Summit 2023

Dementia in a new era:
prevent, diagnose, treat

World Dementia Council
Leading the Global Action Against Dementia

The case for prevention interventions?

Transcript of a session from the
World Dementia Council summit
20 March 2023

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The Council also has multiple associate members consisting of international organizations as well as national governments. They help to ensure that the council's agenda aligns with other global dementia initiatives, providing the council with important strategic advice, guidance and intelligence. As they do not have full membership status, associate members don't vote on issues such as the election of a new chair or new members, or on matters of governance.

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Chair

Philip Scheltens

Professor of Cognitive Neurology and Director Alzheimer Center, University of Amsterdam Medical Centers

Prof. dr. Philip Scheltens studied at the VU University Amsterdam, Netherlands, gaining his MD in 1984, and PhD in 1993. He became Professor of Cognitive Neurology and founder of the Alzheimer Center at Amsterdam University Medical Centers in 2000, which he directed until 2022. Currently he devotes most of time heading the Dementia Fund at EQT Life Sciences, that he started in 2020. He has been the (inter)national PI for over 35 studies, including phase 1-3 multicenter clinical trials. He supervised >75 PhD theses since 2000. He founded the Dutch national plan against dementia and served as chair of the board. He is co-editor-in-chief of Alzheimer's Research & Therapy and co-leads various EU projects. He authored over 1100 peer reviewed papers and > 75 book chapters and co-edited several major textbooks. He is member of the Royal Dutch Academy of Arts and Sciences (KNAW) since 2011. In 2016 he was awarded the European Grand Prix for Alzheimer's Research. In 2020 he was Knighted in the Order of the Netherlands Lion by the King of the Netherlands. In 2021 he was elected honorary member of the European Academy of Neurology and was appointed chair of the World Dementia Council.

Speakers

Matthew Baumgart

Vice President of Health Policy Alzheimer's Association

Matthew Baumgart is Vice President of Health Policy for the U.S. Alzheimer's Association, leading a range of projects at the intersection of policy and programs to achieve an aggressive agenda that serves all those affected by the disease. In this role, he heads the Public Health Center of Excellence on Dementia Risk Reduction, funded by the Centers for Disease Control and Prevention. In addition, Baumgart directs the Association's global public policy efforts, working in collaboration with Alzheimer's Disease International, the World Dementia Council, and the World Health Organization. Baumgart joined the Alzheimer's Association in 2009 and has served in roles overseeing policy development, public health policy initiatives, federal affairs, and state governmental affairs. Prior to joining the Association, Baumgart spent nearly 20 years working in the United States Senate, including as legislative director for Senator Barbara Boxer of California and legislative assistant for over a decade to Senator Joe Biden. Baumgart has a degree in communications with a second major in political science from Washington State University.

Professor Miia Kivipelto

Professor in Clinical Geriatrics, Karolinska Institutet

Miia Kivipelto, MD, PhD, is Professor of Clinical Geriatrics at Karolinska Institutet (KI), Center for Alzheimer Research, and senior geriatrician and Director for Research & Development of Theme Aging at Karolinska University Hospital, Stockholm, Sweden. Her frontline research findings have been published in leading journals (400+ publications, H-index 83) and she has received numerous prestigious national and international awards. Dr. Kivipelto's translational research focuses on the prevention, early diagnosis and treatment of cognitive impairment, dementia and Alzheimer's disease (AD). Through epidemiological studies, Prof. Kivipelto has identified various lifestyle and vascular risk factors for dementia and interactions with genetic factors and clarified underlying mechanisms. Professor Kivipelto is the PI of the landmark FINGER Randomized Controlled Trial (RCT) (Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability), which is the first large-scale trial showing that a multi-domain lifestyle based intervention can reduce the risk of cognitive and functional impairment among at risk persons from general population. This pragmatic model is now tested and adapted worldwide and Professor Kivipelto has launched the World Wide FINGERS network, a unique interdisciplinary network to share experiences, harmonise data, and plan joint international initiatives for the prevention of cognitive impairment/dementia (45 countries currently involved).

Professor Johannes Streffer

CMO, AC Immune

Johannes Streffer is CMO of AC Immune and has previously led the development of a translational space in neuroscience at UCB. He was a member of the Alzheimer Disease Area Leadership Team at Janssen, Pharmaceuticals Inc. He has experience in early experimental trials and biomolecular modalities in Alzheimer's disease (AD) and has initiated a number of methodological and biomarker studies focusing on early diagnosis and translation. He was also the industrial lead for the European Medical Information Framework (EMIF)-AD, which in the Innovative Medicines Initiative (IMI)-EMIF program, fostered understanding of early biomarkers and change in the predementia AD spectrum. He is a member of the Scientific Advisory Board of the Alzforum. Johannes is a graduate of the University of Tübingen, Germany, where he received his medical degree. He also completed graduate studies on neuro-oncology and is Board certified in psychiatry and neurology. He has published more than 100 manuscripts and is a visiting Professor in the Department of Biomedical Sciences at the University of Antwerp.

