World Dementia Council
Leading the Global Action Against Dementia

Global dialogue on dementia and health system readiness: Transcript

The dementia landscape project

7 July 2021

Co-chairs

Dr Margaret Hamburg

Dr Margaret (Peggy) A. Hamburg is an internationally recognised leader in public health and medicine. She is the former Commissioner of the US Food and Drug Administration (FDA), having stepped down from that role in April 2015 after almost six years of service. Peggy Hamburg is Chair of the American Association for the Advancement of Science and is an elected member of the Council on Foreign Relations and the National Academy of Sciences, where she serves as Foreign Secretary. She currently sits on the board of the Commonwealth Fund, the Simons Foundation, the Urban Institute and the American Museum of Natural History. She is also a member of the Harvard University Global Advisory Council and the Scientific Advisory Committee for the Bill and Melinda Gates Foundation.

Professor Howard Bergman

Dr Howard Bergman is Professor of Family Medicine, Medicine (Geriatrics), and Oncology, and Assistant Dean, International Affairs, Faculty of Medicine, McGill University. In 2009, at the request of the Quebec Minister of Health, he authored the Quebec Alzheimer Plan and is presently working with the Quebec ministry of health and social services on its implementation. He co-created and co-leads with Professor Isabelle Vedel, the Canadian team for healthcare services/ system improvement in dementia care (ROSA research team). In 2018-19, he chaired the Canadian Academy of Health Sciences Panel of 6 experts for the Assessment of Evidence and Best Practices for the development of a Canadian Dementia Strategy, assembled at the request of Public Health Agency of Canada.

Speakers

Dr Joanne Pike

Dr Joanne Pike, DrPH, is the chief strategy officer of the Alzheimer's Association. In this role she oversees the Association's strategic plan to advance risk reduction, care and support, research, advocacy, diversity and inclusion, concern and awareness, and fundraising. During her 25 years in progressive leadership in social support and public health, Dr. Pike has developed and executed successful health-focused initiatives while implementing revenue strategies to support those outcomes. At the Alzheimer's Association, she oversees care and support services offered across the organization to those affected by the disease; outreach aimed at creating partnerships with health systems, physicians and other health care professionals; long-term care initiatives focused on person-centered care delivery models; and growth strategies for reaching more individuals through quality improvement, education, and supportive programs and services.

Fiona Carragher

As Alzheimer's Society's Director of Research and Influencing, Fiona plays a pivotal role in the Society vision to create a world without dementia. Fiona has overall responsibility for our Research and Influencing strategy; leading our growing and ambitious world-class research programme and portfolio and our work to strengthen our position as the national charity leader on dementia health, social care policy and societal change. Prior to joining Alzheimer's Society, Fiona was the Deputy Chief Scientific Officer for NHS England, providing leadership for the 50,000 healthcare science professionals in the NHS and expert advice to the health system on science, innovation and diagnostics. She led a broad portfolio of policy responsibilities including establishing the UK Antimicrobial Resistance Diagnostics programme and the system wide Action Plan on Hearing Loss. She is a passionate advocate for women in health and led the establishment of the first Women in Science and Engineering fellowship programme in the NHS.

Dr Maria Tome

Dr. Tome serves as Senior Scientific Officer at the Product Development and Scientific Support Department of the European Medicines Agency (EMA). EMA can provide medicine developers advice on the most appropriate way to generate robust evidence on a medicine's benefits and risks. EMA provides scientific advice and qualification of novel methodologies to support the timely and sound development of high-quality, effective and safe medicines, for the benefit of patients.

Lenny Shallcross

Lenny Shallcross is executive director at the World Dementia Council. Prior to that he was Head of Community Engagement leading programmes across the UK to establish Dementia Friendly Communities. This includes the Dementia Friends programme which is the biggest health social movement campaign delivered by 10,000 volunteers that have recruited 2 million individuals through a community, digital and corporate offer. Before working for Alzheimer's Society he worked in the UK government as a political adviser at the Department for Culture, Media and Sport and the Department of Health, as well as working in Parliament and for the Labour Party.

Global dialogue on dementia and health system readiness

Wednesday 7 July 2021

08:00 PDT	San Francisco
10:00 CDT	Chicago
11:00 EDT	New York
16:00 BST	London
17:00 CEST	Central Europe

Discussion transcript

Lenny Shallcross
Executive director, World Dementia Council

Welcome everyone. I am Lenny Shallcross, Executive Director of the World Dementia Council. I realise many of you have participated in one of these global dialogues before or another Council meeting but for those of you who have not the World Dementia Council was established following the London dementia summit in 2013 hosted by the UK government as part of their G8 presidency.

The Council is chaired by Harry Johns, President and CEO of Alzheimer's Association (US). There are 24 individuals who are members of the Council. Alongside them there are a number of government members. As you know from the invitation and briefing note we sent, the Council will later this year publish a report looking at the progress the international community has made on the commitments that were made at the London summit. To help inform the report, we want to hear from experts around the world on different aspects of dementia policy. We will launch this report at an in person meeting here in London later in the year – if covid allows!

This is the nineth dialogue we have held, previous conversations have been on biomarkers, clinical trials, technology, dementia in LMICs, among others. 350 global leaders have participated in the dialogues. The purpose of today's dialogue is to reflect on health system readiness, where we stand and what needs to be done. No doubt aducanumab will be part of the conversation we have today: whether you think it is the bright star in the ecosystem or elephant in the room it is hard to avoid. But we want to

reflect more broadly on the challenges of health system readiness for the decade ahead that involves different DMT, new biomarkers being routinely used in clinical practice, the need for health systems to diagnose people accurately and timely, and the need for the health market to work.

We look forward to hearing your perspectives on this and more. After this meeting we will produce a transcript of the meeting – which is why the meeting is recorded. For people who contribute live in this discussion we will check the transcript with you. We will also produce a collection of essays reflecting the flow of the discussion today and the issues raised.

I would encourage you to share your thinking either live in the meeting or in the chat conversation. As you will know from the agenda we will kick off with short opening perspectives and then there is a open discussion. To contribute to the conversation just raise your hand in zoom. I am sure you all know this by now but to do that click on the reactions button and select raise your hand.

And with that bit of housekeeping done I would like to introduce and thank the co-chairs of today's workshop: Professor Howard Bergman Professor of Medicine at McGill; and Dr Peggy Hamburg, a member of the World Dementia Council and the former FDA commissioner. And I will now hand over to Howard to start the meeting proper. Peggy.

Dr Peggy Hamburg
Chair, American Association for the Advancement of Science and former Commissioner, US Food and Drug Administration (FDA)

Well, thank you so much and thank you to all of you for participating. This is an unusually expert and engaged audience, and the way this session is structured will have the chance during the moderated session to really hear from all of you and inform our thinking and the products that will emerge in terms of a report from this session. But we will begin with three really excellent speakers and we're very lucky to have them with us. And I'm very fortunate to have a very expert co-moderator as well, Dr Howard Bergman.

So, without further ado, because we really want to use our time to be able to address the important issues before us; as Lenny noted, this is a critical time, really a unique moment when advances in science are offering new, improved diagnostics, biomarkers and new potential and an approved new therapy or disease-modifying agent for this disease. It raises a lot of questions about how best to use these new tools, the readiness of the health system, the understanding of patients, their caregivers and healthcare providers, and how to ensure that we have integrated systems of care that also appreciate not just the medical treatment interventions, but the provision of health and caregiving services and support for this patient population. So really central issues, as we address, you know, the very significant and growing challenge of Alzheimer's in all our countries and around the world. So, with that, let me turn it over to my co moderator, Professor Howard Bergman.

Professor Howard Bergman
Professor of Family Medicine, Medicine (Geriatrics), and Oncology, McGill University

Thank you, Peggy, and thank you all for your participation as global leaders. It's really encouraging to see so many of you and really the diversity of group with your backgrounds and expertise and from so many different countries and continents, I think we've covered even all of the continents across the world. So, let's get to it. You have the biographies in the attached material if you received it. So, the introductions will be very brief. I would first like to introduce our first speaker, Dr Joanne Pike, the chief strategy officer of the Alzheimer's Association. Joanne.

