Alexander Fleming (00:05:03):

We are at the top of the hour and so let me welcome our audience, a worldwide audience to this session of the Targeting Healthy Longevity Conference. I am Alexander Fleming and I with Thomas sir and our conference co-chair, Larry Steinman, welcome you. Without further ado, I want to introduce the moderator of our great session that you'll hear in a moment. George Ridden Denberg, who is formerly general counsel of a O L and C B Ss, but his passion has been more recently looking at ways of preventing and better managing dementia. And in this way, he is founder of us against Alzheimer's and is involved with the Davos Alzheimer collaboration and is a mover and shaker in many different ways. So George, we'll turn it over to you in a moment, but first, Thomas is just going to provide some housekeeping information.

Thomas Seoh (00:06:16):

Sure. Just a reminder to enter any questions for the panel in the q and a function of our Zoom webinar platform. We'll try to get to the As time allows. We've also enabled the chat function for audience interaction. So just for warmup, those of you who are willing, please say hi in the chat and from where you're logged in and Z, back to you.

Alexander Fleming (00:06:38):

Well again, it's a great pleasure to have George moderate this panel, which is just spectacular in the breadth and depth of what it represents scientifically and in other ways. So we're very pleased to have this very important panel. George, without further ado, over to you.

George Vradenburg (00:07:01):

Thank you Zan and thank you Thomas for hosting us on this very, very interesting and important topic with a panel that really is quite broad and deep and it is really my honor to be here with these luminaries of the field. We are hopeful today to introduce the topic of preemptive health and medicine with Lord Ora Darzi of flagship, pioneering, and then followed by a number of individuals, David Ricks the Chair and c e O of Eli, Lillian Company, Dr. Samantha Roberts, the c e o of the National Institute of Health and Care Excellence, friendly, known as nice, mark McClellan, the former F D A commissioner and former C M S administrator, Medicare administrator. Now the director of the Duke Margolin Center all here in the United States. And if I'm Dam June Rain, c e o of the Medicines and Healthcare Products regulatory agency in the uk.

(00:08:17):

And Hillary Evans, who's the chief executive of Alzheimer's Research UK and now co-chair of the UK Dementia Mission. It is quite a lineup of really smart people to talk about this idea of preemptive health and medicine. And what we intend to do today is to have Lord Darzi introduce the topic for 15 minutes or so at the top and then I will ask some questions of each of the panelists that relate to that. But we very much expect the panelists to use the chat function themselves or to use the raise hand function themselves to either comment or ask questions of other participants. This is intended to be a conversation and not a series of monologues, but we are going to start with a description of the topic which has this enormous potential opportunity, but some significant challenges to it. So Lord Darzi, we are honored to have you here. We're honored that flagship is doing this and we look forward to hearing your challenge to all of us with the preemptive Medicine and Health Initiative.

Lord Darzi (00:09:39):

Thank you very much George. And may I also thank Thomas Co and also Alexander Fleming. I have been overwhelmed with Alexander Fleming in the recent months as we approach the centenary of the discovery of penicillin not far away from here. So thank you again for hosting this. Thank you again for inviting me to speak. You really brought up a fantastic group together today and I'm really looking forward to the conversation at the end of this talk. I should begin by saying good morning, but also good afternoon. Since we have panelists and participants on both sides of the pond, let me start by offering some definitions before setting out why I feel that preemptive health and medicine is vital to the sustainability of our health systems. We need to begin by describing what we mean by sickness and health. It actually harder than what you think, and that's because it is somewhat paradoxical.

(00:10:48):

Health comes first. When a child is born, we don't start by worrying about their talents or their looks. We start by asking whether they are healthy, but what does it mean to be healthy? The problem is that human experience is subjective. We can guess and we can emphasize with others about how they feel, but never really know. So health becomes defined by the absence of sickness rather than by the presence of health. We normally understand ourselves to be sick when we experience the symptoms of a particular disease or a condition. Sickness is of course the arena in which most of medicine is practiced diagnosing disease and treating or managing illness, whether it's episodic or chronic. Our healthcare systems aren't in fact healthcare systems at all. They aren't focused on health. 95% of their time and effort and money is spent on caring for the already sick.

(00:12:03):

What we have are sick care systems, not healthcare systems. This observation isn't meant to downplay by the way their importance. Taking care of the sick is of a central importance for any civilized society. But sick care by its nature focuses on the already sick rather than on securing the health of those who are healthy. Indeed, many studies have found that less than 5% of health resources are dedicated to keeping people healthy. This is not surprising today more than 2 billion people globally are living with one or more chronic disease, but the mixing of the categories of health and sickness has some very significant consequences. Above all, it means the urgent need to take care of people who are sick tends to crowd out the important but less urgent need to help people to stay in good health. Now, doctors scientists have understood for many years that reality is much more complicated than a simplistic split into healthy and sick.

(00:13:27):

This is a continuum between health and sickness and the journey from one state to the other is rarely linear. If health and sickness were black and white, there is an awful lot of gray in between. So scientists and entrepreneurs in flagship, and I've had the privilege of being the chairman of this initiative, flagship Piring, as you will know, famously founded Moderna, believed that the same applies at a cellular level in a healthy state. Hemostasis is a self-regulating process that maintains internal stability both at a cellular and a systemic level while adjusting to normal changes in external conditions. Disease is where hemostasis is no longer maintained as either the cellular or the systemic level and symptoms manifest. It is our contention that between there are identifiable biodynamic shifts, that's the term we are using that occurs in response to genetic, environmental and temporal triggers of dysfunction. These shifts are detectable and measurable through various or diagnostic measures. We term this middle phase as pred disease, which occurs in seemingly healthy people. It begins at the earlier stage of cellular dysfunction and encompasses the earlier stages of asymptomatic disease. In all cases, people are on a trajectory towards a disease state but have not arrived at it.

(00:15:24):

People living with pre disease might even be turned pre patients according to identified biomarkers. And the central idea of preemptive medicine is to discover these biomarkers and create new interventions that stops, slows or reverses that journey towards disease and its most impactful. Preemptive medicine aims to reverse the trajectory towards disease and to restore cellular and systemic hemostasis. But we know it is possible that healthy hemostasis cannot be restored, but that further deterioration can be stopped so that person remains stable in their pre-disease state. There will be cases where the trajectory is reversible, but the speed of progression can be meaningfully altered and the progress towards disease can be slowed. The goal is to help people not just to live longer, but to live better. As we say, we want to add life to years as well as years to our lives. So what's new? The traditional way of thinking about prevention strategies maps to this understanding primary prevention strategies aim to lower the incidence of disease in the population.

(00:17:02):

Secondary prevention aims to detect disease in seemingly healthy people, while tertiary prevention aims to limit the severity and impact of disease on people who are symptomatic. Government policies have largely shaped primary prevention through tackling risky health behaviors through smoking bans or tax on alcohol, tobacco, and unhealthy foods alongside health protection through immunization programs and food and water fortification as Queen Victoria did in this country, tertiary prevention is embedded within clinical protocols and routine medical practice. Primary prevention is well-served by public health professionals and tertiary prevention is well-served by physicians and other clinicians, particularly through recent developments in integrated and accountable care organizations. But I believe secondary care prevention has been somewhat of an orphaned child too late for the public health or too early for clinicians. There are relatively small set of activities such as screening programs and blood pressure monitoring that are aimed at detecting subclinical disease. While there are handful of powerful interventions, secondary prevention remains a much more limited area than others. For example, the US Preventative Service Task Force makes just four recommendations for preventative medication at grade A or B. In other words, high or moderate certainty of benefit.