George Vradenburg

Co-Chair, Davos Alzheimer's Collaborative

George is the Chairman and Co-Founder of UsAgainstAlzheimer's (UsA2), a disruptive and catalytic force committed to stopping Alzheimer's by 2020. He serves as Co-Chair of the Davos Alzheimer's Collaborative, a coalition focused on driving global scientific, business, policy and financial coordination in Alzheimer's preparedness, co-convened in January 2020 by the Global CEO Initiative on Alzheimer's Disease (CEOi) and the World Economic Forum. In this role, George provides general oversight and advocacy and works to ensure the Collaborative remains sustainable and action-oriented. In 2011, the United States Secretary of the Department of Health and Human Services named George to serve on the National Alzheimer's Advisory Council on Research, Care and Services for the first-of-its-kind National Alzheimer's Strategic Plan. George received his B.A. from Oberlin College, magna cum laude, where he was elected to Phi Beta Kappa, and his J.D. from Harvard Law School, cum laude.

Discussion transcript

Professor Philip Scheltens, chair of World Dementia Council, Professor Emeritus at Amsterdam University Medical Centers and head of the EQT Life Sciences Dementia Fund

We're going to end today with two very exciting sessions. Not that the other ones were not exciting! But these are even more exciting, I would say! We have very excellent panellists and we are talking about prevention and new treatments. So, we'll first start with the prevention, the case for prevention interventions. I will invite to the podium:

- **Matthew Baumgart**, Vice President of Health Policy for the Alzheimer's Association. Welcome.
- **Professor Miia Kivipelto** or Professor Prevention herself in Clinical Geriatrics, Karolinska Institutet.
- **Professor Johannes Streffer**, he is the CMO of AC Immune. Welcome, welcome.
- And **George Vradenburg**, he's the founding chairman of Davos Alzheimer Collaborative and many, many other things George, welcome.

So you know what is expected from you? Short statements on your view on the topic and then we'll put it out to the audience. Matthew, can I invite you to go first?

Matthew Baumgart, Vice President of Health Policy, Alzheimer's Association

A lot of what's been said in earlier panels today has been clinical-based or research-based and that's not me. I am neither a clinician nor a researcher. I'm a policy guy who does a lot of public health work.

And so, the first point I want to make is that I really think when it comes to prevention or risk reduction, whichever term you feel most comfortable using, we need to separate the clinical and the population-level evidence because I think there are two levels of evidence here. I think the population-level evidence is much stronger currently than the clinical-level evidence. But the lack of – or the less than ideal level of – clinical evidence should not prevent us from moving forward on a population level or a public health basis because I think the evidence is strong enough on a public health basis. And the flip side is, there isn't really any harm. What's the harm if we have fewer cases of hypertension, if we have more physical activity, if we have people who have better sleep, if there's less diabetes, if there's less obesity? I don't think we should let the clinical dictate us not acting from a public health perspective.

My second point is I think we need to shift our mindset. Most of us in this room have worked on dementia for a long time. What that means is, we work with older people or with their family members. And when it comes to prevention, while the saying is, "It's never too late," it's also never too early. We are going to have to think about risk reduction at an earlier point in the lifespan, otherwise we're not going to be as successful. This is something we're struggling with at the Alzheimer's Association. I've had staff say, "Oh, we should go in and talk about risk reduction in senior centers." I said, "Well, why aren't we going in and doing lunch-and-learns in workplaces?" We need to shift our mindset about who our audience is and who we work with when it comes to prevention.

And then the third and last point is that there's a lot of talk about people taking responsibility, and I am all in favour of that. But someone asked the question earlier today about integrating equity into other panels, and here's my attempt to integrate equity into this panel. Individual responsibility can only go so far. There is a big public policy component here. You can't address diet among people who live in food deserts. You can tell them to eat broccoli all you want. If they don't have a store where they can buy broccoli, it's not going to do any good. You can talk about physical activity and exercise, but if people live in unsafe communities – if they don't have access to parks – the chances of their ability to engage in physical activity go down. Similarly, none of us are able to go into our

backyard with a machine that pushes the air pollution out of our yard. There are a lot of public policy components here. So while we often think of the individual when we talk about individual risk reduction, we need to think of the public policy implications and the public policy actions that also need to be taken.