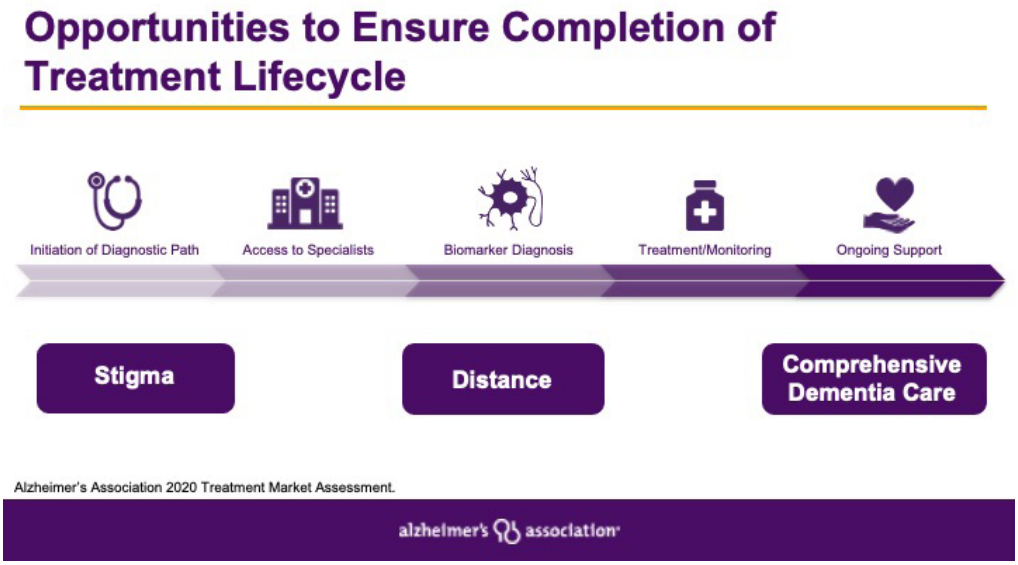
Dr Joanne Pike
Chief strategy officer, Alzheimer's Association

Thank you. And just as I am pulling up a couple of slides, I just say thank you for the invitation to be with you today, and also just want to mention that the health system readiness side of this is something that has been on our mind at the Alzheimer's Association since the moment that we heard the announcement that aducanumab was under review. Certainly not just the health system readiness side, but what was going to have to change about the medical model to support this treatment?

And a few things to think about. Paramount to this were the lessons that we've learned from other chronic diseases, including impact on health equity. And how do we ensure the people who could benefit have a path to access, initiation, and progression throughout treatment? And it's important to consider a few things as we look at health system readiness and that patient population. One most important and certainly something that we hear a lot about is those who could benefit from this specific treatment. Ensuring, number two, access. And three, the ability to progress through

treatment in a health system that is ready and able to ensure that all have the ability to progress through it.

Because we fully recognise that with the introduction of that treatment, health disparities are immediately exacerbated. We wanted to make sure that as people progress through this, that they don't fall through the cracks, that we identify the gaps leading into this, and as an advocacy organisation we consider that system readiness through that lens, that important lens of access. And we have considered (the Alzheimer's Association) five points within the treatment life cycle to consider how that system can be come prepared, what needs to occur to ensure initiation, progression and adherence is certainly maintained throughout for those who could benefit.



So, let's start with the initiation of the diagnostic path. And it's certainly something that we will hear more about through the rest of these short presentations. The fact is the majority of individuals do not initiate diagnosis. And treatment within a health system has the potential, depending on your country's payment model, to increase marketing and revenue for that health system overall. So, they, health systems that is, are incentivized to bring in a new patient population. Now, the diagnosis is important because there are a few factors at play for individuals that are seeking a diagnosis that we will circle back on that make this more complicated.

Access to specialists is another key area. Once initiated, individuals, depending on the diagnostic requirements, are going to need access to a specialist to provide that in depth diagnosis. We know that specialist time and quantity of specialists are limited. We also know that the step between primary care and specialist care results in a drop off of individuals who continue down the path. A system, in order to be ready, is going to have to establish a process to catch and move individuals through the diagnostic pipeline.

As they move towards that biomarker diagnosis, again depending on the requirements, a system's ability to meet PET scan or CSF requirements are going to require increased capacity. Most health systems in the US today report having excess PET scan capacity, allowing special utilisation but also the hesitancy to create additional capacity. In

addition, there is potential again for patient drop off due to these requirements for biomarker based diagnosis. Certainly, we know that CSF alone creates hesitancy, so a capable system is going to have to create a knowledge base to move beyond that hesitancy. Another appointment adds, whether that's for a scan or a CSF, that opportunity for someone not to follow through again. So another crack in the system.

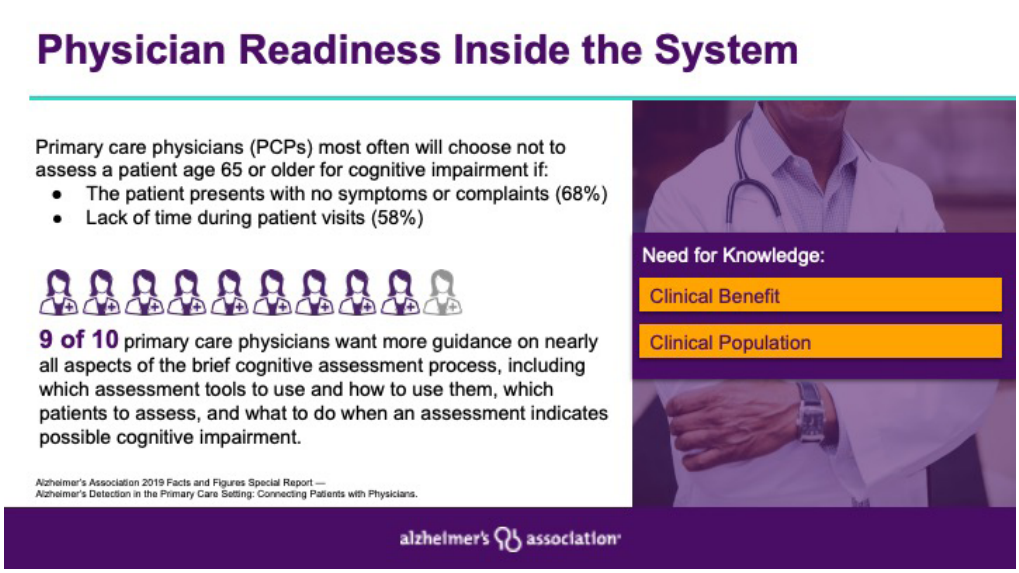
And then treatment and monitoring, and I say this, as the understated description of the day, the biggest requirement for readiness is, as it relates to treatment, infusion. Building capacity and capability for infusion outside existing fusion-based treatments like cancer, and certainly MRI monitoring. Also understanding what a treatment protocol within that health system, defining and creating the quality assurance checks for delivery across it.

And then ongoing support. We know that treatment adherence and the ability to manage full dementia care are inseparable. There is also the question of how long should this regimen last? How long will a system need to keep capacity over time? And where is the best location to maintain this infusion, and infusion with dementia capable care?

Now interwoven, and certainly impacting equity, with these five areas across the treatment pathway within a health system are some crosscutting themes that we have to consider. And here we circle back to that first one in the life cycle around diagnosis, and that is how do we consider stigma, and how do we build a dementia capable health system that moves people beyond stigma? Stigma impacts an individual's ability to seek a diagnosis and certainly culturally, how do we value a dementia diagnosis? In addition, there is trust related issues and concerns. The experience of health care system prejudice. And providers within the medical system creating hesitancy across this life cycle.

One of the single greatest potential moments to create disparity is also going to be distance created within treatments, from an individual who needs it to provider. At every step in this lifecycle the distance to travel is going to create a barrier. In the US, we know this represents a significantly widened divide between rural and urban access. Urban centres that have medical centres that have the capability to become ready, as we've described, are not available in rural areas where individuals have a drive of more than 2 hours is going to create treatment deserts.

And finally, ensuring we create a comprehensive dementia care model, the ability for someone to have that health system that provides all treatments and navigation in one location. Making sure that we maintain connection with caregivers. And as people proceed through treatment, that the increasingly complex delivery of that includes the full spectrum of dementia capable care. We've seen comprehensive care models work in other chronic diseases, and we know that they can flourish. However, system readiness today is going to require us acquiring new models of care that are significantly different than what we have in the dementia/Alzheimer's space right now.



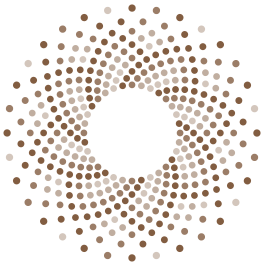
And certainly, we can't consider system readiness without considering the people who act in the system and their readiness also. So I wanted to briefly touch on provider readiness in addition to system readiness. The Alzheimer's Association published in 2019 a special report in particular on primary care providers and the detection of Alzheimer's and other dementias. At the time nearly half of primary care practitioners reported not diagnosing Alzheimer's because of not having a treatment available to them. However, we also heard nearly nine out of ten primary care physicians wanted more guidance on nearly all aspects of the cognitive assessment process, including tools and the capability or knowledge to move people through the diagnosis process. This is a moment we have to double down on our efforts to increase knowledge for providers on clinical benefit and who best will benefit from this particular treatment and how to incorporate this specific change of care in their practice philosophy and delivery. And so with that last thought I will turn it back to you Professor Bergman.

Professor Howard Bergman
Professor of Family Medicine, Medicine (Geriatrics), and Oncology, McGill University

Thank you so much Joanne and I'd now like to introduce the second speaker, Dr Fiona Carragher who is director of research and influencing at the Alzheimer's Society in the UK, and formerly the deputy chief science officer at NHS England. Fiona.

