each of you—we can look at recent decades and say we've been through the era of biology, the era of genetics. How would you describe the next few decades—the era of what? Fill in the blank. Maybe Helmy, we'll start with you.

Helmy Eltoukhy 02:28

Yeah. I started out at the tail end of the Human Genome Project, and so obviously that's something that's very close and dear to my heart in terms of essentially the data deluge that next-generation sequencing technologies enabled, and the fact that we are generating so much biological data, so much data around clinical outcomes and biomarkers and everything related to healthcare outcomes, I think is truly fueling this sort of next renaissance of health innovation. It's certainly fueling our business in terms of the capabilities we have. But the other thing that it's doing is it's—for the first time—creating this ability to compound, just like we see in the tech side of the world. And so that's what's been really exciting.

Alice Park 03:15

What do you mean by compound?

Helmy Eltoukhy 03:17

If you think about what's happened with—the first genome was sequenced for $3 billion. You can now sequence a genome for $100 in a few hours. And you look at Moore's law in terms of semiconductors. You look at essentially the ability for every processor to be twice as fast every 18 months. We've never really had that in the health care field in terms of compounding. You think about the $50 billion of GLP-1s that were sold last year. The 51st billion is not any better, doesn't work any better. It's still another act of invention, another act, another miracle, basically, to get the next compound that's there. So, there's very little leverage. If you look at what we've done, so we launched the first clinical liquid biopsy for late-stage cancer patients. So, this is a blood test that helps advanced cancer patients essentially get to treatment without needing an invasive biopsy. If you look at the first test we launched 10 years ago in 2014, or 12 years ago now, the test we just launched last year is 100 times bigger, 10 times more sensitive, and has an application space that's a thousand-fold larger, but it's the same price. You've never seen deflationary sort of impact. It's like your iPhone. Think about it. In 2007, when it came out, you made phone calls, you listened to music, and you took pictures. Now your iPhones, for about the same price, run your life. They have thousands of applications and so on. And it's the same thing here. So, we're very excited about what the next 10 years holds as we continue to compound with these technologies.

Alice Park 04:55

Taha, I want to go to you next. You come from the world of imaging. So where do you see our next big medical era?

Taha Kass-Hout 05:04

I do believe the future's going to be where autonomous care with high quality and access are more ubiquitous in a way, regardless where site you land on or which shift you arrive at. And that will require also a more progressive and innovation process change. I mean, just picture this for a second. Imagine a patient just walking by. The guidance is automatically done for the positioning of the patient. They get images. While the patient's still there, all the checks and balances are done—the quality, the exposure, the motions—and if anything that just flags, then while the patient's still there, you can now engage, flag it to a technician, for example, that can remotely even assess that. And then the report is generated, and all the findings are there. I mean, that's a future still within our reach. And if you look at the way today how things are, I mean, just the description I've described to you, that would require thousands of models that need to be developed and tens of thousands of pieces that have to come together. Health care today is not a lack of imaging or another lab test that you can run. It's really all the gaps between all these steps that need to be filled, from manual entry to the hands-off to chasing where the decision is now in a tree. That wastes a lot of time, because when you look in health care, aside from you have a basic system to capture electronic medical record or medical imaging, the rest of it spends all just labor. So, the more you can automate these gaps and these steps, the more efficiency the system becomes, especially when you have shortage of clinicians, shortage of nurses, doctors, radiologists globally. Half of the world population don't have access to care today. Not quality care—any care at all. So, you have to think about the future, to be more of that autonomous future that's truly automating all these steps. And one thing I want to touch on, this is an area where we're even investing in that future. So, you can go from one model output where you can look at one organ, one task, to a backbone that can really ubiquitously look at all organs, all certain tasks, and then be able to interact with it, just using natural language. So that way, I'll be able to understand progression of disease and understand how we can ground that in the ground truth and the evidence, and then be able then to hand care where now the access to care becomes more equitable everywhere—so regardless of the sites and the variation. Because when people look at today—at delays—

they look at that as access gap. And when they look at variation, they look at that as a quality gap. So those two areas will benefit the most from the next generation of AI and the next sort of evolution about how we think about we regulate that in that new world. Because they have to look at continuous improvement with guardrails, because it will never going to be like you just frozen models or devices or the other extreme of you continuously freely updating. It really has to be happy medium in between, and the evidence is going to be very critical there.

Alice Park 08:12

Okay. Eric, I think I know what you're going to say coming from the world of mental health.

Eric So 08:17

That makes one of us.

Alice Park 08:21

Coming from the world of mental health. But do you think mental health will finally have its day?

Eric So 08:27

Well, it's interesting. We've all heard the expression that a healthy body is a healthy mind, and I think now more so than ever, it's time to rethink that paradigm, because—I believe, obviously, that physiological health is an important thing. But if you actually look at the continuum of mental and physical health and how the two interact with each other, if you have poor mental health, you probably have things like insomnia. You probably have things like cortisol levels that are all over the place, things that have direct impact on your physiological health. So, I don't think it's as much a healthy body is a healthy mind as much as it is your mind is your foundation for what is going to possibly be how your body will be in the future. And if your mind is off-kilter to a certain extent, that impacts many things. I've been known to be occasionally controversial. So, I look at what I'm excited about for the future in terms of really thinking about the difference between lifespan and healthspan. So, we have, in recent years, obviously figured out ways to extend life through amazing treatments and innovations. What are we doing as it relates to the quality of life? And a friend of mine and colleague mentioned over the weekend that it's an interesting time, because if you look back at the 1950s, how many new drugs did FDA approve in 1950? And I think he said it was around 40 to 50. And he said, "Would it surprise you that in 2025, FDA also approved about 40 to 50 drugs?" I didn't believe him, so I went and I looked it up. So in 1950, FDA actually approved about 226 drugs on about 349 applications. And in 2025, they actually approved about 46 on about 1,500-plus applications. And if you actually look—and then of course, we have access to ChatGPT and all this AI now—so I asked, well, if you look at healthspan and lifespan over the innovation periods of the last 100 years, what do you get? ChatGPT says—I'm citing that, not necessarily myself, because I don't know the exact facts—but in 1950 to 1970, we saw a much larger increase in not just the lifespan, but also the healthspan and quality of life. And of course, a lot of that has to do with the vaccines and eliminations of things that would kill us. But if you look at past the 2000s, it shifted past those things that were more about increasing lifespan—not, I'm going to say over, healthspan, but it just seemed to be a correlation. And so when I look at why I got involved in this health care space to begin with, it was about patient outcomes. As a personal anecdote, my father, who's been an inspiration for much of my life, it's unfortunate, but he's currently suffering from late-stage kidney failure. The unfortunate thing is that it's not the kidneys that are going to kill him. It's that he's lost the will to live, and it's depression, which is