(00:18:57):

I agreed about three years ago. It was actually during covid to chair the preemptive health and medicine initiative at flagship pioneering because I agreed with the founder, the C E O Nuba, who's not with us today, that the potential impact on human health from the pre-disease phase has been dramatically underestimated too little time. Attention and resources are dedicated to examining and exploring the potential of secondary prevention to create value for individuals, healthcare providers and systems as well as societies and economies. So through r and d investment, new detection technologies and novel interventions can be invented, adopted, and I believe scaled if scaled effectively. Preemptive health and medicine would aim to secure the health of individuals, families, communities, and populations. The southern collapse of what might be termed health security during the pandemic revealed how our individual and collective health is the wellspring from which all human experiences follows.

(00:20:15):

Even a particular pred disease could not be stopped or reversed. It is not hard to imagine the enormous value that could be created for an individual and their families and communities if the onset of a chronic disease could be delayed, for example, by five years, five more years of being able to stay at work five more years without pain or disability, five more years of being well enough to play with your grandchildren, just slowing down the onset of symptoms could transform the lives of many. Prevention is a big claim. It is effectively a promise that a disease will never occur at it's bar that is so high that it

dissuades innovation and imposes impossible long development cycles for any possible drug discovery. Preemption though is an action prevention is an outcome. So what is preemptive health? Just as disease is preceded by pred disease, we believe that pred disease is proceeded by the precursor of pre disease.

(00:21:30):

These are modifiable risk factors that can specifically be associated with pre diseases. Preemptive health aims to uncover these precursors and to identify non-drug interventions such as natural biochemicals or digital health tools that can positively impact them to reduce the likelihood that a person develops at pre disease. So I'm aware there isn't long left, so let me just turn to the impact. Everyone here will know that the rising tide of chronic disease, many the result of modern lifestyle means health systems are under sustained financial pressures. When my colleagues who work on the initiative at flagship did some projections, they found if healthcare cost in the US alone grows at the same pace as it has the last next 30 years, then they have as the past 30 years then healthcare will account for 32% of the US economy by 2050. Improving the efficacy of healthcare provision and eliminating waste will not be sufficient response to the scale of this challenge.

(00:22:47):

It is our belief that the only path to sustainability is to improve the health of the population by preempting sickness through innovation with the right investment, the right regulatory frameworks. It is our belief that preemptive health and medicine could have an extraordinary impact over the next decade. And that's why it is so fantastic to have the best regulators in the world at this event. And my colleagues June Rain from M H R A and Sam Roberts from NICE in the uk, their teams are already thinking about what it'll take to create this regulatory framework that enables preemptive medicine to flourish. I know you will want to hear from other panelists, so let me close by saying it has been remarked that most people overestimates what they can do in one year and underestimate what they can achieve in 10 years. Whenever we try to imagine humankind in the far future, we picture a world where scientific and technological advances free us from disease. If we believe that the future is possible, then the only question that remains is not whether but when preemptive health and medicine aims to bring that far future into the here and now that all of us are free to lead our best lives for as long as we can. Thank you.

George Vradenburg (00:24:21):

Well thank you very much Lord. It was a very good explication of both the opportunity. Indeed perhaps the necessity of going earlier in the course of I'd say disease or the pre-disease state in order to prevent treatment costs. Lemme just ask one question then we'll move on to one of the investors in this space. Dave Riggs, with respect to Covid, there was a significant amount of government investment largely in commitments, advanced manufacturing commitments and the like to developing these kinds of rapid interventions. With respect to that pandemic, what do you see as the mix of private and public capital that may be needed to shift the scientific enterprise's focus to earlier stages of pred disease?

Lord Darzi (00:25:17):

I think we're all aligned at the end point of what we're trying to achieve. I think the question is how long it's going to take. Historically, most health systems is the public sector that invest in the preventative side. As we've seen during Covid, the majority, the bulk of the money came from the public sector and from governments. I believe the private sector should be incentivized to do that. The cost of healthcare, certainly in the United States, the burden of that cost is on the budgets of the private sector. In our system like ours, everything is aligned and in the N H s, as you will well know that investment comes

from the public sector, no question about that. But there's a significant amount of investment that goes into the private sector into new drugs and therapeutics. But government beside the investment is the signals you sent out. What happened during Covid, the very strong signaling from government to the private sector and big pharma and the whole life sciences industry that we want urgent solutions to a problem that we could not understand. Whether that happens to be a new discovery, whether that happens to be clinical trials. So I don't have the exact figure of the split, but I think both are incentivized to align, to drive the innovation in this very important area in preventing disease or preventing the progression into a disease.

George Vradenburg (00:26:41):

Dave Ricks chairman, c e o of Eli Lilly has interventions in a number of therapeutic areas in the chronic disease space. He's certainly got one that I am deeply interested in, which hopefully will get approved by the end of the year in Alzheimer's. But with you're emerging drugs and diabetes and weight loss, you're attacking two of the most significant of the chronic diseases of aging and indeed some of the factors that will also drive the risk of Alzheimer's. So you are working in multiple, including cancer I guess, but you're marking in multiple therapeutic areas with respect to the treatment of these diseases. Is what Lord Darzi describes a business opportunity or an impossible goal?

Dave Ricks (00:27:40):

Don't think I'd sign up for the panel if I thought it was an impossible goal. So I think we are on the cusp of beginning to address diseases before the clinical symptoms manifest. I think at some scale, and I think I enjoyed a's comments tremendously there from a drug developer standpoint. Of course the point of origin problem for us is tractability of the science. What we do is primarily in our business is look at identified targets by others and then seek to interfere with biology in a way that can become a widely used product or medicine and then wrap around that the information so people can make appropriate risk benefit. That's sort of the value proposition of our sector. If we don't know the targets, we're really not going anywhere in this problem. But I think if we know the targets, I personally don't see a big difference.

(00:28:43):

If you're wondering as an investor between treating diseases that already have symptoms and treating diseases that don't, if that's, I don't think there's a different calculation for us. There are different problems. I think as I thought about this panel, I think maybe three things to think about from a drug development standpoint and maybe three from a healthcare system standpoint, some of which have been addressed by previous speaker for drug developers. I think the problems in the space, and you've pointed out that we're seeking to prevent cardiovascular disease and diabetes using obesity medications. We're seeking to prevent Alzheimer's disease with an anti-amyloid medication. We run into a few challenges. One of them is the risk benefit in that setting has to be higher or the benefit risk rather than in a treatment setting because the patient's not experiencing symptoms and the probability of conversion to a symptomatic condition is less certain no matter how good our predictive marker is.

(00:29:48):

So you have to have better drugs, they have to be incrementally safer or more effective for both to want to test them in this setting. And the reality is for most of history of drug development, I don't think our drugs have been good enough to be used as preventatives because we haven't understood very well the structural biology and the way that the medicines are interacting with biology. That's changing. I think the speed at which we can get better drugs and iterations of better drugs is definitely accelerating. So

that I think is a good predictor. Another problem we have is in time course. So in most of the important diseases to prevent, we actually don't know the time course of the pre-condition. And so if you pick the wrong point to intervene and it's not a linear relationship between time and the disease, you have a big risk.