Fiona Carragher
Director of Research and Influencing, Alzheimer's Society

Thank you, Howard. And thank you to the WDC for inviting me to speak this afternoon. I'm going to focus on one aspect of what Joanne has talked about, which is around diagnosis, because as we move into a world where there's real hope of disease-modifying drugs, the need for an early and accurate diagnosis is critical. And as Howard has said,



I am a clinical biochemist by background and had the privilege of advising and leading diagnostic programmes within our National Health Service. So as a community, I really believe we have an opportunity to drive change and accelerate progress.

But where are we now? There's no doubt that building a suite of validated biomarkers that can be integrated into clinical practise is a hugely complex challenge, and I think we have to recognise that it's a well-trodden path by many other specialties. For example, we saw significant delays in the NHS in the UK when we look to at scale adoption of the use of natriuretic peptides, that were really pivotal in diagnosing heart failure. So, whilst academic and industry groups make rapid progress developing accurate blood tests, for example, for Alzheimer's disease, we need to ensure that the health system into which they are placed is ready and this will require a coordinated approach that goes in parallel to those research breakthroughs.

So we have to consider the capacity of our clinical laboratories and imaging services to deliver these novel tests. But also the connectivity between our diagnostic providers to the memory assessment services, who certainly in the UK sit in different organisations. There's a need to skill and up train our staff so that once these tests are available, they understand both the use and interpretation of novel diagnostics. So that will mean, as Joanne has mentioned, significant changes in training and attitude of clinicians, but also with the public in terms of the value of an accurate diagnosis.

When we think about dementia care we have to take into consideration the challenge of equity and inclusivity because we know that we've got significant challenges in those areas now. Our starting point is one where there is a challenge getting people diagnosed. In the UK, we have had incentivized case finding initiatives in primary care for dementia over the period between 2013 and 2016, that's meant that we've had a national target for dementia diagnosis of 66.7%. But we have seen a significant decline in those diagnosis rates as a result of the COVID19 pandemic, which has meant that tens of thousands of families are in limbo without diagnosis or having access to have the support that they need. In the UK, we have clear guidance set out by NICE, our National Institute of Clinical Excellence, that says that if there's an uncertainty in diagnosis, PET scanning and CSF testing should be used. But in a 2019 national audit, we found that only 56% of memory services had access to CSF testing and only about 77% of PET CT.

In the UK there are real issues with variability and access to diagnostic capability and capacity in the UK, but also that lack of understanding and value of that diagnosis and in some areas of reluctance to make a diagnosis by clinicians. We know we've got issues with access, but what about the challenges of equity and inclusivity? We know that there's continued stigma attached to getting a diagnosis of dementia for some BAME communities. We also know that the number of people with dementia from our BAME communities in the UK is set to rise by seven-fold up until 2050.

And this is partly explained by some of the increased risks around vascular dementia, such as diabetes, heart attack and stroke. But we also know that we have a significant challenge with getting diagnosis in these communities. A very clear research study has shown that those from Asian and black ethnic communities have the lowest proportion of diagnoses in this country and that it is multi factorial and probably like many countries across the world, it is in part due to stigma around dementia within

those communities, but also lack of awareness of the condition and cultural perceptions around caregiving, for example.

Alzheimer's Society UK has undertaken recent research in the area of diagnosis and showed that there were also significant challenges with our services being inclusive. We have seen issues around access to interpretation, culturally appropriate assessment tools or services, but also very poor collection of demographic data, particularly at primary care level that makes it very difficult for our commissioners to plan appropriately for the services that are going to be most culturally sensitive.

Despite all that, I do think there are opportunities for transformational change. What we're seeing is a shift in national policy because of the critical role that diagnostics and testing has played during Covid. That's meant investment in critical infrastructure, such as the establishment of national network of diagnostic services that include community diagnostic hubs that could potentially open up accessible testing for primary care.

We are also, like many other across the world, seeing and move towards integration, ensuring that our memory assessment services may become much closer to the acute hospital diagnostic capability, but also seeing national policies to incentivise, adoption of new technologies and new diagnostics.

I want to leave you with one final thought and that's the clear role for the voice of the patient here. What we hear as the largest advocacy group in the UK is that people affected by dementia want and need an accurate diagnosis because it enables them now to get the support and care that they need, the opportunity to take part in research and clinical trials, but hopefully also one day soon, treatments that will slow the progression of disease.

So we believe it's vital that we come together as a community, not just in the UK, but globally, which is why it's wonderful to see so many of you here today to take steps to address these challenges. I welcome the opportunity debate and discuss some of the points today. Thank you.

Professor Howard Bergman
Professor of Family Medicine, Medicine (Geriatrics), and Oncology, McGill University

Thank you so much, Fiona. Now I'd like to introduce the concluding speaker, Dr Maria Tome, senior scientific officer at the European Medicines Agency (EMA).

Dr Maria Tome
Senior Scientific Officer, Product Development and Scientific Support Department, European Medicines Agency (EMA)

Hi, thank you very much for having me in this meeting. I will talk as a regulator in the European Union, we give scientific advice to the European Commission who is

the one that gives the licence and make the decisions for drug development. Then in each country, politicians make their own decisions in pricing and health system implementation. And the previous speakers have explained that. Ten years ago I was working in the NHS in UK and I decided that I wanted to develop drugs for Alzheimer's. And I moved to the European Medicine Agency.

Then we realized that the old AD guidelines were really not ready to develop new products. And we decided to create a new AD guidelines CPMP/EWP/553/1995 Rev 2. In EU we described disease modification and MCI to stop the progress to Alzheimer's and other dementias. Why? Because we already have a licensed drug in the EU that stop the decline of cognition in Alzheimer's disease. We decided, we also learned that the diagnostics such as PET amyloid were only license to "in the diagnosis of AD' . And you can only use PET for diagnosis in Alzheimer's, but they are not good enough in the MCI diagnostic context.

Thus we decided we need better diagnostics tools for MCI. Then we work on MRIs, CSFs biomarkers and we keep moving on. What we mean in Europe for disease modification is not only the cognitive decline is slow, but you have biomarkers, not only are implicated in pharmacodynamics biomarkers, you have a drug that target amyloid and decrease amyloid, common sense that will hopefully work, but we hope that we inform the molecular pathway that means that you will include blood, CSFs and another digital biomarkers. Of course, we work with regulators all over the world and we have discussed for years and I think you have several experts in the panels of the meeting that they described in more details.

And I think that regulators have common understanding in Alzheimer' guidelines, but not in all ones, and we have different relations and legislations in all other countries. In Europe, we have big programs that they have finished IMI- EPAD in 2020, for Earlier predementia stages Alzheimer's disease, and we also are working with Japan, United States and Australia in research projects that have informed how we can prevent Alzheimer's disease. We started 10 years ago, and we have been very ambitious. IMI – EPAD have finished and say in early Alzheimer's, the current amyloid load does not changed with the cognitive decline. There is another pathway that are important and is another pathway, and we have another target.

Only from 2020 a biomarkers panel described the same. I say learn from the United States because we are moving quite quickly and it's good news. Some suggestions: we have learned a lot from COVID. It was a pandemic and everybody (academics, clinicians, politicians, researchers, geographers) discovered environmental factors and epidemiologists worked together, and in 11 months we develop a drug for prevention and treatments.

That means that something similar will be done if we want to prevent the AD. And this is the moment. How we will do it? We are learning all the time about predementia stages of Alzheimer's. We are using digital health technologies and we are very advancing very quickly. We diagnosis by apps nowadays. And by the way, we have progress in biomarkers in blood. Of course, we do MRIs.

And with my personal thoughts and reflections. These are my views. They are a lot of drug in developments. My message is of hope. We are ambitious. We really want to stop AD because slowing the cognitive decline in A– we already have drugs for that. Thank you so much.

Professor Howard Bergman
Professor of Family Medicine, Medicine (Geriatrics), and Oncology, McGill University

Thank you. Thank you very much, Maria. So now before I turn over the roundtable discussion to Peggy to chair, just a few reflections. I think our speakers have raised a lot of the key issues for discussion. The approval of biomarkers and disease-modifying medications represent a tremendous step forward but also challenge our health care system from the point of view of the potentially vast demand. The clinical process has been brought out in the various discussions and accessibility in a cost effective and equitable manner in each of our countries, but also globally, of course.

And although nothing compared to the Covid vaccine challenge, the Covid experience gives us an idea of the road ahead. Some of the health system challenges that I think we need to look at are regulatory and financing. So the regulatory framework and reimbursement approval, the financial and fiscal burden on the healthcare systems, both whether they be public, private, or mixed, and the cost concerns individually for patients. The second point, the capacity to clinically manage the process for the potentially vast demand. As the Kaiser report said, this discussion is reminiscent of discussion that took place after the introduction of high-cost treatments for hepatitis C. In that case, the new drugs cure the disease and are approved for a much smaller patient population.