particularly difficult given what I do to deal with. But the point simply is, if we look at patient outcomes, we're trying to ultimately make people feel better, improve their situation. Our company's name is Helus Pharma. It's not Treatus Pharma. So, what I'm excited about is how can we harness the power of technology today to actually transform the outcomes for patients? And it seems obvious that we would want to do that, but that has implications in our universe as it relates to healthy mind, to transforming how people's physiology is, getting them better sleep. Our drug in phase two, for example, showed a 71 percent remission rate even after 12 months, after just two doses of drugs, which we hope will be further proven in phase three. But if you can change somebody's health or mental health for that period of time, the impact that's going to have on their physiology, the impact that that has on the economics of reimbursement and payers that have to otherwise pay for the insomnia, the comorbidities of weight gain, diabetes, cardiac conditions, loss of sexual function—it's a continuum. So, what I'd like to maybe—they say at Milken, he tries to make us think about things a little bit differently. So, I'm excited about the prospect of marrying everything that we're doing in oncology and mental health and scanning and all of these technologies in a holistic way to change patient outcomes, because that will ultimately change our health, but also have impact on, obviously, the sustainability and the finance ability and reimbursement of the American health care system.

Alice Park 13:14

I'm glad you brought up reimbursement because that's a great segue for my question for Abe, which is same question, but from a slightly different perspective. Which is, when we have these breakthroughs and innovations that really are unprecedented in the sense of outcomes and being able to measure, validate outcomes, or even have correlates of what do we consider as success, how well-equipped is CMS to be able to evaluate those completely innovative new therapies that come where sometimes you take a leap of faith to say, "Is this enough? Is it safe enough? Is it effective enough to approve and reimburse?" And obviously, we've seen this back and forth, most recently over the first disease-modifying treatment for Alzheimer's. So, I'm interested in your perspective on how well-equipped an agency like CMS, which has always looked at the traditional therapies, now looks at some of these innovative breakthroughs.

Abe Sutton 14:17

So, we're at a point where there's an incredible range of innovation. And the value of that innovation is going to look different by person. We're going to see a more customized approach to health care in this country than what...[inaudible]. I'll try and project. I don't know if that'll work. We're at a moment where I think there's going to be a large degree of customization in approach to health care in this country. And our orientation in CMS, as a result of the promise of the innovation we're looking at, is to try and say, "How can we..." But I think it's working now, but I'll keep it in reserve. How can we respond to that by ensuring that we're paying for the achievement of an outcome? And we're leaning into what is really our most flexible authority, which is the one in the innovation center that I run, to say let's orient where possible to where something is proven to be safe and effective, and while we're in our reasonable and necessary language of how we evaluate coverage, to orient as much as possible to, "We will do this if it achieves an outcome." Now, the real way we've applied that to date is in digital therapeutics, where we set up via the access model an outcome-aligned payment. But when it comes to things that are really promising on the pharma side, the more traditional approach is that you go through the coverage approach through the Center for Clinical Standards and Quality and get added on. And there, CMS meets that largely by being a price taker, which has benefits from the full wave of development that we've seen for decades and accelerating for anything that'll be covered in Medicare Part B. It's a lot of what's powered

and incentivized the oncology drug development, for example. We're going to continue to have that because there's no statutory barrier to that continuing. I think that's exciting in many ways. It also raises fiscal concerns. We will continue on autopilot to cover that, absent action from Congress, which has pros and cons that people will look at. But as a society, I think it will incentivize further development, and that might be a good thing.

Alice Park 16:25

Okay. Helmy, I am going to come back to you about your perspective of that regulatory aspect. But before that, I want to ask Maha. From your position in being able to look at the landscape of breakthroughs we've seen in the past decade, what are you most excited about? Or where do you see the trends happening as far as the next big group of innovations in health in the coming decades?