Miia Kivipelto, Professor in Clinical Geriatrics, Karolinska Institutet

Thank you, Philip, and thank you for the invitation. It's my great pleasure to be here today. And it has been such good discussions. I'm very happy that the prevention part has been mentioned already several times by the previous speakers as well. Philip, I also liked your idea, not just talking what we have been doing, but what is the next decade? What is needed to give a maximum benefit for most of the persons and the societies?

And clearly, I hope many of you agree, prevention is an important part of the story. I think it's really the key to manage the dementia epidemic globally. In the same way, it's the key for many other chronic diseases, think about diabetes or stroke. And that's my first point. I think we should learn from the other chronic diseases. We should not work in isolation. There is this wonderful 40% dementia prevention potential. And if we are thinking low middle-income countries, I think this number is even higher. So, there is so much we can do globally and importantly we can do it already now. There is something we can offer for all persons. We have this potential, and we have the WHO risk reduction guidelines, my priority would be going to implementation. We have enough evidence to implement, we need to be ambitious, and we need to act now.

How to do that? That's maybe more difficult. We have of course the multi-domain FINGER interventions which can give benefits on many levels. I liked a lot the discussion what is clinically meaningful? And if I'm thinking the multi-domain interventions, we have efficacy on cognition but also on the functional level, quality of life, and even clear health economic benefits. So, we have a model that benefits the individual and sociery and can be adapted for different settings.

What I think is very important now is trying to tailor the interventions on two different levels. On individual level, because we all have different risk profiles, if we are thinking younger persons, at midlife or older persons, I fully agree it's never too late, we can always do something with these interventions. But also, on population levels, different settings, like I said, the population level interventions. And I would say that these both are not enough in isolation, we need to do both individual and population-based interventions, making the healthy choices the easy ones.

And finally for the future I would say my dream would be a precision prevention for dementia. Not only lifestyle or the drugs but combining them to having even more efficacy. I'm very happy that we are now conducting the first combination therapy trials and here the precision medicine approach giving the right treatments for the right persons at the right time.

And finally joint collaborations and data sharing. If I'm thinking how the randomised control trials have been planned and conducted in isolation, I think that time is over. We need to work together. We need to join and share the data. I'm very happy for the support we are now having for the World-Wide FINGERS to make that happen. We are now having around 45 countries in the network and many of those are from low-and-middle income countries. Thank you.

Professor Philip Scheltens, chair of World Dementia Council, Professor Emeritus at Amsterdam University Medical Centers and head of the EQT Life Sciences Dementia Fund

Thank you very much Johannes.

Johannes Streffer, CMO, AC Immune

Philip, thank you very much for inviting me. Great pleasure and honour to be in this elusive room. I do not really understand why I deserve the honour but thank you.

Professor Philip Scheltens, chair of World Dementia Council, Professor Emeritus at Amsterdam University Medical Centers and head of the EQT Life Sciences Dementia Fund

Me neither!

Johannes Streffer, CMO, AC Immune

I thought so! I guess for this audience I do not have to talk about the why, the what and the how may be more important? But it is worth thinking about the why briefly. Steve Salloway I think said once there is nothing mild about mild cognitive impairment. Nobody wants to have that. If we want to start early, then prevention is really what we have to do. Miia and Matthew both talked about the what. And I am fully agree with Miia that it should be lifestyle and pharma prevention if we target it right. It really should come down to the how and I think the how is a critical problem where we all have to work together.

We will have to identify the right people, for instance for interventions. Now, this means having the right biomarkers for that we have confidence in. We have to work on the clinical trial methodology. These trials will not be possible if we do not get a general understanding for instance of surrogate biomarkers that we trust. So first of all, as a community we have to trust these biomarkers and then we have to educate everyone from physicians, to the general public through to politicians, that these are the right things to measure and that we can trust that they will help us to understand these therapies.

And then the question is, how do we develop an intervention that really can get to everybody. So, how do, how can we treat a pandemic. And how can we get the same traction that for instance you had during the COVID pandemic for Alzheimer's. Because this is what we really need. We need traction across the overall world that this is possible. So, I think that how we are going to do that is for me the most critical point today.

Professor Philip Scheltens, chair of World Dementia Council, Professor Emeritus at Amsterdam University Medical Centers and head of the EQT Life Sciences Dementia Fund

Thank you very much. George.