We need to talk about a feasible trajectory to assure equitable access to the biomarkers and disease modifying medications. Issues include clinical capacity, organization, human resource numbers, articulation has been brought up between primary and specialty care. In some of our countries, the Alzheimer care is anchored in specialty care, in other countries like in Canada, my country, it's anchored in primary care. The notion of point of contact testing rather than complex referral systems, and the access for diverse and rural populations.

And finally, global equity and the lack of a framework for dialogue and international dissemination. And the fiscal capacity and health care system capacity from a global point of view.

In summary, some of the key questions for discussion include: how will our healthcare systems, including regulatory agencies and public or private payers, deal with the utilization of biomarkers and disease modifying medications in the context of a certain uncertainty of the real world, patient-centred impact; the very significant individual patient and health care system cost per year, and the complex diagnostic and follow up testing. How will each of our healthcare systems assure equity in terms of access to the biomarkers and medication: cost, diverse population, proximity for the rural and remote populations to specialized resources and technology. And how will we assure equity from a global perspective for middle- and low-income countries?

I particularly like what one of our speakers, I think it was Fiona, who said with all that, there are tremendous opportunities for transformational change. It's now time for you to contribute, my pleasure to hand the chair over to Peggy.

Dr Peggy Hamburg
Chair, American Association for the Advancement of Science and former Commissioner, US Food and Drug Administration (FDA)

Well, thank you so much. And thank you to our speakers for really three terrific presentations to help frame some of these issues and Howard for your thoughtful response to the speakers and sort of overview of the context in which we find ourselves with both challenges and opportunities. I was struck that you said it's nothing compared to Covid. In fact, I think that the challenges of Covid been huge, but we cannot underestimate the challenges that we face here. Covid has many similarities to the challenges we face with Alzheimer's in that there is no nation that will be protected against the burden of this disease and have to find solutions, to manage and to harness science in all as many dimensions, to be able to reduce that burden of disease, hopefully through both important medical interventions, social services, and, ultimately, we would hope prevention.

We also, like with Covid, Alzheimer's represents an enormous challenge on every level. It's not just about the medical condition and the impact on individual patients and their families, but it's also enormous demands on our social structures, huge costs to our economies. And, of course, as we've been talking about today, major, major challenges to our health care system, as we see numbers grow, but also as we really respond to the advances in science and technology that will enable us to apply better solutions. So I think we have an opportunity now to hear from all of you with your thoughts on this set of issues, what you see as key issues, concerns and challenges, key opportunities and strategies going forward.

You're more than welcome, we encourage everyone to just offer their opinions. If you do want to pose a specific question to one of our speakers, I think they're willing to also respond. I'd like to open it up. I don't see any hands raised yet. I don't know if that's because you don't know how to use the hand raise function yet, whether you think all of your questions and comments have already been addressed, or whether I need to look at the chat and call on some individuals who are actually commenting on the chat.

Let's see. I see some hands. Okay. Apologies. George Vradenburg, I can always count on you to have some wise words and observations.

George Vradenburg
Co-Chair, Davos Alzheimer's Collaborative

It strikes me that the widespread use of blood diagnostics, which holds the promise of lower cost and widely accessible, much more primary care friendly, would be a huge

step forward in terms of access and capability. So my question really is, what steps can we take to incent the more rapid and scaled introduction of such blood markers, blood diagnostics, into primary care practice, either as a preauthorization for PET scan or as a substitute for PET scan, but something that obviously would make much more accessible the ability to detect and diagnose this disease.

What should we do to incent the development of those biomarkers. I know scientifically we're there, but they're clearly not yet approved by regulatory agencies, reimbursed or when widespread use.

Dr Peggy Hamburg
Chair, American Association for the Advancement of Science and former Commissioner, US Food and Drug Administration (FDA)

Yeah. Well, I guess there's the issue of developing the products and having them be available, the understanding about their use in the clinical setting and then the payer issues, which at least in the United States, are problematic in terms of sometimes the disconnect between an approved treatment but an actual ability to pay for the diagnostic. I don't know whether we do have an expert on diagnostics, Fiona, who's also worked in the National Health Service. Do you want to just quickly make an observation on this question about how to incent both development and appropriate use of diagnostic?

Fiona Carragher
Director of Research and Influencing, Alzheimer's Society

From a UK perspective obviously we have a different payer or commissioning arrangements. If we learn from where we've been with other diagnostics, where it has been clunky to get adoption into clinical practice, I think there has to be a really strong economic and cost effectiveness argument to make. What we see in the UK is that if diagnostics are seen as part of clinical guidance, so they're not separate, they are clear part of that clinical pathway then they are more likely to be adopted.

What we have also started to see are national policy initiatives that will help to drive this for example the Accelerated Access Collaborative, which is essentially speeding up the adoption of these kind of new biomarkers that could come through. And I think one final point to say is in my 25 years as a diagnostician, you've got to have very strong clinical champions on the local level. And I think in this it will take a combination of not only the primary care physicians linking to old age psychiatry and other clinical specialisms, but don't forget to bring pathology and the pathologist into this, because they will be holding working with diagnostic companies and are often the forgotten group in terms of diagnostic adoption.

Dr Peggy Hamburg
Chair, American Association for the Advancement of Science and former Commissioner, US Food and Drug Administration (FDA)

Great. Thank you. I know there are other hands up now, but on the same topic in the chat, Adesola (and apologies if I didn't get the pronunciation quite right) did raise the concern about how can we also think about access and availability in low-income countries? And I'm wondering if Adesola would like to just outline that set of concerns and perspective quickly before we move on to other questions, observations and our discussion.

Professor Adesola Ogunniyi
Professor of Medicine, University College Hospital, Ibadan

Thank you very much, Peggy. I just felt that these things are so exciting that makes a diagnosis of Alzheimer's disease very easy and you can do so over the world. But we are handicapped in low resource settings. And I was thinking of whether there are considerations of how the technology can be available to health care providers in low-income settings and how patients can benefit. Thank you.

Dr Peggy Hamburg
Chair, American Association for the Advancement of Science and former Commissioner, US Food and Drug Administration (FDA)

And I guess the concern with respect to diagnostics is, of course, a broader one with respect to all aspects of care when we think about translating these emerging new tools and technologies to low-income settings, both in terms of educating healthcare providers and also access to these products, which are not inexpensive and require often high levels of technology in order to fully administer, so an important issue to have on the table. James Rowe, your next on the list.

Professor James Rowe
Professor of Cognitive Neurology and Director of Cambridge Centre for Frontotemporal Dementia and Related Disorders, University of Cambridge

Thank you. Thank you to our speakers, it's a very interesting, exciting discussion. I wanted to pick up on a point that all three of them made, using the words "incentive" and "incentivize", I want to dissect that for a moment, because it seems to operate at two levels. First, as a financial and the other at a clinical level. At a financial level, whether it's digital hospitals or health care providers or national purchasers and commissioners, no new diagnostic or treatment will move ahead quickly, even if clinically effective, if it's perceived as generating a net loss. So we need to link the costs incurred in better diagnosis and treatment with the cost of not tackling dementia. The cost per patient of undiagnosed and untreated unstopped dementia is very high. But often it's a cost to a

different organisation to that which would provide the diagnostics or treatment. And that, I think also makes the incentivization very, very challenging and different, of course, between different countries.

Also on that we need to think not just about getting a diagnosis of dementia. That's the easy bit. Much more effort needs to be put into getting an accurate diagnosis. A high volume of inaccurate diagnoses will be counterproductive. So we do really need to think about how we get accurate diagnoses. We can be inspired in this from oncology, where accurate diagnosis and specification of different disorders has been a pathway to real progress.

I also want to take a moment to think about incentivization from health care practitioners for whom incentive is really around care and quality of life, not the financial aspect. It's quite a different set of motivations and mechanisms here. We need to very careful about rolling out very "high volume, low cost" diagnostic tests, whether it's blood or something else, into primary care or even community or even the members of the public providing. Because we may not do ourselves - or those individuals – a net service. Again, inspired from oncology, we learn that inappropriate screening or widespread screening can do an immense amount of iatrogenic harm if it is uncoupled from proper research and informed advice, on risks and implications of tests and positive predictive values etc. The contextualization and interpretation of results is key. So simply making tests available at scale isn't enough unless it's coupled with access to advice and contextualizing a test result. Only then will it actually be able to take a step towards better quality of life. Those are my thoughts on those two incentivization modes. Thank you.

Dr Peggy Hamburg
Chair, American Association for the Advancement of Science and former Commissioner, US Food and Drug Administration (FDA)

Well, thank you. Very thoughtful set of comments. Nora Super.