(00:30:46):

You're assuming we're assuming this risk right now. As you know George in Alzheimer's we have a study called Trailblazer three going, which takes asymptomatic. People who have high amyloid load are of an AIDS distribution that makes sense and low or no tau and seeking to prevent a new diagnosis of mild cognitive impairment or Alzheimer's disease. And we really don't know very much about how that process of conversion occurs. We learned something more this summer in a four study, which was an earlier effort and it looks pretty linear. So that's good news I think for that condition. But it seems to me it's unlikely that we're going to find that these are everything is a straight line. I'll just point, there's an interesting article I reference a lot in diabetes care medical publication in 2021 that looked at the impact of bariatric surgery on all manner of metabolic outcomes.

(00:31:48):

And it looked at the two primary techniques, sleeve gastrectomy and then gastric bypass, which have a relatively proportional impact on weight loss. It's pretty stable over time. Gastric bypass more effective gets closer to a native of about 30% weight loss, whereas sleeve gastrectomy about 20 and then they looked at all the outcomes and in some cases they have identical outcomes, meaning 20 and 30% was the same. And in others they have very different outcomes like A S C V D or major cardiovascular events, sleep, gas, ectomy did almost nothing. Whereas the difference between 20 and 30% weight loss made a huge difference, almost 58% reduction in these events. So yeah, if it was all linear it'd be easier, but it's not going to be. And I think the diseases where we know more from epidemiology about the progression and the history of disease, the easier it'll be to attract investors to put money behind those conditions.

(00:32:45):

The final thing I'll say is regulatory frameworks. And I think here we can work with the regulators, maybe some of them on the line here to make it easier to take on these approaches. And in the case of the A four study, which was a failed study in preventing Alzheimer's, but that was a public-private partnership. But I think we're an industry of followers and I think if there are initial efforts needed, that was a pretty good model where it was sort of one third, one third, one third and private philanthropy industry money and N I H money to get something going. And now we didn't succeed in that effort, but we can iterate and improve. I do think and era pointed to many of these, there are other problems even once you succeed. So let's say our trailblazer three study succeeds or all of our outcome studies going with tsce peptide show, we can prevent kidney failure, liver disease and strokes and heart attacks and really big portions of the population by treating obesity earlier.

(00:33:42):

I think first of all, the health systems aren't particularly ready for the volume that may be coming their way. As was pointed out, they're built for treating sickness, not preventing sickness. And so that's a big question. In the case of obesity, the intervention cost is really light. I think it's a lot of pharmacy and maybe digital health. In the case of the Alzheimer's treatment, it's pretty heavy. You need scanning, you need intensive therapy for about a year. That may be worth it, but it's a restructuring for sure. And I think when we show up with positive data, it's going to be a challenge to restructure health systems to actually deliver these things. Or as Ara pointed out, maybe it's a different system altogether needed more consumer directive perhaps. The second thing is diagnosis, and I think I lead a pharma company.

We have a nascent diagnostic business which we assembled in Alzheimer's disease because there's a problem in diagnostics, which is there's really no money in it.

(00:34:39):

I think the totality of global diagnostics profitability is something like 1% of pharma. So sometimes the cart needs to come before the horse and in this case the cart is the diagnostic. And if no one's working on it or deploying it, we'll never know who these people are. That shows up also in clinical trial problems. And then the final is knowledge dissemination. I think the confidence has to be pretty high for physicians and consumers to use drugs in a preventative setting. And I think what we've learned through covid is through government intervention industry. I think that was a high point probably in 2021 for a lot of us working in that space. But we've seen since what can erode that confidence and I'm not really sure that that wouldn't happen again even in a space like obesity or Alzheimer's prevention where conspiracy theories and misinformation and low confidence could really undermine something that could actually change life expectancy. So that's a topic and maybe another panel can take on that topic, but I think it's much harder in a preventative setting.

George Vradenburg (00:35:52):

I'm curious as to what you would see as regulatory challenges. We'll turn to the regulators in a second of being able to, assuming you could detect the disease at this very earliest stage and assuming you were able to target that successfully and interrupt this pre disease state, how in the heck are regulators going to deal with that? Well,

Dave Ricks (00:36:24):

I can tell you where I was raising it. I'd love to hear Mark's point of view on this as well. I mean, we lived through this with Alzheimer's, right? So the primary thing a regulator could do is use a logical precursor to study versus the end disease, thus really changing the math for investors on waiting for an outcome in a preventative setting, which in some important diseases could be closer to a decade. Of course patent lives in W T O countries are 20 years. So that by itself it would eliminate that disease from study really. But we could use a logical precursor that's a risk that people need to hold hands on. I think the F D A attempted to take that risk in approving early drugs for Alzheimer's by looking at amyloid reduction. I think it will turn out that that was a wise choice actually, but generated huge controversy even in the treatment setting, let alone the prevention setting. But if we want to make progress in a broad swath of preventative diseases, that kind of risk would be by regulators in this case would I think really induce a lot of investment because it makes the problem much more attractable.

George Vradenburg (00:37:33):

Well, just as a comment, we're seeing now a number of companies who've come back into the Alzheimer's space as a result of FDA's aggression aggressive attitude there. I'm going to now turn to a Dame June regulator regulatory issues. How in the heck do you approve the efficacy of a drug when you're so many potentially years away from actual demonstrated deferral or elimination of symptomatic presentation? How do you accept the prediction of clinical benefit as opposed to the showing of it in a predeceased state?

Dame June Raine (00:38:15):

Well, let me first say how important it is that we're identifying the regulatory role upfront in a really timely and important discussion. And we've heard so clearly from Lord Darzi of the really important

population health gains and health service gains and living longer and healthier life gains for the individual. So it's a problem we need to crack and I do believe that we can crack and we've already heard from Dave some of the ways that you've built on George about risk sharing. But if I step back to some of the simple principles, and in fact Dave has talked about them, the regulatory role is a simple one and it's geared to assuring the public that standards of quality, of safety, of efficacy have been met for a particular use and herein lies the challenge that we are facing. But before I talk about that challenge, regulators I think have a role and a duty to enable innovation not to keep patients in the public and payers waiting to follow the science.

(00:39:22):

And this is why we would like to put our, if you like selves in the ring and say that regulators to have a duty to help the preemptive health agenda to flourish. Especially now that we have the pipeline coming of really interesting new entities around, as we've heard already, obesity, dementia, risk modifying drugs. So critically important for us is going to be robust data that links this early diagnosis based on say biomarker evidence with predictors of benefit at particular points at that stage going from the pred disease state against balancing it against the products risk. So it is a risk benefit, but a particularly interesting one and I'd look forward to seeing some modeling around that that might help us all to embrace the risks as you say. And the time element is going to be pretty important. And it may well be a very long time.