George Vradenburg, Founding Chair, Davos Alzheimer's Collaborative

George Vradenburg. I'm chairman of the Davos Alzheimer's Collaborative, which many of you don't know. So, a word of introduction here. This is a partnership between the biopharmaceutical industry on Alzheimer's, through a global CEO initiative, with the World Economic Forum. It is creating a global mechanism through the establishment of a Swiss-based foundation, that basically is along the line of GAVI and CEPI. Now, why a global effort? Because all the efforts that we're making in

individual countries, individual labs, and individual efforts are not linked or scaled in a way that solves the problem. As Elias Zerhouni who is on our board, said we are trying to solve a 100-foot problem with 10-foot ladders. And so, unless we link and scale what is going on around the world, particularly in low-and-middle-income countries, we are not going to solve this problem for the people of the world.

So, that is what we do. Our programme is threefold. One is on global clinical cohorts. I will come back to that in a second because it's relevant to this. Second is on trials where we do combination trials and we're partnered with Miia to try and figure out that problem around the world and with health system readiness. And you've heard from Phyllis Ferrell earlier about some of the work that we're doing and trying to drive new technologies into health systems around the world. But all of it is built on the notion that no one researcher is going to solve this problem. No one government is going to solve this problem. No one advocacy organisation or company is going to solve this problem. We want every company to make money by curing this disease. We want every researcher in this room to get a Nobel Prize for curing this disease. But we need to work together. It's a whole of society approach.

When it comes to prevention and the sense of risk reduction, much of the work that my organisations are doing is doing out of our U.S.-based advocacy organisation called Us Against Alzheimer's, where basically we're working there to bring both advocacy in getting the United States government committed to a healthy aging and reduction of risk of dementia goal. It's now a goal of our national government to link this notion of healthy aging and reduction in the risk of dementia. And so, the public sector through HHS, working with Matthew, is very much looking at what the federal agencies can do on that regard.

I want to bring business into this because I think business has a much more likely possibility of changing our behaviours than the United States government. So, we have efforts as business, as employers. They care about the workforce, they care about the health of their workforce, so how do we encourage them with data and with practice to determine how better to improve the quality of care, quality of health for the brain in their workforce? Business also an is innovator of products and services. If you want to eliminate food deserts, you don't go to the United States government, you go to the food industry and say, what incentives do we need to put in place to eliminate food deserts, to reduce the amount of processed food, and to increase the amount of fresh food? So that means working with industry, potentially with the Food Drug Administration, the food part of the FDA.

Let me give you an example of why I think business has an important role. We just recently deregulated the ability to get hearing aids through normal pharmacies and over the counter as opposed to having to go through experts. That's going to increase hearing aid use. That's going to reduce loneliness because we know that hearing, loss of hearing is one of the factors that leads to social isolation. So, business should be part of this. The challenge is to do it. The UK has been ahead of us on the Business for Leadership effort of Tina Woods, and so we're partnering now with them.

On the cohort front, we're adding Alzheimer's measures to existing cohorts around the world. These are very large cohorts on infectious disease, cardiovascular, metabolic disease and so on. If you begin to add cognitive measures, digital cognitive measures, blood for both genetics and biomarkers you can make progress. We now have the suite of things that can link all of these chronic diseases of aging that are linked together and so create a global platform, a global architecture for how it is that we can get to healthy aging around the world.

Professor Philip Scheltens, chair of World Dementia Council, Professor Emeritus at Amsterdam University Medical Centers and head of the EQT Life Sciences Dementia Fund

Thank you very much all for these very brief comments, although the word brief has a different meaning.

George Vradenburg, Founding Chair, Davos Alzheimer's Collaborative

We're now in the stage of the day. Everything has been said, but not everyone has said it.

Professor Philip Scheltens, chair of World Dementia Council, Professor Emeritus at Amsterdam University Medical Centers and head of the EQT Life Sciences Dementia Fund

He announced already that he would say this, so I got you this. So, audience, come on, challenge them. I mean, this is all true but what! Oh, Brian, you haven't said anything this afternoon yet, so I'll give you the floor immediately. Brian Lawlor, over there. Does he have a microphone yet? Oh, okay. Sorry. Myrra took the microphone, so you can, Myrra, really, really briefly, briefly, because there are many people who want to comment.

Participant | **Myrra Vernooij-Dassen**, Professor emeritus Radboud University Medical Centre

Briefly. Okay. Well, one of the important elements of Miia's comment is the importance of treating dementia as a multifactorial syndrome, and this is something which has not been said too much today. We can deliver improved interventions in the future if we have a better understanding of mechanisms and we better use the evidence there is, because there is evidence on the level of association, of epidemiological association and so on. We have to know more about the mechanism in order to improve our interventions and to know what we are really doing and what is important in these multifactorial interventions.