Nora Super
Senior Director of the Milken Institute Center for the Future of Aging (CFA)

Hello. Thank you. I'm Nora Super with the Milken Institute, Alliance to Improve Dementia Care, and I wanted to follow up on Joanne's presentation and perhaps get Fiona to respond as well. The focus of this is system readiness, and I know Biogen for one have been studying that for a long time. And when people ask me, is the system ready for this, the short answer is no. And I think that one of the things we haven't talked as much about is really the specialists that aren't available in the US and the UK and I'm sure across the world there's very low access to specialists of geriatricians, geriatric psychiatrists, neurologists. We have some data in the US about the wait time just to even get a neurologist appointment is very long. So I think the biomarkers and everything are really encouraging. But I think to the point about the being able to get an accurate diagnosis is incredibly important. And I was really struck by what Dr Bergman said of

comparing this to hepatitis C. It's not a cure. It's just one of many treatments that might be considered for this complex disease. And so I wonder when we think about system readiness, how do we incentivize getting more specialist in this field so that we can get accurate diagnosis? We can get people the proper treatment, whether or not if this particular drug. So I don't know, Joanne, if you have a response to that or Fiona.

Dr Joanne Pike
Chief strategy officer, Alzheimer's Association

First of all Nora, it's great to see you. And I agree completely with you. When we thought about the need for specialists a couple of years ago, we certainly looked at what ways can we incentivize individuals to go into this field overall in the US, there's certainly policy related initiatives related to enhancing medical education on this topic. I would be interested in hearing if there are avenues of increasing specialists outside of the US that goes beyond policy initiatives, but also thinking about how can we incentivize the system to bring in more students or to increase the number of advanced practitioners that are not MDs. But how can we increase individuals who have access to do care and screening that are nurse practitioners or physicians assistants who have the ability to do this so that we are increasing the pool of people who can provide this level of care, but not relying only on medical school education as well.

Dr Peggy Hamburg
Chair, American Association for the Advancement of Science and former Commissioner, US Food and Drug Administration (FDA)

Thank you, Fiona. Do you want to make any?

Fiona Carragher
Director of Research and Influencing, Alzheimer's Society

I think just very similar within the UK based as well, this real challenge within that specialism. But I think the other bit that we can't, which I kind of put in my comments, is that we've taken a massive step back during Covid. We've now got significant waitlists for our current memory assessment clinics, and certainly in the UK, we're finding that our diagnostic capacity is not prioritising dementia. It is cancer, cardiovascular disease and other clinical specialties. So, I think that it's been made worse by Covid, if I'm really honest Nora and this something that really concerns us at Alzheimer's Society. It is not going to be an overnight transformation, but the opportunity of looking at multi professional teams and approaches would be really important.

Chat function

The chat function was available throughout the dialogue for participants to ask questions of presenters and to hold discussion amongst each other. It began just under 54 minutes into the event and is displayed below. It does not necessarily correspond with the adjacent transcript in this document.

George Vradenburg
Clinical use of blood diagnostics holds the promise of lower-cost, widely-accessible, and primary-care friendly protocols for detection and diagnosis. What steps, in the view of the panelists, might we take to invent the more rapid and scaled introduction of such blood diagnostics?

Dr Peggy Hamburg
Chair, American Association for the Advancement of Science and former Commissioner, US Food and Drug Administration (FDA)

Great. Thank you. Let me move on to some of the other people with hands up. Let me also ask if you could just identify yourself and your institution or line of work that is often helpful, although many of you, of course, know each other or at least know each other's work. Also, a lot of people are saying interesting things on the chat. I encourage you to raise your hands and say them to the group as well, in the hopes of making sure everyone can benefit and also perhaps stimulating other comments. So now I'd like to turn to Henrik Zetterberg.

Professor Henrik Zetterberg
Professor of Neurochemistry, University of Gothenburg

Hey, Hello. My name is Henrik Zetterberg, professor of neurochemistry at University Gothenburg and University College London. And my speciality is fluid biomarkers and especially the blood tests that have been developed recently. I just wanted to give a brief update on what's happening right now in this field. Because, as George pointed out, there is so strong science behind the use of both in the CSF p-tau/ABeta ratio and CSF tau as blood tests for Alzheimer's disease. And also of course [indistinct] general neurodegeneration marker. And these tests are currently done with rather specialized technologies, [indistinct] techniques, which are not available in general clinical chemistry.

But the concordant results now from many different research groups strongly as support that these are clinical chemistry, valid tests that most likely will be of great importance in general medicine and in general practice. So the big clinical chemistry companies are right now making efforts for these biomarkers on their clinical chemistry workhorses. And that is happening at the moment in close collaboration with FDA and European agencies, and it is looking good. So I would encourage you to listen into AAIC in the coming weeks and for example look at the presentation by the NIH where different beta methods are being compared, and they are one of the methods that really work well in general clinical chemistry labs is actually performing at the level that, for example, the C12 does.

So I hope that the recent developments in therapeutics will give the biotech companies incentives to produce tests that work in general clinical chemistry practice. And some of these molecules are also quite stable. So, for example, we have recently shown that dried blood spots work to measure [indistinct] works well as well, which would facilitate these types of measurements in remote settings. And hopefully we will together in the clinical and lab communities, develop algorithms with which we can improve the detection of patients with amyloid pathology and with the neural reaction to that amyloid pathology to make it more cost effective to identify these patients and eventually put them on treatments and monitor those treatments where A/Beta and plasma markers, from my point of view, will most likely they should work, but we have no proof of that yet. But if

Professor Gustavo Alves
Is very important the situation of this countries as Brazil, because here, the aging is ocurring ver very fast, then we don´t have public policy for the elderly people before the "magic drug" for Alzheimer´s disease, we need strong diagnostics.

Professor Adesola Ogunniyi
Follow up to George's comments above: How can patients and health care providers in low-resource settings benefit from these advances in the management of individuals with dementia?

Professor Gustavo Alves
Colleagues, being born in Latin America is an inclusion factor for Alzheimer's due to the issue of education, educational level.

you treat the patient with an amyloid targeting drug, the amyloid toxicity is reduced, then the expected reactionist of plasma tau will go down.

If it doesn't go down, there might be something wrong. I want to just conclude that we have a number of tools at hand and they are being developed into tools that will be similar to how we work with clinical chemistry tests in other disease areas that we should put forward, and we should also try to get them implemented as a prerequisite. In order to prescribe a drug against a pathology, you need to have evidence of existence of q pathology and also ways to monitor the treatment effect. Thanks.

Dr Peggy Hamburg
Chair, American Association for the Advancement of Science and former Commissioner, US Food and Drug Administration (FDA)

Well, thank you. We're fortunate to be able to have gotten an update direct from the bench, so to speak, on some of what's going on in that realm. And it is very exciting. Let me turn now. Martin Rosser?

Professor Martin Rossor
NIHR National Director for Dementia Research, UCL Queen Square Institute of Neurology

Thank you. I am Martin Rossor, neurologist and director for dementia research at the NIHR. My comment is an observation and it's already been picked up or touched on by James. and it relates to the dialogue and how we speak about the problem, which I think has the danger of creating some further problems. The first is the category error that many people make. Not this group of distinguished individuals, but politicians and the public make a category error of thinking that MCI and dementia are the same as Alzheimer's disease.

And the problem I think here is that people move into a binary view: the diagnosis is about Alzheimer's or not Alzheimer's? And quite a lot of the discussion around the diagnosis and how we identify the Alzheimer group is around that. The problem is that there are numerous causes of cognitive impairment and managing those will not be met if we have a binary view of the diagnosis. And as we move to having people referred with mild cognitive problems, the proportion who have Alzheimer's disease will be less. And we mustn't forget the vast number of people who will have a cognitive problem who don't have Alzheimer's.

Dr Peggy Hamburg
Chair, American Association for the Advancement of Science and former Commissioner, US Food and Drug Administration (FDA)

Thank you. Very important point to remember. Next on my list is Andrew Law. And I'm told that Soeren Mattke also wants to speak, but I don't see a hand up for her. But let me turn to Andrew first.

Dr Iracema Leroi
Might we clarify who exactly we are referring to - ALL people with AD, as per the FDA indications, OR the more specific group as per the inclusion/ excl criteria reflected in the trials (which most clinicians would support)?

George Vradenburg
@adesola, digital cognitive assessment tools are increasingly promising as are blood diagnostics for low resource settings

Dr Isabelle Vedel
Another topic is what is the role of research in this transformational change? Cost-effectiveness studies, implementation studies

Professor Gustavo Alves
We must to think about fast test,, prodromic, point of care

Professor Andrew CK Law
Professor of Psychiatry and Head, Department of Psychiatry, University College Dublin (Malaysia Campus)

Hi, this is Andrew from Malaysia, a geriatric psychiatrist and professor with RCSI & UCD (Malaysia Campus). Wonderful to be here. Just picking up on Joanne's presentation, one of her slides showed the significant number of PCPs being not comfortable in diagnosing or managing dementia or Alzheimer's disease. Those figures, I don't know if they are actually from the US? If there were, then I am actually quite surprised! In Malaysia, we have very similar problem, if not worse! In view of that, could you let us know, how are we going to equip our PCPs, bettering them to be ready to take care of dementia patients? For us, and surely for the rest of the world, we have rapidly rising aging populations and Alzheimer's prevalence will also increase.