Maha Katabi 16:51

I think the theme for the next decade is going to be about integration. So, we've learned so much, for example, from oncology because it has benefited from huge investments over the last 10, 20 years. There has been regulatory acceleration of approvals in oncology. There's been access to so many different modalities that get tested first in oncology, just because of the faster access to patients. And now we're seeing these technologies being applied elsewhere. So, for example, in the autoimmune disease setting, everything that we learned in oncology with T-cell engagers, with CAR-T cells, with in vivo CAR-Ts, has now been applied, and we've had a few examples of drugs that have made it into clinical trials, not onto the market yet, where you're resetting the immune system. So, you're not just tackling the symptoms that you would see in a patient with autoimmune disease, whether it's rheumatoid arthritis, whether it's lupus, whether it's Sjögren's disease. It's a really broad range of chronic conditions. But at the core of it, it's an over-reactivity of your immune system to whatever antigen is driving any of these diseases. And so understanding the basis of the technology of CAR-T cells, where you can essentially wipe out your B-cells and then reset your system to repopulate with B-cells that aren't autoreactive, has enabled essentially patients to come in for a few treatments and be cured. When speaking to clinicians that have treated patients with RA or with lupus with these technologies, the vast improvement in their condition—and they essentially don't have to get any other treatment for two years, and now they're tracking the durability of these therapies. Is it going to be five years? This is a vast change versus somebody that needs to take an injectable every month or even every three months if we can make them longer-acting. So that's on the in vivo CAR-T side. We've seen that integration, as well, happen as we were dealing with the pandemic. So from Operation Warp Speed and mRNA technologies being at the forefront of how we manage the pandemic, now mRNA technologies are actually a very exciting area of investment in a variety of disease areas, whether it's oncology—and hopefully it will be CNS and neurodegenerative diseases—as we figure out shuttles to bring these modalities into the brain where they need to act. So, from my standpoint as an investor, there's just a vast area of modalities that have seen their prime time now with different applications, whether it's in infectious diseases and oncology, and being able to bring them to areas where patient need is just significant, is very exciting. But I'd love to hear from Abe and others about how we're going to pay for all of this and have patients afford it. So that'd be great.

Alice Park 19:38

Yeah. And Helmy, I wanted to ask you about that as we delve into that issue of the cost. From your perspective as an innovator, liquid biopsies are something that we haven't had before. The ability to

detect, and potentially even prevent cancer, to look for the earliest signs. Give us a little insight into what it takes when you're going into uncharted territory here, especially with regulators, as far as what kinds of challenges did they pose as far as how do you define effectiveness? What is the threshold of success, and how do you know when you've got something that is good enough?

Helmy Eltoukhy 20:23

Yeah. How long do we have? It took us—I'll just put it into perspective. There's many aspects to that. There's a regulatory side in terms of actually getting the technology over the finish line. I would say that part is probably the most straightforward because both the CLIA/CAP side of things as well as the FDA, I think, has been pretty transparent in terms of the requirements, where the bar is. It's always hard when you're a trailblazer, because sometimes the orthogonal validation studies you do haven't been defined. You have to define some of that, and it can take longer and longer, and to—

Alice Park 21:04

So there's more back-and-forth, right? And even educating, perhaps.

Helmy Eltoukhy 21:07

There's education. When we first started with the first liquid biopsy for late stage, it was much more sensitive than any other technology out there. So how do you validate that what you're detecting is a true positive? So, we had to come up with different analytical methods and agree with the FDA in terms of how many studies we do, some of the replication of that, the guard band studies, and so on. But it was a good partnership, I would say. I would say that there are other aspects, though, that are less straightforward and less transparent. So, we launched Guardant360 in 2014. It took us 10 years to get up to 300 million covered lives from when we launched it. And so, Medicare was great. We got that. They're the first to cover the test. But we now have, I think, 600 peer-reviewed publications. We've tested over a million patients with Guardant360. 90 percent of oncologists order that test, and yet there are still some indications that are not covered by some private payers that are out there. And so that part, I think, that uncertainty in terms of what is the bar to actually get covered, I think is a disservice to the entire diagnostics field in some ways. I'd rather the bar was even somewhat high, but at least clear so that upfront you know exactly how much investment is required to get over it.

Alice Park 22:37

What are some of the reasons that those private payers are giving you for why they're not covering?

Helmy Eltoukhy 22:42

It's a variety of reasons. I think there is an aspect of deny first and pay later, or deny first and ask questions later. And...

Alice Park 22:56

Because it's new.

Helmy Eltoukhy 22:57

Because it's new and because the more they delay it, the more they won't have to pay it, even though it may be inevitable eventually that they have to get there. I don't think the diagnostics industry does itself justice in the sense that there's conflation between utility and information. So, I was involved—I was at Illumina where we went from genome sequencing costing millions of dollars to about $1,000. And it was a great time, and we got to the $1,000 genome. There were all these companies launching that were saying, "We're going to sequence everyone's genome. We're going to sequence everyone. It's going to be great." And then at the end of the day, what did you get when you sequenced your genome? You got 3 billion letters. You knew that maybe your ear wax was wet or dry, your eye color, and a few things that were kind of obvious and self-evident if you just looked at your family tree. And that's the difference between utility and information. Are you actually going to change a clinical decision that's being made at the point of care? And that's something we've been very laser-focused on as a company. But I don't think that sort of demarcation between the two is quite as clear in the overall space.

Alice Park 24:24

So Abe, Maha raised the issue of cost and reimbursement. So, as we see these innovative technologies like liquid biopsies, which are meant to give us a less expensive way to track cancer. But some of the innovations and breakthroughs, gene therapies, things like that, we're talking millions of dollars. The latest Alzheimer's treatment, over a million dollars, which is way out of reach for most people. How do you balance that issue of accessibility, in terms of cost affordability and innovation, and having something that is as breakthrough and game-changing as a disease-modifying drug?

Abe Sutton 25:13

So, important to just note the statutory basis, which is the Center for Clinical Standards and Quality, and CMS will not consider costs when determining if something should be added in Medicare. And that is something where then we've referenced the commercial market, imported those prices, and that's how it works for drugs in Part B of Medicare. In Medicaid, states will closely consider what they cover, what they do not, and have formularies and cost containment mechanisms. And Medicare Part D plans and MA Part D plans will do a similar thing for Medicare Part D. But when I think about new defining categories—whether it's diagnostics, whether it's cell and gene therapies for Medicaid—a lot of that might be areas where the innovation center comes into play. And there we will consider—can we lay out a pathway that is potentially deflationary for our country as this onboards? Often in health care, as opposed to other parts of the economy, we see new innovation be something that is costly. The concept of a new technology add-on payment is familiar to many folks here. But if you just spoke to someone who's—let's say—from the tech world, they're like, "Hold on a second, but why would that be necessary? People should want to adopt this." And then you'll explain all the distortions of how we pay rebates and how we actually have a bundle for the services of the DRG that the hospital gets, and it all starts to make sense after you spend a couple of hours with them. And they'll feel a little depressed.