Miia Kivipelto, Professor in Clinical Geriatrics, Karolinska Institutet

Thank you. Fully agree. I see late-onset Alzheimer's and dementia as a multifactorial, quite complex disorder, and probably we need to target several mechanisms and risk factor targets at the same time. But really to move to the personalized or precision medicine approach. I agree, we need to study more and understand more about the mechanisms. What we are doing now in the World-Wide FINGERS trials, and this comes back to the blood-based biomarkers, is we can analyse the blood samples to try and understand what the exact mechanisms are. So, this kind of network gives us opportunities for a new kind of, I would say, findings when it comes to these underlying mechanisms.

Participant | **Brian Lawlor**, professor of old age psychiatry at Trinity College Dublin, and deputy executive director of the Global Brain Health Institute

They say that brain health is the new heart health. And I'm just wondering about the panel's views on a societal-wide approach to prevention. The concept around brain healthy communities and brain health across the life course. What are the panel's views on that?

Professor Philip Scheltens, chair of World Dementia Council, Professor Emeritus at Amsterdam University Medical Centers and head of the EQT Life Sciences Dementia Fund

Yeah. Can we go for the panel? Matthew, you first.

Matthew Baumgart, Vice President of Health Policy, Alzheimer's Association

Sure, I'll answer that. I am completely in favour of it. When you look at a lot of the risk factors, you're right. A lot of them are heart-related, whether that is an actual heart-related condition – hypertension, diabetes, obesity – or whether it is a lifestyle factor that affects the heart – diet, exercise, smoking and so on. I think given the resources of public health, the better way to go is to try to integrate dementia messaging and a dementia focus into a broader health effort. Kill two birds with one stone. That also helps on the resource side, at least when you're talking about the public health world.

Miia Kivipelto, Professor in Clinical Geriatrics, Karolinska Institutet

Yes, I fully agree. And what we have been saying for years, what is good for the heart is good for the brain, is still true, and this vascular part is probably the one where we have already so many treatments, both non-pharmacological and pharmacological. There are still questions. For example, what type of blood pressure medication or diabetes medications are the best for the brain? So more research is needed, but absolutely we can give these recommendations. And I think, brain health, it motivates people to maybe take better care of these risk factors.

Matthew Baumgart, Vice President of Health Policy, Alzheimer's Association

Can I make one other comment on the previous point about multifactorial? Most of the multifactorial components is also heart-related. You rarely find people with only one of these health problems. You have people with hypertension who are also obese or who also don't exercise or who have a bad diet. So that multifactor approach, doing it across the board on health, I think is our best public health approach.

Johannes Streffer, CMO, AC Immune

Yes, obviously, fully agree. And I think brain health is critically important. Everything we can do to keep the brain healthy has to be done. And this is the way to go. It's certainly true on a population level where we have a lot of easy wins in a way, because a lot of things are just not done.

What I would like to mention as well is that if you are not a healthy brain, and an unfortunate model is for instance brain trauma, then you're at much higher risk for aggregating proteins in the brain. So, the diseases we are talking about, are as well associated with less good brain health not necessarily caused by lifestyle. So, these things go together. And I think we talked about multifactorial interventions.

Where we need to end up is having multifactorial lifestyle interventions for brain health and multifactorial pharmacological interventions. Very similar to the heart, right, there is no way of solving this by starting late or starting one dimensional. And then the question for me is, how are

we ever going to prove anything like that? So how are we going to prove? And then I would like to come back to that point. And that is the education, for instance, on biomarkers. Can we find markers that, and take it very broad, we believe are predictive of the treatment effect. And we do not need a thousand patients for five years for everything, but we have something we can track. So, if we say multifactorial, then biomarkers, again, the only way to prove it.

George Vradenburg, Founding Chair, Davos Alzheimer's Collaborative

I would say the only intervention or comorbidity that at least the NIH thinks is significant is diet and hypertension. They don't believe that a lot of these other stuff in Lancet, all these other 13 factors, have been shown to have much of an impact on disease risk or progression. They have over 100 lifestyle clinical trials and are trying to understand the biological change associated with a wide variety of other different lifestyle interventions.

But in a sense, we know that in fact, a healthy lifestyle is probably good for a lot of reasons, so why not go after healthy aging in addition to talking about therapeutic approaches to dementia? Or talk about brain health. When you go to the doctor, you typically get a checkup from the neck down, you rarely get a checkup from the neck up. So again, it comes back to the health system that a number of us have been railing about, and I will reiterate that the health system is just not yet prepared to think about the brain yet.