(00:40:25):

And here I think we have the opportunity of real world data, large data sets, and let's bring on more international collaboration in this space because can I say it loud? Regulators are increasingly more comfortable to base labeling decisions on real world data. I think one of the issues to think about now is where regulators have gaps. We've heard about the gap in prevention from Lord Darzi, what are the regulatory gaps? And it may be a personal perspective, but I don't think we communicate risk very well in accessible ways for patients and the public. And as we've heard, we are going to need to take the public with us on this journey. And I'd really like to see this opportunity grasped by regulators to help the public come with us as we move forward with preemptive health, particularly as we've got these important new entities, we want to realize their potential.

(00:41:26):

So I think let's mainstream preemptive medicine, preemptive health, the science is driving and the science is being done. I'd like to raise the flag for the UK here. We have the newborn genomes program really bringing some interesting results but also the attitudinal change that parents will have to work through. And then of course we've got our Future health, which is the program that's going to look at disease risk scores in 5 million people. And my PA was coming in just earlier to say, I'm signed up, I'm going down to boots. This is our chemist that's local to us and getting her blood test. So 5 million disease risk scores, what are we going to do with that evidence? So I think together is the way we will do it. I think this panel is a fantastic start and I hope it is the starting point for some specific discussions, international discussions to how we crack the issues and gain the opportunities. So I'll stop there.

George Vradenburg (00:42:30):

Well thank you Dame June. I am curious now I am not inside the regulatory world. I am outside of it and a consumer or a victim of it depending on one's perspective. But are there understanding international regulatory collaborative systems or would you suggest that perhaps we have an odd hoc one focused on preventive medicine?

Dame June Raine (00:43:00):

And I would say luckily the answer is yes. We have the International Coalition of Medicines regulatory authorities, which is having its summit in November in Melbourne, Australia. And that is actually beginning to spin off some important discussions say around rare diseases where this is very similar to the idea of what the newborn genomes project will do in identifying genetic predispositions at a very early stage. So we've got the tools, the technology and the data, and we have the international collaboration. So let's get going.

George Vradenburg (00:43:39):

Great. My sense may be wrong is it that international mechanism does not include business or patients or scientific researchers? That is to say it is a regulatory collaboration. So I question, given the value of this panel and having so many different perspectives, whether or not there could be, if not ad hoc, a spinoff of what you're talking about or a work group that's spun off what you're talking about that involves other sectors of the fields.

Dame June Raine (00:44:14):

Certainly there is an open door while the regulatory, if you like panel is a large number of regulators from around the world. The interface both with industry, with patient organizations, with the World Health Organization is in place and the

(00:44:30):

Product of this is the spinoffs such as the one on individualized therapies. So let's keep going and maximize the opportunities.

George Vradenburg (00:44:41):

Terrific. Well I am going to turn briefly here to not so briefly, it doesn't know I have to busy so brief to Sam Roberts because I really wanted to get the payer's perspective here because the payers are being told, gee, if we do this right, we can reduce the heck out of the costs in the healthcare world. So this should be a delightful opportunity for you to say, let's go get it. Do you see this as easy, hard, what do we need to do to get at this from a payer perspective?

Sam Roberts (00:45:14):

So I mean as you know, we think that's a huge opportunity, have probably two pleases and one caution, and I think I'm going to answer your question on you're challenge directly to us, Dave, because we see exactly the problems that you described but from the other side. So I think the first thing that you talked about was the risk associated with intermediate endpoints in that we are not going to know whether these interventions affect length and quality of life was sometimes decades. And I think the real you were sort of saying where does the risk of that not knowing lie? And we think that it's a shared risk obviously between yourselves and ourselves, but the way that we can significantly mitigate is by properly investing in research on intermediate endpoints. We've seen this in two of your big preemptive medicine launches, right? On the one hand you've got for obesity where we've got beautiful data on if you reduce body mass index, it leads to this reduction in cancer, this reduction in cardiovascular disease, this reduction in musculoskeletal disease.

(00:46:27):

So us as payers or people who make decisions on behalf of payer can feel confident say we're going to take that risk. On the other hand, you've got diseases like Alzheimer's where you've got intermediate

endpoints like amyloid that haven't really been a hundred percent valued that they quality of life. So that's what I'd love us to see us working together with scientific community industry regulators or what are those intermediate end points that we can all invest in getting right, but correlate with length and quality of life. So that's where I'd focus. And unsurprisingly George, we are indeed working with other H D A agencies around the world on validating some of these intermediate endpoints. That's the first thing. The second thing is we see exactly what today is describing, which is once you're talking about interventions that firstly need to identify people who are not presenting to the health system because they are not sick and two affect large sways of the population.

(00:47:26):

So for us, for example, in the uk, the anti-obesity medicines could have an eligible population of 4.3 million people. Any cost of intervention is really significant overall. So we think about prevention as saving money in the health service, but actually when we looked back on all of our recommendations at NICE on prevention, only one in five actually do save money and the other five cost money because the cost of delivering the intervention is so expensive. So you have to identify everybody, you have to figure out, ask people to provide medications, some applies, others weren't, others will be intolerant, et cetera, et cetera. So the number that you initiate in the program and the number who benefits are quite unbalanced. So that's the other thing I'd say as a way of mitigating risk is it really think files about what is the total cost of delivery of these things at massive scale that will really mitigate the risk for the payer.

(00:48:31):

So those are my pleases. I don't think they're insurmountable incidentally. I think the GLP ones for example of how those risks have been mitigated. And then my last one line of caution would be often people say with this kind of profile of saying, well not to worry, we can do coverage with reimbursement and we can do our based pricing, our experience, we now are now 70 year coverage with reimbursements medicine, you can do that, but the time periods for these are typically much shorter, two to three years. So you'll get into a new coverage with reimbursement. And then the second is outcome-based payments. Absolutely you can do them. They are pretty hard to transact. So they tend to be the, we look at a hundred medicines a year of those hundred. We rarely get one that is an outcome-based payment because it's so hard for. So I wouldn't say those things are off the table, but I wouldn't think of them as simple solutions that mean we don't need to deal with these other kind of cautions that I raised.

George Vradenburg (00:49:35):

As I remember you also in our prep session mentioned the challenge of keeping people on drugs over a long period of time to achieve the clinical benefit. So that adherence is a real problem. It's one thing to get people to start going through all the costs associated with identifying the right people and the right product. It's another to keep them on that drug for the period of time you may need to keep them on the drug in order to get the benefits that you hope to achieve. Just speak a bit about that.

Sam Roberts (00:50:06):

Yeah, exactly. And I think we've had some folks in the chest have spoken from the diabetes community in the UK where we've had two great programs there. One is diabetes prevention program and then the other is a low calor. And in both of those, I'm not going to get the numbers exactly right, I can't remember the trials, but basically of a hundred people who enroll only 10 to 20% of the a hundred people who could be eligible, only 10 to 20% final benefit because of this issue of identifying people who are not actually sick. So they're not presenting themselves, where do you find them? What's the

mechanism you use of those people who you find how many initiate treatments of those people who initiate treatments, how many complete the course and of people course, how many is it effective in? So I think that's why we're saying the funnel of costs is actually quite large and that's not a problem that has happened with preventative treatments for many years. But that's just something for us to think about If we think that all of these interventions are going to be cost saving, they won't unless we address that kind, the funnel of cost and help system input.