Alice Park 26:45

And then Eric steps in.

Abe Sutton 26:47

Not to scar anyone, but I do think it would be good if we could say that as we're on the verge of a lot of innovation, we link together the data that Taha references, we are able to personalize things. Well, let's

see if we could lay out a pathway where we adopt it if it's really helpful at preventing unnecessary utilization, at doing needed services to prevent unnecessary expenses down the line. And so, if the diagnostic is going to detect something that we could treat today, that's great. But if it's going to send us on a fishing expedition, covering it isn't great. Which is why I like accountable care. Because if we set up a framework where somebody will evaluate it and say, "Yes, it makes sense to adopt this, let's do this," that's good. I also like if an entity wants to come in and say, "I will take risk on do we lower the cost trajectory of it, give us preliminary coverage," that's a pretty good thing to engage in as well. And so those are the types of conversations I'm having actively now. We have a cell and gene therapy model in the innovation center focused on Medicaid because, frankly, there are a lot of things in the FDA's pipeline that are in this space that have many Medicaid beneficiaries, and the economics of commercialization of those products are quite challenging. The delays of going state by state, the coverage just for the individual patient to get as opposed to the broader population, doctors not knowing to push it.

Abe Sutton 28:05

Well, on sickle cell, my predecessor designed something incredibly thoughtful, and we did a big campaign in the early days of 2025 when I came in to say, let's make sure we're recruiting every state. Red state, blue state, doesn't matter. And letting them know, "We're continuing this. Please come in and join." Because she had signed the deals with the manufacturers, and it was my job looking at this model, which I looked at and said, "This is a really innovative approach," to try and get as many states as possible. My goal was to get states to cover 50 percent of Medicaid beneficiaries with sickle cell in the country in the scope of the model. In the end, we got 84 percent of Medicaid beneficiaries with sickle cell in the scope by reaching 33 states and convincing them to come in. That's something we should expand on. We should do more. We should take the sickle cell approach and say, let's extend that to other disease areas and have that be the reimbursement pathway for cell and gene therapies that have a large Medicaid population. And that accelerates coverage post-FDA approval for those categories. It also makes it easier for states to come in. It gives a standardized prior authorization and step therapy regimen. There's nothing else to coordinate across different areas, standardized coverage criterias. It's a win-win for the state Medicaid program and for the manufacturer when we come in and align incentives. And we did it with an outcome-aligned payment, so it's tied to patients staying in remission. That's the type of framework that we can do to work. It doesn't work for everything. It does reshape the incentives. If treating something is not going to link to cost savings, if we adopt this approach as a country, it does change where investment dollars will flow. But I think every regulatory reimbursement framework that we could possibly adopt will do that to some extent, and this is one that could put us on a fiscally sustainable path and continue to push forward innovation. So that's why I believe in it. Eric could give you a counter, though.

Alice Park 29:57

But it's fair to say, probably, that the current model doesn't always work that way. So, sickle cell and what you're doing there, that's more the exception than the rule, right? Because the current model still isn't looking at, for example, the cost of a lifetime of treatments and hospitalizations for that patient with sickle cell versus the several million, perhaps, one-time gene therapy, which is an upfront cost, but perhaps advertised over their lifetime is far less expensive than the cost they would have incurred with repeated episodes. But that still isn't the mindset or the structure of how these new therapies and breakthrough therapies are looked at.

Abe Sutton 30:37

So, that is correct. The sickle cell is the exception, not the rule today. I recently wrote with some of my colleagues a piece in the *New England Journal of Medicine* endorsing the idea for more Medicaid categories doing this reimbursement approach. And so, that's something we've said we're working on publicly, and so we can say that. But you're right, every state currently has their own approach for how they would evaluate this, and as more cell and gene therapies are approved, particularly ones that are oriented towards Medicaid, there'll be a diversity of approaches. With Medicare, I think this is less of an issue just because people are very familiar with our policies and how to get coverage and how to manipulate those rules, frankly. And so, there's a lot more predictability there. But I think the promise of this in Medicaid is really large. So, laying out a framework like this and putting it into payment models or regulations to the extent we can, would have value.

Alice Park 31:31

So a lot of this too, I think when we're talking about innovations and breakthroughs now, and especially as we look ahead to the next decade or so with things like liquid biopsies and advances in mental health and imaging, is that we're focused now, shifting a little bit more toward cures versus treatments, right? And a cure sets up a very different kind of cost-effectiveness scale, I think. So, Taha, I wonder if you could comment on the role that imaging can play in really detecting disease early and even preventing them.

Taha Kass-Hout 32:09

Yeah, absolutely. Imaging is a big part of the decision tree, right? You can't really make a decision if you don't have a lab test or a medical image, right? But when you think about just a holistic approach, it's not just taking an image, you're really trying to understand that treatment plan, the entire diagnostic pathways, try to scan more for, for example, you want to get earlier with screening, like mammography and lung cancer screening and all that. So, the way we think about it is in a number of tiers. First of all is, for example, if you look at advances in medical imaging over the last decade, we owe a lot of that not just to the physics, but also the software and AI that we embed in our devices and embed in care pathways. For the last 10 years, we can see a huge revolution in medical imaging that can be attributed just to that, especially radiology and cardiology is another area, and cancer is another. And a lot of that sits upstream of the process. So, you want to be able to, for example, reduce the—as I mentioned, we have a huge capacity issue globally. A lack of technicians, lack of nurses, radiologists, et cetera, to serve more and more population, let alone now widen the spectrum around disease state from screening to diagnosis, to treatment, to follow-ups. So, when you look at it from that lens is—upstream work is going to be super important because you want to reduce rework. Any bottleneck happens where you have, for example, a read is going to be delayed, or an image has to be retaken because the quality wasn't checked the first time, or you have variability across sites, or whatnot.