Professor Philip Scheltens, chair of World Dementia Council, Professor Emeritus at Amsterdam University Medical Centers and head of the EQT Life Sciences Dementia Fund

I'm gonna come back to you. Mark, you are first.

Participant | **Mark Roithmayr**, Chief Executive Officer, Alzheimer's Drug Discovery Foundation (ADDF)

This question is a question for Miia and it's about the future of precision prevention. And Miia you are doing a combined trial now, right? Prevention with a repurposed drug metformin. Can you tell us a little bit about that? But even more importantly, take us out three, five years, and do you see other repurposed drugs or other single molecule drugs that you could work with in FINGER trials?

Miia Kivipelto, Professor in Clinical Geriatrics, Karolinska Institutet

Yes, it's a great question. So, the MET-FINGER trial is the first trial where we combine the FINGER model with the repurposed drug, metformin, a diabetes medication. And the idea is simple. We thought that if you combine, you could get the better efficacy. Not for all, but for those who have the risk profile. So, all are getting the FINGER intervention or are included in the control arm which is regular health advice. In the multi-domain intervention group, those who have a pre-diabetes or a certain risk profile, then they get metformin in different doses. I think this is a model for the next generation of clinical trials where you could test, for example, the new diabetes medication, for example, GLP-1 agonist, or maybe some other repurposed drugs.

This is a pragmatic trial, and at the same time, using the precision preventive approach. We also use ApoE4 enrichment. So, we try to really get people before they have symptoms, but who have a clear risk profile. It will be exciting to see how the model works and to use the platform design to other clinical trials.

Professor Philip Scheltens, chair of World Dementia Council, Professor Emeritus at Amsterdam University Medical Centers and head of the EQT Life Sciences Dementia Fund

Thank you. Rhoda, I think you have the microphone. Any question?

Participant | **Rhoda Au**, Professor Anatomy and Neurobiology, Boston University

Yeah, well, you cut me off in the last one! So I'm gonna use this opportunity now, right? And it turns out it might work better!

We talk a lot about dementia as a life course disease, but we actually don't study it that way. Because if you look at the data, we tend to look at people 50 years and up, and we don't look at 50 years and down. If we're trying to think about how we make this relevant to all governments, to all public policy makers, it turns out that everything that's bad for the body is bad for the brain, right? The only reason we think about heart-brain is because of things like Framingham. We started with the study of heart disease and stroke. And look, we collected lots of data for a really long time, and then we realised, oh, it's related to the brain. Well, it turns out, so is probably almost everything that we study.

We need to figure out how to bring true life course data into this and bring in, again, public health, which is our government leaders, right? And really take sort of the whatever disease, I don't really care what you're interested in, I already know it's relevant to the brain. So why don't I make that connect? Why don't we just start with wherever your interests are and connect that to the brain, right? I think that gets us to the much bigger public health agenda.

And to that, because I wanted to address this to Andrew last time, I want to point out, we are all working with really biased data, all of us. Everything we know today is on biased samples. We don't actually even know something as basic as blood pressure and its real relationship to the brain because we don't study blood pressure in the right way. That's where technology comes in. Technology is not supposed to be doing a better version of what we are doing. It's supposed to be doing what we're not doing. And if we get the data that we really need, then people like Andrew can move forward with the AI, that's going to get us to the solutions that we're talking about.

Professor Philip Scheltens, chair of World Dementia Council, Professor Emeritus at Amsterdam University Medical Centers and head of the EQT Life Sciences Dementia Fund

Thank you. If you just pass the microphone to Tetsu, so, but wait a while, so, so, I first have the panel respond quickly to, so George.

George Vradenburg, Founding Chair, Davos Alzheimer's Collaborative

Yeah, you've just heard from the manager of the DAC global cohorts work. One of the things Rhoda is doing, based upon the responses DAC has had in Africa, raises an intriguing challenge. African researchers are working with a demographic profile that's quite different from Japan and Europe. And so, they're saying, we're working in maternal health, working with young people. And so, as a consequence, they're saying, let's think about starting now what will be the ADNI of the future in which we look at all of these factors as they relate to brain health across the life span. Early childhood problems, education levels, sex violence in the home, all of these factors which over a period of one's lifetime you could begin to accumulate and marshal the data which in fact will demonstrate the basis for potential precision interventions and on brain health more generally. The challenge for us in the field is we don't have methodological research on how to do this yet, but we have an appetite to explore this perspective in those countries of the world who have a demographic profile quite different from Europeans, Americans, and Japanese.