Dr Joanne Pike
Chief strategy officer, Alzheimer's Association

Just to comment really quickly. That was US specific and it was prior to that research study was done prior to aducanumab going to the FDA for approval. So one of the things that we heard within that was that there was a belief that primary care physicians didn't believe their peers were ready, but they felt ready themselves, which was an interesting dichotomy to learn that they saw themselves different than they saw the profession overall. But we do believe that there is a significant opportunity to make sure that at this moment, primary care understands the potential patient population who could benefit specifically based on the clinical trial information, and also what the protocol would be to move them either to specialist or, dependent on the model, for moving them to treatment. That is a significant opportunity for us moving forward.

Dr Peggy Hamburg
Chair, American Association for the Advancement of Science and former Commissioner, US Food and Drug Administration (FDA)

Thanks for that clarification. Now I'm going to turn to Soeren, who I guess is on the phone, and that's why I can't see him. And I apologize without that visual I got the gender wrong! So Soren.

Professor Soeren Mattke
Research Professor of Economics at USC and the Director of the Center for Improving Chronic Illness Care

Thank you, Peggy. That always happens to me. In first grade, I never got tested in sports because then the gym teacher knew that this was not a girl's name and the other teacher thought it was girl's name, so I kept wondering where I ended up! I wanted to pile in on the blood biomarker testing. We had shown last year at AAIC that at least for the US

Dr Adelina Comas-Herrera
Particularly when thinking about Low and Middle Countries, it is very important we understand how cost-effective different treatments/care approaches are in those countries. Of course it would also be good to know how the new treatments will compare with existing ones in high income countries too. There are a lot of relatively affordable existing treatments for which access could be improved at relatively modest cost, in both high and low-middle-income countries

Dr Michèle de Guise
To be able to accelerate the introduction of these innovations with a high degree of uncertainty, we must have the capacity to measure or estimate the

context, with a blood based biomarker with specifications that Henrik mentioned, you can pretty much abolish the specialist constraint in the diagnostic pathway because you make the triage at primary care so much more efficient: with a brief cognitive test you know that there's likely cognitive decline, with the blood test you know that there's likely Alzheimer's pathology, and therefore you are referring mostly patients that have a likely treatment indication later on.

That's particularly important given the nature of the treatment, at least as approved now. We have made the analogy to Hep C, but it's not quite right because in Hep C, we had plenty of time. In, Hep C we could treat all the way up to manifest liver cirrhosis and still cure the disease and return to normal liver function.

In Alzheimer's disease that's not the case. We know that once we are beyond mild dementia, the treatments are most likely not effective. So we actually have to speed up and get people into and through the diagnostic queue rather quickly. And that leads me to my second point and that is the economics of this. The unfortunate fact - back to James Rowe's comment - is that the economic burden of dementia is enormous but a disease modifying treatment that addresses the disease at a stage of manifest clinical symptoms is not going to reduce that burden all that much.

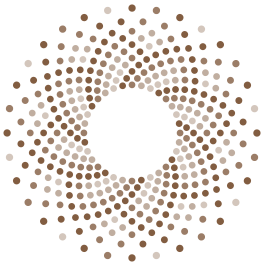
Caregiver burden is already high in MCI and mild dementia, and it's not going to be changed much by keeping patients longer in that state, the same for medical cost of cognitive decline. So if we want to make this a cost effective treatment, we have to go into the preclinical stage where we can actually arrest a disease before it becomes symptomatic, much like we treat cardiovascular disease now.

Dr Peggy Hamburg
Chair, American Association for the Advancement of Science and former Commissioner, US Food and Drug Administration (FDA)

Thank you. Those observations are very helpful. And I guess where you work, you have a chance to be thinking about them on a daily basis as you address how best to care for chronic care patients. Let me turn now to Jacqueline Hoogendam.

Jacqueline Hoogendam
Dementia policy co-ordinator on Long-Term Care, Ministry of Health, Welfare and Sport, The Netherlands

I work at the Ministry of Health in the Netherlands, and I'm among other responsible for the governmental funded dementia research in our country. It's very interesting to hear all your comments and I'd like to draw your attention to a recently started research program, ABOARD, which is a public private partnership in the Netherlands with researchers, of course, but also hospitals, industry, health insurers, patient organizations, focusing on a number of issues addressed this afternoon. It's research to make more accurate diagnosis of Alzheimer's, but at the same time looking into possibilities to come to a personalized treatment for this patient and, as it's working with hospitals as well, immediately transfer the research outcomes to clinical practice,



global value in the real context of care, to have a learning health care system providing the opportunity to provide "living guidelines"

Professor Ricardo Allegri
I believe that in LMIC the first problem is the access to biomarkers, we need something like blood BM, few centers have access to BM in Latin America located in big cities.

Dr A Mark Clarfield
Could someone please comment on the controversy re FDA approval of a drug (aducanumab) with very doubtful clinical efficacy ? 3 committee members resigned in protest including Dr Aaron Kesselheim from Harvard who was quoted as saying that the FDA decision was "probably the worst drug approval

providing the right treatment. But also working on awareness and prevention of stigma for people with dementia, so stimulating them to go to a doctor or a memory clinic in Netherlands as well.

So it's a very promising research project, and the researchers are really looking into possibilities to have similar project started in other countries. Of course, our aim is to make it a worldwide project, similar to the Finnish Finger project, but to start they're very willing to cooperate with other researchers in other countries as well. I'll be happy to give more information and provide a link to the project website (Project ABOARD | Alzheimer Nederland (alzheimer-nederland.nl)) . Thank you very much.

Dr Peggy Hamburg
Chair, American Association for the Advancement of Science and former Commissioner, US Food and Drug Administration (FDA)

Thank you. And your comment reminds us, we've been talking a lot about advances in biomedical product innovation research, but it's also important to do health systems research and to really understand more about the context and organization of care to really support Alzheimer's patients at varying stages of disease. Ivan, let's turn to you.

Ivan Koychev
Clinical academic psychiatrist, University of Oxford

Hi, I'm Ivan, an academic psychiatrist at Oxford. I wanted to pick up on a few points. Firstly, I think this is a great opportunity to make diagnosis of dementia more specific through biomarker pathways that will allow us to move into treating dementia before its clinical stages which is where I believe the greatest potential lies. But I do want to point out that essentially the situation where we're in now is that a disease modifying treatment has just been approved. I think it's fair to say the decision has been controversial. So I do wonder in the context of health care system preparedness aout how do we prepare the public and the healthcare providers for potentially disappointing initial stages of treatment? Where, for example, the efficacy isn't particularly well pronounced, while at the same time healthcare providers have to deal with side effects they haven't dealt with before. The context is that the higher dose of aducanumab associates with significant incidence of ARIA and this is the dose that we are likely to be prescribing.

So I think at least in the initial stages, when we think about preparedness, we have to also think about how do we open the conversation that this is going to be perhaps a treatment of limited efficacy and high side effects that people haven't had to deal with before?

decision in recent US history"

Dr Elisabetta Vaudano
Unfortunately I have to leave now, but I would like to ask the speakers following with Martin comment, how could be addressed the fact that there is a risk of creating silos of patients, those that fit and can easily navigate from diagnosis to an effective treatment and all the "rest" where this will not happen or will not happen timely enough, and in particular the patients with comorbidities? Bye and thank you for interesting conversation!

Dr Isabelle Vedel
We need more evidence to help decision-makers, clinicians decide where to invest their limited funds and time to have the greater impact at the individual and

Dr Peggy Hamburg
Chair, American Association for the Advancement of Science and former Commissioner, US Food and Drug Administration (FDA)

Yes, we do need to think about educating the public and the patient population as well as health care providers, for how to think about what is known about new products, including this recent approval here in the US and what isn't known and the balancing of risks and benefits potentially for different sub populations of patients, and so a lot that we continue to need to learn even the context of a drug entering the marketplace. George, I see your hand up, but I'm going to turn to a couple of other people first and come back to you just so that we make sure that we hear from a range of participants. Adelina, thank you.

Dr Adelina Comas-Herrera
Assistant Professorial Research Fellow, Care Policy and Evaluation Centre (CPEC), London School of Economics

Adelina Comas-Hererra from the London School of Economics and I work as a colleague on the STRiDE project that we've discussed in some of the previous sessions. I wanted to make a point about the importance of when we think about how to prepare health systems that we need to have also put evidence to help us understand which treatment and approaches are more appropriate in different contexts and settings. And part of that requires that we have a good understanding of the cost effectiveness of the different treatment opportunities that we have and that we need that this information is also available in this type of research and evidence is available for low- and middle-income countries because the structure of the health systems and the relative cost of different options are very, very different in different parts of the world.