Taha Kass-Hout 33:55

This is where AI is really amazing at helping reduce that, because that translate into two things: Translate into access and more equitable care globally, but also translate into how you can now scale this across many sites and as change happens. So, the advent now of—and I can give you a few examples. For example, in MRI, this is an area over the last few years we've invested heavily in. A full body scan can take now half the time it used to take prior to 2020, yet twice the resolution out of the same scan with a software upgrade. That's huge for patient experience, huge for diagnosis, but also for consistency because you're not jeopardizing on the quality. You look also in certain areas like the heart, where 86 percent of

that scan reduction in time and more than 55 percent resolution. That's a great example about how this AI is really helping now with standard of care and also open up the funnel. But when it looks for now—how can we accelerate the evidence, right? This is an area where working closely with the FDA is a great—I'll give you a couple of really great examples. On one hand is, software needs to be updated. If you have a smartphone, you don't upgrade your hardware every cycle you need a software upgrade, right? Well, FDA has a great tool for that called PCCP—Predetermined Change Control Plans—which is really amazing tool because it's basically a safety iteration contract with the FDA between manufacturer and FDA. Say, "Look, here's my device. Here's where I'm going to agree I'm going to update over time. Here's how I'm going to measure the delta, and there's how I'm going to generate the evidence to track it. And if there's anything that deters from that, I can roll it back." That's an amazing tool because now we can bring more innovations that are continuous. Imagine every three to six months now you're rolling out something new, whether that's for screening, for lesion detection, for resolution, scanning time, and that sort of thing.

Taha Kass-Hout 35:51

The other thing is also, think let's say, breast cancer or lung cancer. Oftentimes here is—doctors deal a lot with variation when it comes to volume, huge volume. Like, for example, out of 1,000 mammography scans, there are five interesting ones, and two thirds of those biopsies are normal. So you're constantly chasing a normal. In that world is—you don't want to also deal with the volume and also increase false alarms. So you need to be able now, before you even expose patients to screening, is be able to stress test all the edge cases possible. Right? From high-risk cases to rare cases, and that sort of thing. Because you're looking for motions, you're looking for resolution, you're looking at how small the lesion is without jeopardizing the resolution of the image and the exposure for that patient, because you want less and less radiation or less exposure time for the patient. Well, how you do that without having to wait 20, 30, 40 years to generate every one of those use cases? Similar to how smart cars, when they move and like—well, you gamify a lot of these simulation and synthetic data becomes big, big contributor to that innovation and evolution in the process. Because now you can, before you expose the patient, you can stress case all these issues. You can actually—part of the clinical trial is you have synthetic data that mimics the reality because you understand the ground truth, you understand the resolution and what are you detecting for, and you understand the variation. That way, you can accelerate innovation in a matter of months or years, rather than decades, to bring that technology forward.

Taha Kass-Hout 37:27

Now, let's fast-forward now about how that all translate into the health care system of today. The operation efficiency is top of mind for every health system we talk to globally. How can you get more out of the same resources that you have in a way that you have a full view of your entire system end to end with care coordination? So, every one deviation along the process, whether a read had to be redone, or a scan had to be redone, or a read took a little longer, or if there's a hiccup in the length of stay because of the emergency room, or whatnot. The more you solve for that, you can automate the next step. You can now actually stretch the resources to accomplish more, which means that translates into more patients taken care of. To give you a few examples. The Queen's Health System, where we're working together. In a matter of 10 months, we were able to increase 22.2 percent of their admissions, reduce the length of stay by one day. That translates to a $20 million ROI in less than 10 months. Duke Health is another great example about how they were able, since 2020, reduce their temporary labor by 50 percent and increase by 66 percent about time to assign a bed from the first time you identify that patient. Those things translate because you're looking at the whole problem holistically. But the next evolution of regulation

needs to evolve is around this continuous evidence generation with these guardrails. So that way, you can now afford a future. We can even go all the way to autonomous care, where there's checks along the system. You predict what's the next action, you understand where the flags are. You only involve human [inaudible] resources when it's really needed, and be able then to have full traceability in every action and audit that was made along the system. And that's really how we can now take that to the next generation. But with that is—you need to look at regulatory pathways that are going to be reimbursable. As the chair for AdvaMed Digital Health for the last couple of years is cross-med tech and big tech. We're looking for predictable pathways for reimbursement. Second of all, today in health care, there doesn't exist a multimodal population representative data that we can actually go and test against, and with continuous monitoring efforts being generated. And third of all is, how can you keep the human in the loop—human, the clinician—that's not only accountable, but the decision always come back to, so that way also we can have full accountability and traceability into how the actions are being made. So that's how we really think about it more holistically end to end.

Alice Park 40:11

And I think that model that you just described is particularly relevant, Eric, in the mental health space. As we're seeing more digital coaches and wearables that are able to detect perhaps even when people aren't aware of potential early signs of depression, if they're not moving, or by the words that they use, the language they choose, and things like that. When you look at that, do you see what Taha just pictured for us, this world in which people are much more empowered and much more informed, I think is the other thing about what's going on with their mental health—that we will be more effective in treating things like depression and really be able to intervene with more effective therapies as well?