George Vradenburg (00:51:27):

Thank you. No, thank you for making those points. I think they were important. I'm going to move across the pond now to Mark McClellan who uniquely, at least certainly in the United States uniquely has both an F D A regulatory hat and a payer hat. So Mark, you've heard the conversation, what's the thinking over in the uk, your reaction regulatory talking

Mark McClellan (00:51:50):

About the UK too, but in the us? George, let me pick up on some of the great discussions so far and as thanks to you and Zen and Thomas for bringing us all together. And I want to try to build on some of the comments from Dane, June and Sam and going back to where Lord Darzi started us out. I totally agree that there are greater opportunities for preemptive medicine and that we need the right investments and the right regulatory framework. I do want to build on some of Sam's comment about needing healthcare payment and delivery changes. And all of this is hard because it is not only a approach that's challenging compared to dealing with tertiary prevention and complications under our current regulatory frameworks and payment frameworks. But these long lead times and the need to be confident and effective in intervening in people who are still relatively healthy has just been challenging for our traditional paradigms.

(00:52:55):

And maybe it could start with just another area that's come up a lot recently is an area for preemptive medicine and that's cancer care. Remember, the usual regulatory approach to bring a drug to market is start with the most complex advanced patients where no other treatments work, where you can give a new drug in a big dose and because it's such an urgent need, single arm studies, short follow up since you're trying to prevent death within a matter of weeks to months, that's a relatively easy pathway for scientific development. Contrast that with where cancer care should be headed with new development of multi cancer, early detection tests that should be able to shift diagnosis to earlier to treating cancers in earlier stage patients where the dosage may be different, the side effect profile may be different and the time to follow up and need to monitor for adverse events is longer and harder.

(00:54:00):

You can see that as you go further and further back, those problems get compounded. And we've talked about some of the ways to address that. Obviously the science around biomarkers, both for people who are at particular risk of the disease progressing and particular risk of side effects are very helpful in people who at least for some months or years may not have any more serious health consequences. So we've talked about the value of biomarker development there, but I also want to move to, I know time is limited to the importance of changes in the delivery system. And Dave mentioned some of these things too. Remember that both in the US and the uk, our financing paradigm for healthcare is about tertiary prevention and helping people who really need help. We've gotten good at that. We're getting even better in the us. The medicare law, that program that I oversaw is defined to cover treatments for an illness or injury or actual dysfunction in a body part to cover preventive services.

(00:55:14):

It takes acts of congress even to cover prescription drugs. That was 40 years later after Medicare was created. So there's that underlying feature in the US healthcare financing system that we still haven't really moved away from. I think the same thing is kind of true in the N H Ss, I guess you can't call it sort of a constitutional emphasis on making sure people who have urgent needs in hospital get those addressed. But it certainly puts an emphasis on limited resources. I think the good news is we've seen some progress, but I think we need to see a lot more Ara mentioned to move towards accountable care. And just to keep it very simple, that's about paying for outcomes, not for specific services. It helps downstream in maybe supporting shifts in sites of care covering digital technologies or ai things that may be hard to cover under traditional medical services, but where it can really make a difference is moving more upstage.

(00:56:16):

Good news is in the US we've seen some examples in other countries as well of organizations that move towards being paid more on a longitudinal not just six months or a year, but preferably longer basis at the person level with accountability for results has freed up a lot of innovation and culture change in healthcare to not just say we intervene early and advise people when they come in for their office visit to lose weight and eat a healthier diet, but really build community health systems around them. Digital apps that people can use, team-based approaches of care, including reimbursement for a lot of lower costs, but effective providers and connecting with patients and making those early interventions happen. It's just very hard to do that on a fee for service basis. And the second comments that I think everyone else has made, early awareness with accurate information, attention to adherence when people have so much else going on in their lives is really hard.

(00:57:19):

And you have to build systems around that just like we will build excellent systems around safety when people go in for a major surgical procedure, it takes that kind of support. And we're really just getting started on that with respect to what that means for drugs in this space. So there's not only the challenge of the costly long studies to get to approval and the time and effort to validate markers once the drugs are approved. As Dave said, our healthcare systems aren't set up to use them well and have trouble with the math. For example, just yesterday our CDCs advisory committee recommended booster vaccines for covid for essentially everyone in America for over six months of age. Well, we're not going to get close to that. I mean the US had this great system for developing even testing clinical trials, the very promising mRNA and some other vaccines had a military based distribution system to get those vaccines out around the country.

(00:58:26):

And yet in 2020 and especially 2021, we had higher rates of adverse outcomes from COVID than much of the rest of the world. And that gets back to the delivery system problems. As Dave mentioned, we do have some health systems that have proven ability to work with community organizations to pay more for not just clinicians or not just physicians, but other clinicians, pharmacists, others who are trust in the community, convey accurate information, are still very, very trusted. But that's a whole infrastructure that needs to be built and it requires a different kind of financing. Again, this is about paying for outcomes more at the person level. And I think you see that in some of the drug pricing challenges that we're facing now, understandably, if a healthcare system isn't going to be able to deliver a product very widely, especially prevention oriented ones, you're going to tend to see high prices to recover investment costs.

(00:59:26):

And frankly because lowering the price won't make that much of a difference. We've been involved in some drug outcome pricing models like for hepatitis C drugs and Medicaid programs in the US where the price is actually zero. None of the states that have implemented those programs actually triggered the zero price. Why? Because finding patients doing the screening and diagnostic tests for Hep C and then helping those individuals who often are in low socioeconomic status or using intravenous drugs or having other issues in their lives have a very hard time with adherence. So what I'm hoping to see is finding a way to better math for these drugs where the price per drug might be lower, but there can be real confidence on the part of the drug manufacturers that they will have partners in healthcare systems that can drive up use. And frankly, those healthcare systems and the real world data that they generate in these longitudinal care models are the main source of evidence on things like what can go wrong when you intervene early with patients, what are the rare side effects that you'd like to rule out? And for validating those early stage biomarkers, very hard to do that in the academic clinical trial context. The N H S and then working with NICE has taken some very good steps at the population level in the UK to address some of these issues. And we definitely need to see more of that kind of work on both sides of the pond.

George Vradenburg (01:00:59):

Thank you, mark. I just want to acknowledge that Dave has to leave. He has a plane to catch. And so I appreciate his being here and I hope he will take up the June's invitation to continue this discussion and to invite his industry colleagues to join in some collaborative fashion to really uncover the challenges here and whether we could really make headway on this preemptive medicine health initiative. So thank you Dave for coming and appreciate

Dave Ricks (01:01:31):

All in on that. And I would say actually to Sam Roberts as well, happy to work on some of those problems together. I think it's possible we could make the UK the first obesity free country in the world.

Mark McClellan (01:01:41):

Whoa.

Dave Ricks (01:01:42):

If we started with that

George Vradenburg (01:01:43):

Goal, there's a claim

Dave Ricks (01:01:45):

We could work backwards and solve it together. Well, we have a drug that's highly effective, but it will require two things. One is time horizon for the assessment because these drugs do go generic, but hardly any h t A organization in the world accounts for the generic period and their cost effectiveness. But if we're preventing disease 30 years from now, most of the time the person's taking the drug, it'll be generic and pretty cheap. So if we could get through that as well as figure out ways to get out of our own pricing paradigms, I think we could solve it. So it's possible. Think of what that could be. Happy to

talk about that further outside of a panel. But anyway, thanks for having me, George. And exciting times, definitely for human health ahead.