Miia Kivipelto, Professor in Clinical Geriatrics, Karolinska Institutet

Just a short note, I like a lot the concept life course perspective and it's never too early to start to prevent. We are now working with the concept Family-FINGERS, trying to take FINGER to the schools where you shape your lifestyle, and also multi-generation FINGERS so that the caregivers, who is also a risk group, could take part of that. So, these are some new concepts we are working with.

Participant | **John Gallacher**, Professor of Cognitive Health, Oxford University and Director of Dementias Platform UK

I'd like to congratulate George on focusing on cohorts and the theme of life course, which is currently coming up. The problem with the population cohort is it's optimised to detect the causes of diagnosis. The problem with the clinical cohort that it's optimized to detect the effect of a treatment. Bringing these two together is extremely difficult. And using just legacy data, I really don't think it's going to work. So how about a dedicated disease progression cohort going from, designed to go from earliest detection through to diagnosis, through to trajectory, and then through to death?

George Vradenburg, Founding Chair, Davos Alzheimer's Collaborative

I think that's great. One thought: perhaps we should start now with what you got. We indeed have cohorts around the world, remarkably, that have been collecting data on their populations for a wide variety of reasons. And, in many cases, that data goes back 20 and 30 years, in some cases with cohorts with 100,000 persons. So, in fact, if you work with it and then try and patch it, fill it in, and begin to try

and think of the research methodology of what it is that you want systematically to collect through time, you at least start somewhere. Because one of the problems that all of these meetings tend to have, at least in my opinion, is that we tend to have a vision but we don't have action. Was it Emerson who said, that 'vision without action is hallucination'?

Professor Philip Scheltens, chair of World Dementia Council, Professor Emeritus at Amsterdam University Medical Centers and head of the EQT Life Sciences Dementia Fund

Trust George to have a quote.

George Vradenburg, Founding Chair, Davos Alzheimer's Collaborative

Someone here said it's the people in this room who will make change. If you look at people in this room, however, this is not the people that we ought to be working with. The people in this room do not reflect the 75% of the people of the world with dementia who are in low-and-middle income countries. That population is not significantly represented here. So, we all can act very effectively in Europe and the United States and Japan, but the people outside of this room are the people we should be working with much more effectively. That means Africa, the most diverse legacy populations in the world. It means Asia, much more diverse than the United States or Europe. So, I would suggest that we have got to act, not just think about what we want to do, not making the perfect the enemy of the good, but to act with what we have now and build upon it.

Professor Philip Scheltens, chair of World Dementia Council, Professor Emeritus at Amsterdam University Medical Centers and head of the EQT Life Sciences Dementia Fund

You haven't even mentioned China actually for that matter also. Tetsu.

Participant | **Tetsu Maruyama**, Chief Scientific Officer, Alzheimer's Disease Data Initiative (ADDI)

So, I'd like to ask about the elephant in the room. It's great to have identified the risk and even for individuals the things that you can do. But, we know that almost everybody in the developed world who smokes knows that it's bad for them. And people at least know that they ought to lose weight. But some of the interventions that have mattered have been policy ones. Banning smoking indoors has had a huge effect on heart health. So the question is, should we be emphasising policy that's going to have people follow the recommendations that research is producing right now? Or is education really the answer here? Or how else are we going to get people to take up these recommendations and use them to prevent dementia?

Professor Philip Scheltens, chair of World Dementia Council, Professor Emeritus at Amsterdam University Medical Centers and head of the EQT Life Sciences Dementia Fund

Quick comments. Yeah, so quick.

Matthew Baumgart, Vice President of Health Policy, Alzheimer's Association

That was one of the points I made in my opening statement. We cannot forget public policy here and the significant role it has. I was talking about it more in the context of social determinants of health and health equity, but the example that you gave is perfect in terms of smoking. In terms of access, George mentioned another example: the hearing aid policy in the United States having changed. So, Tetsu, I one hundred percent agree with you.

Miia Kivipelto, Professor in Clinical Geriatrics, Karolinska Institutet

Yes, fully agree. Both individual level and population level approaches are needed, but either is insufficient alone. You need to have them both. And I think, again, the nice thing with the multi-domain interventions is you don't need to do a huge amount of everything. It can increase the layer of protection if you do several of those interventions. So in that way, I think we need both.

Johannes Streffer, CMO, AC Immune

I mean, this is a great point, and we were discussing that earlier in the coffee break with John. It is about motivation right. So policy can do a lot. You can say we stop this we forbid it! But that is very difficult on lifestyle in a free world, we do not want people to tell us how we live. We have to motivate people instead. So, it's about motivation and finding the right motivators. And this is something to motivate all of us family and friends. It is about education and awareness. So, do people know that these risk factors are really important for dementia? And I think most people don't know.