Eric So 41:04

Yeah, I've always told folks that there's a spectrum of mental health. One doesn't go from having a bad day to suddenly wanting to end their life tragically the next. And I think to a certain extent, social norms and stigma have played a large role in that. And we all can talk about the negative things associated with social media and things like that, but one thing that I think has come out of this generation as a result of that is everybody has a voice, and it is okay to be heard. And we live in a universe now where, to a certain extent—I won't say it's more favorable, but some of the stigma's gone away—and we've obviously seen the recent executive order as it relates to psychedelic research and drugs. And, I want to make it very clear in that executive order that we are still very concerned, and the administration is still very concerned about safety. These are companies that had breakthrough therapy designation already. So, we recognize a very large unmet need. They had promising data. It's just a matter of how do we accelerate that? So, from my perspective, our awareness and de-stigmatization of mental health has allowed us to embrace a culture where we talk about it more. Why do we call it Alcoholics Anonymous? Oh, you're not supposed to talk about that. There's something shameful about it. So, we need to break out of these types of social norms that have been put on us. Growing up in my household, my very early experience with mental health is if you complain that life was hard, my father would tell me that, oh, I just got to have a stiffer lip, and you got to be tough. And for those that haven't experienced mental health or depression, that's not how it works. It's not how tough your brain is. In fact, what we're finding out, and you probably heard the term chemical imbalance over the years, it's not as much about brain chemistry as it is about brain circuitry. Certain parts of the brain don't talk to each other anymore because of trauma or other things. What we're finding out through our R&D and our drugs and our development is that parts of the brain that previously weren't speaking to each other are now speaking to each other because of the neuroplasticity and neurogenesis

that's occurring with the compounds that we're working with. So, I think a combination of social awareness and understanding of a more holistic acceptance and de-stigmatization all lead to an environment of greater support. That greater support allows people to come forward and seek help and part of that detection, part of that—they say an ounce of detection is worth a pound of cure. That's very much the case.

Eric So 43:44

And I think—I have the benefit of traveling around the world and seeing how different cultures respond to health care. And I can definitely tell you that, historically in North America, we've been very grounded in cause and effect, ailment and pill, that kind of universe. Other parts of the world are much more focused on preventative medicine. And again, improving that quality of life and how does nutrition impact your health? How does that impact your mental health? How does it correspondingly impact your physical health? What are the environments where we do want to do more early detection, whether that's oncology, liquid biopsies, whether that's checking up on mental health. In North America, your employer historically pays for your gym membership because they think that if you go to the gym and you're healthier, you'll have less reimbursement on your medical insurance. When was the last time you checked out how healthy your mind was? Now with things like WHOOP, and it's very fashionable to have this, and I got an Apple Watch, so sometimes they have conflicting data, but I always track my sleep. And yes, if you've had a bad night of sleep, you're going to have a bad next day. And these insights and how AI and other technologies, like I say, can conflate to help us get a more holistic picture of one's health and what we can do about it, that makes me very optimistic about the future. And just to throw in my little controversial comment on reimbursement, because I couldn't resist. I live by two mantras, which is: Is the juice worth the squeeze? And how much would I actually pay for that? And what I mean by this is years ago, there was this tiny little fruit company that changed the paradigm on how you bought your cellphone. Right? So in 2006, before the iPhone came out, you used to be able to get your cellphones primarily through reimbursement from your mobile carrier, because they wanted you to just sign up for the monthly cell phone bill. And that's how you got your phone reimbursed. Then the iPhone came out and Steve Jobs said, "This is something that everybody's going to want to have. So let's go direct. Let's create the Apple Stores. Let's market this product directly. And you can buy this phone without getting a cellphone plan." And years later, we're all lining up for when the next iPhone comes out and paying 2,000 bucks for it. But the point is, people are willing to pay for things that they want. They're willing to pay for things that'll transform their lives. And where this comes full circle in health care is if people actually feel that a drug or a treatment or a detection is something that can change their lives immediately, that they feel benefit from, they'll figure out how to pay for it. Right? Whether it's reimbursed or not.

Eric So 46:24

And I know there's a whole complexity and Abe's going to jump all over me on this one. But the point is, at the end of the day, it's a question of value. And I think as a statement, I guess on health care over the last couple of years, is people are not feeling they get value out of health care. They feel they're a lifelong treatment, not lifelong changes in their patient outcomes. And if they felt that there was that—and I think what's great about all the folks on this panel is we're all working towards things that will transform patient outcomes. And there is a value there. And there's something that I would pay for there. Early detection, it's very unfortunate, but—Helmy knows this story—a friend of mine last year unfortunately passed away because he felt that there were certain pains in his stomach, and he was very quickly diagnosed with late-stage colon cancer. That is something that could have easily been fixed had he detected it earlier with

Helmy's technology, for example. And it's an absolute shame. So, we need to educate people about the state of technology and what it can do to transform their outcomes. We need to make them aware, and we need to make that accessible, because ultimately, that will be the cost savings in the system that's going to pay for it all. Right? If you can detect cancer before you have to treat it, if you can transform mental health so people don't have to gain weight or lose sexual function or all these other comorbidities, and you can make that happen for 12 months at a time, that's going to have an impact on health and it will have an impact on the numbers.

Alice Park 47:59

Right. And I think, though, the issue—just to play devil's advocate here a bit—is that in our US health care system, though, the person who's making those decisions about what's of value to them is not the same person paying for it. Through our insurance system, we have third-party payers. So there's one degree of separation there, and that I think has led to a lot of disconnect and inflations in prices and questions about reimburse—but that's a whole different session, so...

Eric So 48:27

But to a certain extent, it's the employer that actually pays for that even.

Alice Park 48:30

Exactly.