George Vradenburg (01:02:29):

Good, thank you. Thank you Dave for coming. We'll continue. Now I want to ask Mark, to what extent is disruption in the delivery system going to occur outside our traditional health system direct to consumer products, whether in the diagnostics or the other self-help products? I mean, we have a huge supplement market, which is direct to consumer. To what extent is disruption? I mean, I came from a O l where a disruption in a wide variety of businesses by the internet occurred outside of the existing then business structures. Is there a direct to consumer sort of way to disrupt or other mechanisms to disrupt the healthcare system outside of it rather than trying to work through Medicare?

Mark McClellan (01:03:19):

Sure, George. I think there are a lot of examples, especially where people are willing to pay on their own and some employers that are doing kind of add-on efforts to address clear specific gaps in the care that their patients are getting. Whether it's in the case of employers access to behavioral health services, which can be really hard traditionally, but thanks to telehealth and other supports are much easier to do as add-ons, whether it's for basic primary care services, then investment and companies ranging from one medical to virtual primary care. The challenge though, George, is that each of these efforts typically is only once piece of a very large system that just needs to get better at helping people get coordinated longitudinal care to address all the problems we're talking about. It's not something you can do with just a quick, maybe we'll get better at that.

(01:04:24):

And there are very successful companies and pieces of this work. But remember a unicorn company in healthcare, one of these early startup successes, billion dollars is literally a drop in the bucket of our 4 trillion health system where most of the resources and supports are still in hospital-based care, still are not really widely adapted, these reforms. So I think there will be some further innovation and there are companies that are working with hospitals to help them modernize primary care practices to help them be more comprehensive. And I hope we can keep encouraging that. So private sector innovation really important, but it's hard to see it really succeeding at scale without Medicare getting even further behind these early. So supporting early studies to track whether drugs really and devices and diagnostic tests really are having those intended long-term benefits and support health systems and getting that longitudinal data structure in place to really help people identify risks early, adhere to steps to do something about those risks and be accountable for better outcomes over time.

George Vradenburg (01:05:42):

I'm going to turn a second here to Hillary, but I also want the other panelists to give some thought to whether there are any analogies. 50 years ago, 70 years ago when we said, Hey, we ought to get in front of this thing called polio. We ought to get in front of this thing called cardiovascular disease where we've actually done preemptive medicine, didn't even call it that at the time, where in fact we've gotten some results, whether it's cost or efficacy that is really had been historic and demonstrably. So I'm going to turn now to Hillary, who as a co-chair of the UK dementia mission, really in a country that has extraordinary life science assets, whether they be viewed as the academic world and now a number of industries who've invested there. N H Ss as obviously a life science delivery company, the Biobank, a lot of really extraordinary assets.

(01:06:48):

Can UK put something together? You're charge of the dementia mission, but I invite a more general comment or in dementia alone that really could sort of take on this notion of preemptive health and medicine in a therapeutic area or multiple areas and say, this is what we want to achieve. We want to be the first obesity free nation in the world. I mean, that's quite a claim as a goal. And then figuring out how to get there. I'm just curious as to whether the head of a UK mission has some thoughts about what a nation might do if it put together all of its extraordinary assets.

Hilary Evans (01:07:29):

Thanks, George. Yeah, really great to be here. I mean, I think this is just hugely exciting, isn't it? I think that the opportunities here are huge and across a lot of different disease areas. So the UK government mission that George talked about is one of, there's seven missions now in the uk. I co-chair the dementia mission. But there's an obesity mission, cancer mission, respiratory mission addiction. And really that's what the Office of Life Sciences in the UK government have tried to do. So we're sat between Ministry of Science and our department of health and social care and we have been set up in a way really to take some of the learnings from the COVID taskforce. So we've charged with being disruptive, thinking about what we need to do in our disease space, but actually also working across the piece in terms of these different missions and where we have some similar sorts of challenges.

(01:08:30):

So we are working with the obesity mission, actually, it's a mental health mission as well, which I think is really interesting and exciting. I think the UK does have huge, huge opportunities, the N H s, the clinical data that we've got, the data sets and really rich data sets that we've got. But there are, and I guess the sort of the size, population size that we've got in the uk, but there are some hurdles and there's some big challenges. And I think that talking about dementia specifically, huge global challenge with dementia. If we don't do anything in terms of developing interventions and treatment for people with dementia, we know in the next sort of 20 years the numbers of people with dementia will triple. And the cost of supporting looking after people with dementia on a human societal economic cost is incredibly high. But we are making strides.

(01:09:25):

So I think the disease and modifying treatments are starting to come through. Kinumab, Don Umab is really exciting. And I think that the ongoing trials that Dave talked about in terms really understanding what some of those disease modifying anti-amyloid therapies might do in a pre-symptomatic population will be really, really interesting. And I think this is where the dementia mission at the moment really is focusing. So what could these treatments and future treatments, preventative medicines, potentially vaccines in Alzheimer's disease and other diseases that cause dementia look like, and what are those opportunities? And they're, where have we gotten opportunities in the uk? So what can the mission do to support these kinds of trials? So we need larger sample sizes, we need better biomarker stratification, we need better risk identification and we need the tools to do this. So actually blood tests, digital tools. And so what we want to do in the dementia mission is look, I guess from a biomarkers actually, how can we then work in collaboration with industry and how can we work in partnership with regulators and our health services to think about actually how we detect and diagnose, how we stratify patients for trials, how we make the UK the go-to place to do dementia trials or do large scale preventative trials that could be really, really exciting.

(01:11:11):

And what is the data platform or vehicle that we could use? And actually if we are talking about going presymptomatic and aligning a lot of the data that we know that we already have and that's coming through in UK Biobank and our future health was mentioned, do we then naturally pull some of the data that we've already got off of a number of these different platforms and start looking at what that's telling us? That could be hugely exciting, but then what does that look like for our public patient population? And I think that's then the conversation in terms of ensuring that we are making progress in the detection diagnosis as we are with some of the disease modifying treatments. And then I think for me, the other big challenge here is around our health systems and how we view as a sort of clinical pathway, how we treat and what those interactions with people who maybe have a diagnosis or have the higher risk of developing, say Alzheimer's disease and what that looks like.

(01:12:28):

And so for me, that's where there's a big opportunity. So we have three key pillars of the dementia mission as a sort of roadmap. So the first is in the biomarkers space to develop them and to do that in collaboration with industry who are already very much in this field and other players who I think are very interested in coming back into neurodegeneration and then looking at bigger clinical trial platforms, looking at how we can work on a population level screening potentially because we know some of those tools are starting to come through. So we're really interested in those early digital detection, blood tests, genetic screening testing much earlier along in midlife. And then the third pillar really is around systems. So actually what do our health care services need to look like to start to deliver on some of these treatments, which are potentially going to be treatments to a presymptomatic population.