And quite often we will only have evidence from high income countries, then that led us to think that yes this treatment is cost effective in the UK therefore everybody in South Africa should also be accessing it. But it may be that in South Africa there are, because of the different prices of different types of care, this is not at all the case. I'd like to make a strong plea that whenever we make decisions or we make recommendations about adoption of treatment approaches in different parts of the world we're careful to be using data and information that is appropriate to the context.

And the second issue I wanted to raise is that some of the findings that are emerging now through STRiDE looking at the care pathways available to different segments of the populations in seven middle income countries. And in many countries what we're dealing with is with people who go to the faith healer, they don't even go to primary cab. So here we're talking about people having a blood test as a cheap option. Actually, there are many steps in many parts of the world before a person with dementia will reach even the opportunity of having a blood test. And there's a lot of work to be done in these countries to get to this point, and I just wanted to flag that up. I know it's come out also in some of the other comments by other people I just have to raise this again. Thank you.

societal level. eg. Is it more cost-effective to develop support systems, improve the capacity of primary care clinicians to follow-up the evolving needs of PwD or to invest in bio-markers ?

Professor William Reichman
A paper on the superior predictive value for MCI using the Cogniciti Brain Health Assessment vs. the MOCA will be published (open access) in the next edition of the "Journal of Gerontology: Psychological Science". The data will also be presented virtually at AAIC and CTAD this year.

Dr Adelina Comas-Herrera
I agree with @ george, there are huge opportunities to reach people in LMICs, both for supporting detection and for offering support

Dr Peggy Hamburg
Chair, American Association for the Advancement of Science and former Commissioner, US Food and Drug Administration (FDA)

Thank you. Two important issues to be explicit about as we think about this. Kate Possin, you're next thank you.

Dr Katherine Possin
John Douglas French Alzheimer's Foundation Endowed Professorship at the UCSF Memory and Aging Center

It's great to be here with you all today. I'm a neuropsychologist at the University of California, San Francisco, where I do both work on digital diagnostics using TabCAT, the brain health assessment and supportive care models like the care ecosystem. And perhaps because I have a foot in both camps of diagnostics and care models, I have come to observe that there is an artificial dichotomy between these areas of research and policy, with some folks focusing on diagnostics and others on supportive care as if they need to come in that order for the patient.

And I think it's time that we focus on integrated care models that are scalable that start with early detection. I think we need care navigation programs, supportive care that focuses both on the person with cognitive impairment and their caregiver from early stage to provide an additional layer of support to primary care. We know that this type of supportive care can improve quality of life for people with dementia and improve quality of life wellbeing for caregivers as well, while reducing health care costs.

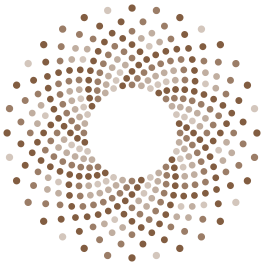
And it can be delivered in a scalable way. It can be delivered in a telephone-based format by trained dementia care navigators who are supported and supervised by licensed professionals from hubs where these specialists can work. I would like to propose that we think about integrating supportive care with early diagnostics to try to move patients, including patients from health disparities populations, through the pipeline to support earlier, more accurate diagnosis while always attending to quality of life.

Dr Peggy Hamburg
Chair, American Association for the Advancement of Science and former Commissioner, US Food and Drug Administration (FDA)

Thank you. Sean Kennelly.

Professor Sean Kennelly
Consultant physician in geriatric and stroke medicine, Tallaght University Hospital

Hi. And thank you for a really informative discussion. I'm a geriatrician based on Tallaght University Hospital in Dublin in Ireland, and I suppose I just really want to make



Professor Paulo Caramelli
Excellent point or suggestion Isabelle!

Professor James Rowe
There is a potentially valuable connection between progress in LMIC countries and better inclusivity & diversity in European and US studies

Dr Adelina Comas-Herrera
Agreed @James!

Professor Adesola Ogunniyi
I agree James

Gustavo Alves
Primary care, chronic disease!

Professor Sean Kennelly
I think it's an integrated care model which will have elements in primary and secondary care

comment as this has given us the opportunity to really present Alzheimer's disease, and it'll be viewed through a totally different prism by the general population, by other clinicians, and one of our first challenges is winning those hearts and minds about people viewing Alzheimer's disease as a pathology-based condition. And that's going to be one of our first challenges and even for primary care physicians and things like that and have that education piece and how we bring people along that pathway is going to be very important.

I think the other thing is as a stroke physician also, I think there's another awful lot for us to learn from other conditions that we should really take stock of. I think when we look at stroke of where stroke thrombolysis medicine was a therapy that was for a small number of people, really 10 to 15% of people, but on the back of it, we managed to develop stroke units, which made a seismic change towards the overall care paradigm for people with stroke. And in that context, I think these new therapies are an opportunity for us to present brain health clinics and that brain health piece as an adjuvant therapy, regardless of whether or not somebody is getting treatment.

We really should be thinking about that narrative around what Gill Livingston and her colleagues have really presented about the importance of brain health. While we're having a discussion about molecular therapies, I think is also MS also presents us with a learning opportunity for where we had disease modifying therapies, some people who are eligible, other people who are not, and there is a slight inequity that can creep into the pathways for people with the same condition as to whether or not you meet criteria for the disease modifying treatment or if you don't, and the level of care and attention you might get if you're going into disease modifying treatment pathways. So we need to be cognizant of those lessons.

Then oncology. I think James mentioned it earlier on that the future in a decades time is probably that we have this group of people who are living with Alzheimer's disease and the other dementia subtypes with their pathological classification, where we may be looking at an infusion based, radiology based, very, very similar model of care to which cancer does today, that we learned the lessons that we did with cancer care, that we should really developing around a centre of excellence model and that we shouldn't really be going with an adhoc, "everybody does their own version" of this. I think that was some of the points that were coming through that we really should be probably promoting a centre of excellence model around the diagnostics and initiation of therapeutics, maybe then to decamp a hub and spoke type model as a delivery piece first, and also bearing a mind from oncology the importance of care and the other holistic aspects that were maybe a secondary thought as oncology evolved, and it's probably a closer relationship now than it was at the beginning.

Dr Peggy Hamburg
Chair, American Association for the Advancement of Science and former Commissioner, US Food and Drug Administration (FDA)

Well, thank you. Your comparison to multiple sclerosis is very interesting. I was also thinking about HIV AIDS, and it may be that early on, as new treatments and diagnostic and monitoring strategies become available, that centre of excellence approach is

Neil Drimer
Thanks so much for an engaging discussion

Dr Michèle de Guise
I would like to thank you for this fascinating conversation. It was a real privilege to be able to participate in this exchange.

absolutely crucial. It may become less so when we have new, better products and more familiarity and we sort of normalize use. But I think right now that is a very compelling argument you make. We got a couple more people hands up. Christopher Chen.

Dr Christopher Chen
Associate Professor, National University of Singapore

Good evening. Christopher Chen, a neurologist from Singapore. Really nice to be here. I just wanted to take up points that were made by Martin and Sean about dichotomy and about not neglecting patients that are already demented. In conversations I've had with my patients who have come to ask me about this new disease modifying treatment, the disappointment on their faces when some of them realize that they may not be the kind of patients that could benefit from this advance is actually quite dramatic. And I think that we can't allow ourselves to neglect patients who already have established dementia and neglect the need to continue to go and sort of see better treatments for them, both in terms of disease modification and symptomatic treatment. Thank you.

Dr Peggy Hamburg
Chair, American Association for the Advancement of Science and former Commissioner, US Food and Drug Administration (FDA)

Thank you. Let me see where we are on our list. I think, George, back to you.

George Vradenburg
Co-Chair, Davos Alzheimer's Collaborative

I just want to pick up a point to that line made about blood tests themselves as much of an advance that they are over current methodologies, they do not fully respond to the detection and diagnostic problems of low resource countries. Through our Davos Alzheimer's Collaborative we are using digital tests, at least for cognitive assessments we have picked a particular one, but Bill Reichman in the chat has mentioned others. Digital technologies are lower cost yet than blood and rely on devices and instruments which are the most penetrating technology in the world. And my guess is that Adelina's Jamaican faith healers carry a cell phone.

So I do think that we need to understand better the quality of these digital assessment techniques. Some are already exceeding the quality of MOCA in terms of their ability to detect a cognitive decline. They have the added advantage of being a more continuous mechanism of assessment, as opposed to assessments done periodically by going to a clinic. Obviously, the problem of understanding the pathology of the disease, even if you're in cognitive decline, is another question.