Eric So 48:27

So the employer—

Alice Park 48:31

—and makes decisions about what's of value and—

Eric So 48:33

Yeah. What does the employer want? The employer wants a—

Alice Park 48:37

Healthy workers, yeah.

Eric So 48:37

A worker that's healthy, that's coming to work, that's producing. How do you solve the national debt? Sure, you can collect more money from people, or more appropriately, maybe you take all the people that are oppressed, you make them better, make them functioning and wanting to contribute to their communities and their companies, and you add to the income productivity of the country. So, there's lots of different ways to skin the cat. But sometimes I stir the pot a little bit. I've been accused of that.

Alice Park 49:03

No, that's fine. And I just want to take a quick minute to remind everyone that if you have any questions for any of the panelists, feel free to submit them through the app. Maha, I want to ask you, as you're looking at investment opportunities, how important and how much of a role do really innovative strategies in validating and testing things in medicine? How important are they? Things like—we've got technologies now, the ability to perhaps do disease in a dish, model the disease without any human intervention. We have the ability to perhaps do studies that can obviate the need for animal testing, all of which are very expensive. How big a role do these types of strategies play, and are you seeing them increasingly in the ways that companies go about developing innovative treatments?

Maha Katabi 50:00

Yeah, absolutely. So, there is an entire industry in clinical research organizations like Charles River and others, for example, that aim to integrate all of these advances in the service offering that they provide to therapeutics-focused companies. So, it's not that therapeutics-focused companies are both investing in the development programs that they're running and the innovative technologies that they're using to discover and develop these medications. It's rather that they're leveraging service providers. So, what we see is that we don't need to invest in companies that have 500 FTEs to be able to cover everything from improving how the discoveries are being tested and evolved to designing the clinical trials and identifying the right patient populations and asking the right questions about which patients should work or should fit in this treatment paradigm. And so the ability to outsource—and there was a session earlier about where the outsourcing is happening, it's also not all in the United States—is such that there's plenty of technology and efficiencies to be captured in the drug development process. So whether we integrate AI, whether we integrate the non-animal-based preclinical testing, whether we are able to streamline the clinical process and have the FDA support—actually, a more streamlined clinical development process, both early on as well as, for example, not necessarily two large trials are required for every drug approval. There are so many more efficiencies that can be gained across the entire value chain in health care that I do believe that—I don't know if it's going to take two years or 10 years to see all of this being implemented, but it should translate into meaningful efficiencies. And from my standpoint as an investor, each investment firm has its own kind of remit and experience in what we can leverage to help the entrepreneurs that we back. So, what we've decided to do at Sofinnova is to focus on clinical innovation. It's very important to us to be backing approaches that are not just bringing incremental improvements over standard of care, but really changing the way we think about treating a disease, or, for example, enabling patients to never have to go to end-stage kidney disease, for example, and be transplant-eligible, but be able to reverse the conditions that they're suffering from so that they don't get there. And so that's what we're focused on, and we're focused on understanding how we can design novel endpoints to show the agency that we don't need to stick to the traditional endpoints, but there's a new endpoint that can be implemented to capture the value that's being created with these new therapeutics that we're backing. But I think what you said is going to be leveraged multiple times over as AI is implemented, novel preclinical testing, and the desire to remain competitive on a global stage. So, the acceleration in drug development globally just has been tremendous over the last three years. And so seeing how that can be reimported back and implemented across the biotech industry here, I think is going to be very key to remaining on top of it.

Alice Park 53:13

And just as a segue from your mention of outcomes, I've got a question from the audience. How much of our health innovation should focus on productivity that drives economic outcomes versus patient and provider outcomes?

Maha Katabi 53:29

Well, the two aren't contradictory. Essentially, a patient outcome that matters, for example, in a disease like schizophrenia, is the ability to treat symptoms not just of psychosis and hallucination, but also of depression and apathy. And once you treat all of these symptoms, the person becomes a more contributing member of society and their families in general and their communities. So, I don't think the two are contradictory. Actually, in patient-reported outcomes, what we as investors and the FDA as a regulator is trying to capture is an outcome that enables the person to be functional, and functional in every sense of the word. It's not just essentially functional in terms of being able to, for example, in a muscular disease, to be able to walk faster. But the ability to walk faster actually will give you the energy to take on a job and to help yourself and help your family in a more effective manner. So, there is a great connectivity between outcomes that are captured in clinical trials and productivity, and we need to do more of that to be able to essentially make sure that these products are accessible to everybody. So, once you demonstrate the value that is being captured beyond the immediate functional clinical outcome that you corrected, you're able to distribute it much more broadly because the reimbursement is going to be there for those outcomes.

Alice Park 54:53

Okay. Abe, you have anything to add to that?

Abe Sutton 54:57

I want to go back to something Eric said, if that's okay, which is on how a consumer-driven health care system is one where people perceive value in something and therefore pay for it. And yes, some goes through the employer, some goes through the insurer, but we do have examples in America of things that don't go through that, and we do see price discipline come into play. You referenced a device you're wearing. I'm not supposed to say names of products, apparently, in these things. So, I tried to stop myself from doing it, but he said the name, so reference back, I didn't break the rules. But there are multiple different options like that. LASIK surgery and how costs to clients have occurred there. The issue that I have is that works for people who have the resources to pay and buy this. But I think Maha touched on something critically important, which is how do we expand access to people who are dependent on Medicaid for their insurance or dependent on Medicare for their insurance? For the first time for digital therapeutics, we're paying for that in Medicare, and we did it through the outcome-aligned approach. And look at the entrants. There were 150 companies preliminarily accepted onto the list for the access model. A bunch of medical device companies who are taking the monthly payment we're setting out for driving outcomes and giving away their devices or renting their devices for free in order to get that subscription payment, which is just turning their economics in a different direction, but it works. When we see really promising things that are driving health outcomes for people who have been paying for them, we need to say, "All right. We see the improvement there. People are voting with their feet. Let's have those companies now go and engage the people that we as taxpayers have accountability for." Because I think that if we could get them engaged in their health journey, engage them earlier, we will see the prevention that Maha was talking about, and therefore, we'll benefit as well over time. And so, when you get to that segment, it's a win-win that's very easy. It's harder when we get to things that are massive quality improvements that are categorically different from what we have coverage policies, because there Congress needs to step in to initiate coverage, which makes it harder to underwrite those things. If it falls within our existing coverage policies, it's easy. We just add it on, and then it's an inflationary thing in our

system. It's when we get to that other category that I think there's still a question that we need to answer of how we as a country want to deal with that.