(01:13:29):

So the current way that we would maybe think about diagnosing and triaging patients to a treatment for Alzheimer's disease, which we've never done in this way, probably would be outdated and isn't going to work with disease modifying treatments in terms of the way you would administer say non umab treatment in this space via regular infusions for an intensive period. So looking at those sort of investments that are needed in the treatments of tomorrow, but also that future healthcare model. And if we can do that on a sort of dual track, I think that would be fantastic. But I think for dementia there's a big opportunity because of the challenge that we've got. I think there is the political will and I think that you need all of those things to make that change. So for me, I'm a real optimist and I'm really excited about what it is that we can achieve. George and I have been working on this for a number of years together, but for me the time is now to see what we can do but align this with some of the other disease areas as well. But if we can start in dementia and show what we can do here, actually you can replicate this way of working in other disease areas.

George Vradenburg (01:14:47):

I'm going to ask, I know I asked before whether there were some historic examples of where we may have engaged in preemptive medicine and didn't even call it that, but I want to ask another question first. Most of the diseases we're talking about here affect low and middle income countries and low resource socioeconomic groups within each of our high resource countries disproportionately. So we have a situation where we tend to have clinical trials that are very well designed for white Caucasians and yet do not include the diversity of populations that both within our countries, let alone the world, it may be that we're going to discover things or could discover things about these diseases which are hugely informative about identifying those at risk or those who have a lower risk by going outside Europe and the United States. So I'm curious as to whether or not there's any merit to that and equity within our respective continence is important, but global equity I think is important.

(01:16:02):

For some reason, we're now finding in some of our work that in the Alzheimer's world that the cutoffs for diagnostics for African-Americans are maybe different than they are for white Caucasians. And which suggests immediately should we be looking at Africa as well as African populations at the same time that African-Americans in the United States are twice as likely to get the disease. So something else is going on. So I only say that to say how do we assure as we go forward if we're going to have this conversation that we include the populations within our respective countries or continents that are of lower socioeconomic status and how do we include the rest of the world in our work? Because if some of the low and middle income countries around the world go bankrupt because they can't deal with the chronic diseases of aging, it ain't going to be good for the world economy. So I'm curious, and I'm not sure who, let's, Lord Darzi, could we start with you? How do we assure that your idea is taken and thought of as a global proposition because the cost savings or the economic growth associated with being successful in your initiative is going to nure to a wide variety of countries and the global economic growth that's much broader than our two continents.

Lord Darzi (01:17:34):

Absolutely. I mean that challenge remains whether we are talking about disease or preemption of disease. And historically though, if you talk about public health, we've done a reasonable job when it comes to public health in many lower and middle income countries, thanks to major foundations like the Bill Gates Foundations and other W H O and others. But when you are moving to a completely different sphere in which what we're talking about here, preemption, although in the long term will save many of our health systems a lot of money, but the upfront investment needed if you to roll this out in lower and million income country is going to be of significant cost. Unless technology becomes cheaper, unless the use of AI and other digital applications may make accessibility cheaper, that's a major issue. Could I just say the other thing I worry about too is not just lower and middle income countries, but also in health systems, including ours, which has a single player system with all the advantages, there are serious challenges when it comes to health inequalities and access to these technologies.

(01:18:40):

That's one of the interest of our accelerated access collaborative. There are subgroups of the population which are impossible to access even in a single payer system in which everything is provided to you for free at the point of need. So there's a lot of policy thinking that needs to happen here and how we drive such innovations through, if you go back to the Victorian era, all the public health interventions at the time affected populations as a whole, whether that was clean water sanitation and could you replicate that in modern age with these new platforms of technology is the question that's yet to be answered and it needs a huge engagement from our political elite. And how do you improve access to these technologies either in high income countries within cigarette inequalities like the US or the UK or Europe or lower embedded in countries?

George Vradenburg (01:19:38):

Well, Darzi, I'm going to put it to you. Most of what we're talking about are global issues. That is to say industry is global, patients are global drug development. To some extent academic research is global nation states tend to invest in those things which are within their countries. If there are benefits to our nation states and to the world that aren't captured by the health economics of NICE or of Medicare, should we be thinking about some global funding mechanism that basically says we can understand the cost of these chronic disease of aging at a global level, but no one nation is going to be able to invest in a

way that really reflects the value of getting transformative changes on these chronic disease of aging and therefore should there be a global fund directed to preemptive health and medicine?

Lord Darzi (01:20:45):

Absolutely. The answer is yes. Is that feasible? Potentially. We've seen historically some amazing political leadership examples. Take H I V for example, what the US did, what the criticism that the US president had at the time in terms of his policies, interventions, that's the type of leadership we need and it's happened in the past. I can see why it shouldn't not happened in the future. And this global fund looks and invests in many lower million income countries for all sorts of reasons. So yes, there's precedent to this and the answer to your question, yes, I think there should be one.

George Vradenburg (01:21:28):

Well, I'm not going to come back to the other, and this is sort of a health economics issue that I should have asked Sam about. She can't invest at the level because of her budget. She can't invest at the level that would capture the values to the globe and to the global economy. So I am suggesting, and maybe Sam, that you lead the effort in the UK to get the UK to back a global fund. We're working here with our congress to do that ourselves and we're working the Japanese government, but the UK government stepping up as it has in the past would be provide some of that co-leadership perhaps on developing a global effort around these chronic diseases of aging. So I'm going to come back now to the question I was positing and then deferred. Do we have examples in our history, health history?

(01:22:22):

Lord Darcy mentioned some public health interventions, but if you think of polio, you think about statins. Are there things where we actually have done this in the past and where you could model or demonstrate at least the benefits of going earlier and solving a health problem earlier in the course of its disease to say, Hey, it's been done before, we just haven't called it this, but now we should do it more systematically and with greater focus. So I'll put this to anyone who wants to answer the question. I'll start with Lord Darzi, but anyone else is certainly invited to step in and respond. Okay, Sam?

Sam Roberts (01:23:15):

Yeah, I can have a go. I mean I'm going say the obvious one, which is smoking cessation, but it's quite interesting how different a paradigm that is, right? It's the avoidance of a harmful activity. It's not the identification and prescription of an intervention. Although I'm wondering now that I'm saying that there are some similarities in that with smoking cessation support, you need a range of interventions that can be delivered at a range of times. You need opportunistic screening, you need both individual interventions as well as public health measures. But I think that, remember when I said 21% of the preventative interventions are cost saving? Actually smoking cessation is one of those. It is cost saving five years.

George Vradenburg (01:24:05):

What is another one other than because that's an interesting public health slash intervention kind of thing.

Sam Roberts (01:24:14):

Oh, so now you're testing my memory, George, but I actually think contraception, but depends on whether you consider that offensive. That's another one. There's some debate in the UK about whether

diabetes prevention programs are cost saving. There's some evidence that suggests the cost effective. There's others that say it's cost saving. I can go away and do some of my research while the panelists are answering.

George Vradenburg (01:24:43):

Mark, you have a good sense of history. Where might we say that we have done preemptive medicine? Oh, I'm sorry, you had your hand up Dame June. I missed it there for a second. I

Dame June Raine (01:24:57):

Was going to suggest aspirin. I think the story,

George Vradenburg (01:25:04):

I think you've frozen unfortunately. Okay, you're back. Can

Dame June Raine (01:25:10):

You hear me? Aspirin in cardiovascular, first of all, secondary prevention then primary, and that took a long time to get into practice. I think the theme is that when we have these opportunities, we tend to take a long time. We've only now introduced testing newborns for Gentamycin ototoxicity, and that's been a genetic link known for a couple of decades, whereas 200 babies in the UK every year would end up deaf without that testing, I think we could have a very fertile discussion building up a sort of bank of examples that would actually make getting a global fund very convincing.