Professor Philip Scheltens, chair of World Dementia Council, Professor Emeritus at Amsterdam University Medical Centers and head of the EQT Life Sciences Dementia Fund

Good point.

George Vradenburg, Founding Chair, Davos Alzheimer's Collaborative

I would also say that, in fact, you can make a lot of money with safe cigarettes, right? We're moving that direction with vaping. And, in fact, you can continue to go down that path. And I'm suggesting business innovation can solve this a lot faster than public policy.

Professor Philip Scheltens, chair of World Dementia Council, Professor Emeritus at Amsterdam University Medical Centers and head of the EQT Life Sciences Dementia Fund

Question from you.

Participant | **Lucia Crivelli**, Neuropsychology Coordinator, FLENI

I'm part of the World-Wide FINGERS Network. We are working in the LATAM-FINGER Network, which gathers 12 countries across Latin America in an effort to follow multi-domain intervention. We have been funded and supported by the Alzheimer's Association. One of the things that was more difficult for our initiative was to recruit participants. We got there! We have now over 1,000 participants already being recruited. This is a very diverse population. We have more than 50% of our sample is mestizo. So, it's ethnically diverse, but it's also culturally diverse. When we wanted to apply the multi-domain model to our population what we found is that it was impossible, very difficult to import the knowledge gained in Finland to Latin America. So, we had to do modifications, but these modifications had also to be done within Latin America because of the heterogeneity of our own population. There was no single modification that worked for such a diverse population. So, when I think about bringing this in public health policy on a much bigger population group than a trial population, I cannot imagine how can we implement, how can we bring to earth all of these differences, all of these things that are part of our richness but are also big challenges. So, I wanted your comment on that.

Professor Philip Scheltens, chair of World Dementia Council, Professor Emeritus at Amsterdam University Medical Centers and head of the EQT Life Sciences Dementia Fund

Question on implementation Miia.

Miia Kivipelto, Professor in Clinical Geriatrics, Karolinska Institutet

Yes, it's a great example about diversity. While we use the same model, it should be adapted to the local circumstances and to that population. One size does not fit all. So, I think this practical experience is very, very important. And I really think implementation research is so important. And it is true for the behavioural changes, what is needed for that person, what is needed from that society. It is not the same everywhere. So, I really would like to highlight that we need to work much more with these questions, both research, implementation and policy.

Johannes Streffer, CMO, AC Immune

Very short, that is the same for every pharmacological intervention. They as well have to be tailored to be available everywhere. So it cannot be a treatment that is not affordable for the world. It has to be a treatment that is affordable for the world.

Professor Philip Scheltens, chair of World Dementia Council, Professor Emeritus at Amsterdam University Medical Centers and head of the EQT Life Sciences Dementia Fund

Last question from the audience.

Participant | **Dominic Trepel**, Assistant Professor (Health Economics), Trinity College Dublin

I think that there's a lot of potential benefit in prevention that we haven't realised. I've been working as an economist in dementia for 15 years. I just wanted to hear from the panel if there is a case to divest what's currently being invested in post diagnostic dementia across all of the things that we've heard about today and to start putting into prevention, how will that happen?

Professor Philip Scheltens, chair of World Dementia Council, Professor Emeritus at Amsterdam University Medical Centers and head of the EQT Life Sciences Dementia Fund

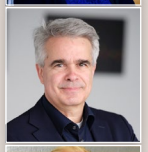
That brings me to the question that you can end the panel with. So, should we divest the investments that we do in other things into prevention? Matthew, you first?

Matthew Baumgart, Vice President of Health Policy, Alzheimer's Association

No.

Miia Kivipelto, Professor in Clinical Geriatrics, Karolinska Institutet

No.



Johannes Streffer, CMO, AC Immune

No.

George Vradenburg, Founding Chair, Davos Alzheimer's Collaborative

No.

Professor Philip Scheltens, chair of World Dementia Council, Professor Emeritus at Amsterdam University Medical Centers and head of the EQT Life Sciences Dementia Fund

Okay. No. No. Well, that ends the panel today. Very nice. It's actually right on time. It's 4.15 and we have to hard stop at 5.00. I don't want to allow the last panel the same amount of time as you have. Thank you very much. Thank you.

The World Dementia Council (WDC) is an international charity. It consists of senior experts and leaders drawn from research, academia, industry, governments and NGOs in both high-income and low- and middle-income countries, including two leaders with a personal dementia diagnosis. The WDC has an executive team based in London, UK.

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UK charity registration number: 1170743