Alice Park 57:20

Okay. And in closing, I just want to ask each of our panelists here—the US has for decades been the leader in innovation in health and medicine. Do you think the US will continue to be that leader and play that role in coming decades? And if not, who do you think will step into that role?

Helmy Eltoukhy 57:43

Yes. Maybe I'll start. Yeah, absolutely. You look at R&D budgets of US companies in the healthcare space, and they dwarf most other—even GDPs of many other countries around the world. I think the big risk, though, that we have is we're spending, I think, something like $5.3 trillion in health care in the US, growing at 67 percent per year. And so it's just not sustainable to be able to grow at this level. And I think the part that we really need to think about is how do we turn it from this Mexican standoff we have with these entrenched incumbents all taking a piece of the pie and completely reshape the system so we can bottle that innovation in a way that is accessible to patients in a much more cost-effective way.

Alice Park 58:31

Okay. Maha?

Maha Katabi 58:33

Well, we have a great resource, and that's patient data. And we don't leverage it because it's all siloed, whether it's within companies or within agencies. And there are other countries that have a single-payer system that have been able to centralize data and leverage it to accelerate further innovation and further novel treatments being brought to market. So, I think that's one of the areas in which we can improve to be able to capture and remain at the forefront. But there is no shortage of other countries that want to play that role.

Alice Park 59:05

And many even feel we're losing ground in some areas, right? Do you agree with that?

Maha Katabi 59:10

I don't agree with that currently, but I can project what would happen in 10 years' time if we don't correct course.

Alice Park 59:17

Okay. Taha?

Taha Kass-Hout 59:19

Yeah, maybe a glass half full, but for me, yes. If you want to go to the moon, you can't keep thinking about building taller buildings. You have to really think, you have to build a rocket ship to get there. And for that,

there are many ingredients that can be a tailwind. We cannot continue this model of one organ, one task, for example, when it comes to advancing our imaging diagnostic. If you want to go and screen more population, you want advanced treatment, you want to connect all this data, multimodal data together with majority of it is unstructured, you have to think differently, right? Like foundation models that are purpose-built for health care. How can you have many tasks together? How we can stitch all this data together and operate more efficiently, so that way, clinicians can really operate on top of their license and not be dragged into yet one more pop-up screen that they have to deal with and that sort of thing. And so I really believe that. And then with that, the reimbursement has to align. Now the next generation of regulation has to evolve with this continuous iteration and scaled evidence and have a public-private partnership to generate the evidence continuously, continue to ensure that the clinician is the center of the decision accountability, but really understand how these models are operating. So that way we have full visibility into the decisions that are made, and most importantly, always think about the patient first and put that in the center. I think we have a bright future if all these parameters come together, providers work together towards that goal, so we can really scale globally.

Alice Park 01:00:48

Okay. Eric?

Eric So 01:00:50

I'll answer the question very quickly but provocatively, which has been par for the course for pretty much everything I've said this afternoon, which is, to a certain extent, I don't think it matters as much whether we maintain our lead in innovation. It matters whether or not we are able to become leaders in making our people healthier. And companies leverage technologies all around the world. It doesn't help if we have the best education institutions in the world if literacy is at an all-time low. So, I'm much more concerned about are we making people or helping people get healthier or not, whether we are the innovators in that, or whether we take innovation from other parts of the world and apply that to us. I think that's the important thing in—

Alice Park 01:01:28

So how the innovation's used—

Eric So 01:01:29

Exactly.

Alice Park 01:01:29

—rather than just innovating for innovation's sake. Abe, I'll give you the final word here.

Abe Sutton 01:01:35

I remain optimistic. I think we've driven much of the innovation or incentivized much of the innovation because the development has really been proven out by reimbursement that you could achieve here. The challenges that we see now on that are, one, our labor costs of delivering anything here are very high, and that's reflected in the cost of anything here. And two, that we do protect patient privacy and we have data

silos, and there are a number of factors that make it harder to do things for better or worse here, and I think there's a balance of equities that we've achieved. There are three things that you need to put together to encourage continued innovation, whether it's on the AI front or on the pharma front, whichever wave we're talking about. One has been spoken about a lot here, which is the data in order to drive and direct how you're approaching things. And there are frameworks for how things could be made more accessible on that, and there's a lot of people working on that. Two is the clear regulatory framework for market access that people could depend on and trust. And we do still have something that is truly dependable in this country, led by the FDA on this. And then the third thing that I would highlight is a clear reimbursement framework. For that, where we are trying to get to the cutting edge, I think there have been distortions in a fee-for-service structure. There's a lot of benefits of an integrated HMO approach, which many other countries have to some extent. They put different names on it. But I think we're getting there also with our move to accountable care or how Medicare Advantage plans function in our system. And so, I'm optimistic that we have the pieces together to actually incentivize the next generation of development.

Alice Park 01:03:06

Okay. On that optimistic note, I want to thank all of our panelists for a very lively discussion. Really appreciate your time.

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