George Vradenburg (01:25:55):

Well, I'll invite that as a follow-up item. Mark, you have any thoughts on where we can say that we have done this as a globe? We know that extending life during the 20th century has produced enormous amount of economic growth around the world to the benefit of hundreds of millions of people. So this notion of extending life, gee, why are we trying to do this? Extending healthy life has an economic consequence, not just in cost savings potentially it may be more costly, but the benefits may well exceed the costs. If you could capture in one place the analysis and the investment associated with cost, increased cost, but a magnitude of multiple of those additional costs in global economic growth and the benefits of that.

Mark McClellan (01:26:50):

And I would make a distinction, as you said, between cost saving, which is very hard to prove, especially within just the healthcare silo and cost effective when you consider these other dimensions. And our goal should be cost effective, but hopefully with sustainable healthcare systems too. I put in the chat covid, covid vaccines having lived through, that's an incredibly fast effort to take a base platform, particularly in R N A and turn it into human clinical trials at large scale in very diverse populations, big enough to do detection of even rare side effects followed up by surveillance systems to further understand those side effects. Well in many countries and large scale production, not under typical pharma fee for service approaches, but under population level essentially procurement models. And then we did stumble a lot on equitable availability of the vaccines and especially stumbled on, it's not as simple as you build the product and I just saw Oppenheimer recently, so you build the product and drop the bomb, it can all be in military operation.

(01:28:13):

This requires, especially for chronic diseases, really getting out through trusted mechanisms to reach people and for chronic diseases, track them over time. We had trouble with that even with the Covid vaccines. But I think overall the arc seems to me to be going in the right direction. We're paying attention to the right issues clearly here. Hopefully the findings from this discussion can make it out more widely and there are growing examples of building real world evidence development systems and the UK and other countries building payment methods for healthcare that sustain and support these earlier intervention models. So while I don't think there are any examples of really fixing these chronic disease problems, people have mentioned statins and early stage non-drug diabetic treatments. David, if he was here, would remind about being able to get to pre-diabetes and obesity perhaps through medications. But the track record of those is mixed. Most people who have diabetes or pre-diabetes or hypertension in the US either don't know it or aren't on regular treatment even though the treatments are close to free at this point. At least the first line treatments are close to free. So we still got some more work to do, but maybe I can temper that with some optimism that we're headed in the right direction.

George Vradenburg (01:29:44):

Great. So we have about five minutes left and I want to be respectful of all of you extraordinary panelists. So I'm going to hand it back to Laura Darzi. I sense hear a lot of lean forward from everyone that you have raised an important issue and it is an issue worth continuing focus and figuring out how to construct the process by which that focus might take place. But I would love to hear your reactions to the discussion and how if at all, you would like this discussion to continue.

Lord Darzi (01:30:22):

Thank you, George. Thank you everyone for a great, great debate. And I have no doubt we have something that we should try at least to get it to a place with policymakers, with funders, with commissioners of services, with insurers. I don't think there's any losers in here. I think the biggest challenge I see is how do you transition a healthcare system from where it is today to a system that you can design for the future. That actual fact is intervening at a pre-disease, very early stage and also intervening with the sets of therapeutics, whatever it happens to be in preventing that progression of disease. So this is not just a scientific challenge. This is not just about a new discovery of a new therapeutics or a biomarker. This is about a whole transformation of health system. And historically that is the most challenging thing when it comes to healthcare reform.

(01:31:29):

It is virtually impossible. I mean, I remember from the days in which I was asked to produce a report in London to look at the capital city of London, which had the best financials capital center in the world. It had the best entertainment and tourism. It has some of the best universities there. When you come to the healthcare system, you see this huge inequalities that existed in a very rich capital city. And then when you come up and say, okay, we have 32 stroke centers here, out of which there's only three actual meeting the baseline criteria of becoming a stroke center.

(01:32:14):

That is the fact that was all in front of us. And the conclusion was we need to have six comprehensive stroke centers. Now, you would not believe the people who had the plot cars out in the streets weren't the public. They weren't the doctors who will hate the idea of losing stroke services from their own institutions. And anyhow, to cut the story short from the 32, we moved to six and that was we saved 200

lives a year. We saved huge amount of disability adjusted life years from stroke victims, and we reduced the cost by about 35 to 40%. That could only be done. All of these major changes could only be done by true engagement with the public. It's a big debate. This needs a big debate. Empowering the public working through the policy changes the regulatory framework that is needed. It can be run by one. It can't be run by wonderful organizations like Flagship or by big pharma. It needs to come, the demand needs to come and the change has to happen at a local level. So it's a huge steep mountain to climb, but it's feasible. It's possible. And I think history will suggest if you go back to the more than a century ago, some of these transformational changes happened and they did happen. And that is why life expectancy has doubled. The question we have now is how do we improve the quality of that extended life expectancy.

George Vradenburg (01:33:47):

Thank you for that. Really excellent and quick summation. I'm going to turn it back now to our host, Alexander Fleming or Thomas show you wrap us up and give us any homework assignments. And we're obviously putty in your hands or puppets at the end of your string. You just tell us what you'd

Alexander Fleming (01:34:09):

Like to do. Well, George, we cannot thank you and our panelists enough. This has just been an amazing discussion and it's so frustrating as has been expressed by many of our listeners that we just have so little time for the abundance of expertise and insights that you brought to us in this short time. We will follow up in different ways, but I'm going to ask Thomas to give some practical ways we're going to make available the fruits of this particular session to the audience and those beyond. Thank you again panelists.

Thomas Seoh (01:34:49):

So first of all, a recording of this session. The link will be sent to all registrants within a day or two. We hope we're working hard on that right now. And we will prepare a transcript and the chat log will be posted@alis.org. In addition, I believe the panel is discussion or George's discussion about producing a white paper or some follow-up or publication of the event as well as a continuing conversation or convocation on this very important topic. This is not a one and done topic because we have today's discussion. The problem is solved. It's something that's going to be going on for a number of years, and so hopefully people will tune in for developments on that. I also want to, if you don't mind, make a quick commercial for the remainder of the targeting healthy longevity season. We are planning additional sessions if you like this one.

(01:35:48):

If you are a registrant, you'll receive information about this. We have a session upcoming, actually a two-parter on loneliness, shockingly as big a risk factor apparently as smoking or obesity. That'll be co-chaired by a cod by Lucy Rose of the Cost of Loneliness Project. And Jeremy Abba, publisher of the Scientific American Magazine. And later in the fall we will have a two-parter on the Cosmos trial. Probably the largest randomized controlled trial. You've never heard of that in 21,000 plus people that suggested cardiovascular and brain health benefits from a flavonol supplement and a multivitamin. So I think Sam, with that, I want to thank the panelists and you, the audience, and we are delighted to be able to bring this to you. We wish you a great day wherever you are in the globe or on the globe. And with the closing of this session speakers, the virtual hall will be left open for a few minutes for those of you who are able to Terry, but the formal proceedings are closed. Thank you so much.