And we're going to have to get at that problem as well with much different techniques in low resource countries than in high resource countries. As we know, 90% of the genetics

work in Alzheimer's has been done in Western European ancestry populations when 90% of the world is not Western European legacy. So we're going to both find differential tools for cognitive impairment, differential protocols for assessing longitudinal cognitive change (impairment) in different parts of the world, but we're also going to need completely different techniques for both the detecting and then treating those with cognitive impairment, no matter how (what) it's caused elsewhere in the world.

Dr Peggy Hamburg
Chair, American Association for the Advancement of Science and former Commissioner, US Food and Drug Administration (FDA)

Well, thank you. And I think you remind about a lot of important issues about how new technologies get adopted, how we think about these advances, the recognition that we need to make sure that we fully understand the context of disease in different places and under different conditions around the world. And at the end of the day, that we really try to help support health system readiness and public patient and healthcare provider awareness or appropriate uptake during this really exciting transformational time that brings with it all kinds of opportunities, but also major challenges.

As we come to the end of our time, I wanted to just go back, if I may, and I didn't warn them ahead of time to our presenters just to give a very brief concluding thoughts. Just a couple of minutes each, either a couple key takeaways from or discussion or points you want to make sure are part of the ongoing work of this organization. So, Joanne, first to you.

Dr Joanne Pike
Chief strategy officer, Alzheimer’s Association

Thank you. I think the few things that I would highlight, and I would actually start with something that you mentioned, Peggy, was the need for health services related research to make sure that we're establishing protocols around diagnosis and models of care that really can integrate, as Kate mentioned, across the full spectrum from early detection through palliative care long term. I think a key piece to this is we know there are models from other chronic diseases that work within treatment to make sure that health equity does not get exacerbated long term when a treatment is initiated. And it's a matter of using those same types of navigation models to make sure people do not fall through the cracks long term. So thank you for the opportunity to add that, and I appreciate the opportunity to be here.

Dr Peggy Hamburg
Chair, American Association for the Advancement of Science and former Commissioner, US Food and Drug Administration (FDA)

Well, thank you. Now, Fiona, over to you.

Fiona Carragher
Director of Research and Influencing, Alzheimer's Society

One of the area that really struck me is a point in that Kate made, which is about we can't disaggregate the diagnosis from the kind of the care support piece because not everybody who is diagnosed will have access to disease modifying therapies if we're going to stratify at an earlier stage. So really thinking about how we have that joined up care support pathway, I think again, some of the comments Adelina made reflect what we're seeing in the UK in that we've got to think about this being as equitable and inclusive as possible. We have to think about the diverse communities that we are all serving across our countries. And I think the final point I would make and particularly if we think about if we look to the transformation in HIV AIDS, is that we should really think about the voice of the patient in here and how we bring together communities that can advocate at the strongest level to ensure that that we are taking new diagnostics and novel treatments into care as fast as possible. I think the voice of the patient is something that we probably haven't touched on as much, but I think is going to be key to this going forward.

Dr Peggy Hamburg
Chair, American Association for the Advancement of Science and former Commissioner, US Food and Drug Administration (FDA)

Well, thank you very much. And our last speaker, Maria Tome, welcome your observations and thoughts.

Dr Maria Tome
Senior Scientific Officer, Product Development and Scientific Support Department, European Medicines Agency (EMA)

Thank you so much for inviting me, excellent ideas and thank you for the open discussion. I say we are really scientific advisors, we hope that the policy makers and the rest of the groups, but we are you have here a huge community of people with a lot of expertise and I think we really need to think beyond cognitive decline and really move forward. And people mention HIV, I worked in HIV prevention. And I can tell you that, again, biomarkers are very important. Thank you so much for having me, thank you.

Dr Peggy Hamburg
Chair, American Association for the Advancement of Science and former Commissioner, US Food and Drug Administration (FDA)

Well, thank you. And I think this has really been an excellent discussion and a lot of rich conversation in the chat as well. I did just get a note one more person wants to say something. Charles Scerri, so quickly and then we will conclude this session with my turning it back to Howard.

Professor Charles Scerri
Professor of Dementia Studies at the Faculty of Medicine and Surgery, University of Malta

Thank you very much. Thanks for the invitation and just a brief observation, because an important issue which has been not mentioned really so far, we definitely policy in leadership making the fight against Alzheimer's disease and dementia a priority. Unfortunately, only a handful of countries so far worldwide have a dedicated dementia plan and healthcare system readiness should form an integral part of such plans and policymakers obviously need to come on board in order to be successful. Some countries have succeeded in just doing that, but other countries still lack momentum, and they know, and they are fully aware that they have increasing numbers of individuals with dementia within their countries.

If Covid taught us something, it taught us that we can find ways with which we can move forward. How can we transfer what we have learned in Covid to dementia, in terms of research and in terms of policy? Another thing is that we also need to communicate with them in a language they can understand and that means policymakers and the general population as well. For example, following the FDA approval of aducanumab, a lot of people contacted me trying to understand what this was all about.

Basically, they couldn't understand what was actually happening, whether it's good for them or not. So if people cannot understand, how can we be confident that they would be those same people to participate in future clinical trials? So it's very important to find a common language with which we can communicate with these individuals and with policymakers, because what we have said so far depends a lot on policymaking as well in order to be successful. Thank you very much.

Dr Peggy Hamburg
Chair, American Association for the Advancement of Science and former Commissioner, US Food and Drug Administration (FDA)

Well, thank you. And unfortunately, we have come more or less to the end of our time. We could, I think, have a lot more discussion on this topic, and I think we probably will, because this issue about health system readiness is so essential to our success in dealing with Alzheimer's disease across its life cycle and all of the many manifestations. And hopefully, all of the opportunities we'll have in the future to actually improve care in meaningful and enduring ways. Let me turn now to Howard to finish up our session. Thank you.

Professor Howard Bergman
Professor of Family Medicine, Medicine (Geriatrics), and Oncology, McGill University

Thank you, Peggy. Just a few remarks for this excellent, excellent discussion. And I'm thinking back to the days of the first cholinesterase inhibitors. Whatever we thought

about their effectiveness, how they promoted and stimulated a change in our healthcare systems and our ideas about Alzheimer's disease and the development about Alzheimer plans and in many of our dementia strategies in many of our countries. And I think the present situation of the advent of biomarkers and disease modifying medications, whatever you think of the effectiveness of the present one on the table, I think it's going to do the same stimulation of thinking of our health system readiness.

One of the important issues, and there are many important issues that were raised in the discussion, I want to comment on two. Where is care going to be anchored? Is it going to be anchored in specialty care or in primary care? And this is the debate we're seeing in many countries. In my country, it's anchored in primary care, so the diabetes model versus the cancer model. I think there's been different points of view that have been expressed in this meeting, but that's going to be I think one of the important issues. We have taken the point of view in Canada of saying anchored in primary care with the support of specialty care, and finding ways and means to empower and enable primary care to detect, diagnose and treat Alzheimer's ease with support of specialty care. So that's an issue I think that was raised with the idea of centres of excellence versus primary care. And I think that's going to be an important discussion.

The second thing I think that has been said and that reset is the importance of implementation policy and economic research, as rigorous as all the basic science and drug discovery research. And it's as if we have we shouldn't have to wait to have these medications ready to go to say, okay, now we have to do this research, and I think it has to go hand in hand. And hopefully when we talk about research funding, we're going to talk about the research funding for implementation research, rigorous implementation research. Finally, I think we need to have dialogue in each of our countries and at an international level as Adelina said on this issue, on how we have to adjust our Alzheimer plans, but bringing together the major stakeholders, people living with dementia, clinicians managers, industry, the decisionmakers, etc to continue this discussion as we move forward.

And hopefully this will not be the last discussion, but hopefully this will stimulate discussion in many of our countries. Thank you to all of you. I turn it over back to Peggy or to Lenny, to perhaps Peggy for some closing comments, and to Lenny to close the meeting.

Dr Peggy Hamburg
Chair, American Association for the Advancement of Science and former Commissioner, US Food and Drug Administration (FDA)

I think I'll turn it right back to Lenny so that we can end on time.

Lenny Shallcross
Executive director, World Dementia Council

Great. Thank you, Peggy and Howard and thanks to the speakers. There's been a lot of talk about HIV. And there's a great Instagram account, for people who are on Instagram, called the AIDS Memorial. And I suggest you go and look at it, because it's postings by the partners, the siblings, friends, and even parents of people who didn't survive the pandemic. And one of the great stories in it is the search for treatment and the desperation that the people living with HIV had before the FDA did the first drug approval. And it's a great thing to reflect on, that people really want treatments. The story of people who campaigned in the 1980s on HIV and many of whom went on to die before treatments arrived was "give me access to treatment and I'll try it". So that's an aspect of the HIV story that was beautifully told and recorded online. And there are many others that are worth looking at. With that brief observation encouraging you all to look at the Instagram, I'd like to thank you all for participating, we'll send round a transcript of the meeting for your comments before we publish online. We'll have a series of essays too. On that note, I wish you a good morning, good evening and good night, and enjoy whatever is left of your day. Thank you very much.

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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