

Summit 2021

Looking to the future:
The dementia landscape



**World Dementia
Council** Leading the Global Action
Against Dementia

Are we on track?

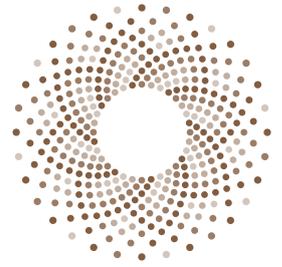
Transcript of a session from the
World Dementia Council virtual summit
6 December 2021

Johnson & Johnson

**SCIENCE
FOR MINDS**

Lilly

Chairs



Dr Maria Carrillo

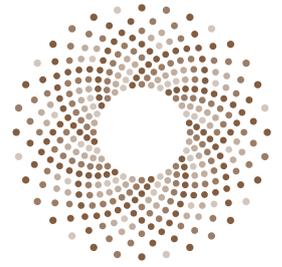
Maria Carrillo is chief scientific officer at the Alzheimer's Association (US), setting the strategic vision for the Association's global research program. Dr Carrillo has published extensively on early diagnosis and biomarker standardization efforts, as well as on the global challenges to progress for research in Alzheimer's and dementia. She is a co-author of the "Appropriate Use Criteria for Amyloid Imaging," published by the Society of Nuclear Medicine and Molecular Imaging and the Alzheimer's Association. Dr Carrillo earned her PhD from Northwestern University's Institute for Neuroscience and completed a postdoctoral fellowship focused on Alzheimer's brain imaging and risk factors at Rush University Medical Center in Chicago.



Professor Philip Scheltens

Philip Scheltens is professor of cognitive neurology and director of the Alzheimer Center, Amsterdam University Medical Centers (The Netherlands) and member of the World Dementia Council. His main clinical and research interests are Alzheimer's disease, vascular dementia, frontotemporal dementia, magnetic resonance imaging, PET imaging and fluid biomarkers. He is active in the field of biomarkers and clinical trials and has been the national principal investigator for many studies, including phase 1-3 multicenter clinical trials. He founded and directs the Alzheimer Center since 2000, from which over 70 PhD theses have appeared since. In 2013, he co-founded the Dutch national plan against dementia (Deltaplan Dementie) and serves as the chair of its board.

Speakers

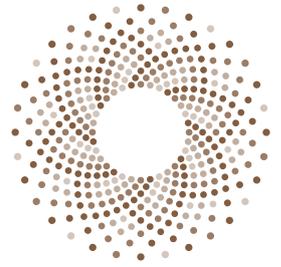


Dr Richard Hodes

Richard J. Hodes, M.D., is the Director of the National Institute on Aging (NIA) at the National Institutes of Health (NIH). Dr. Hodes, a leading researcher in the field of immunology, was named to head the NIA in 1993.

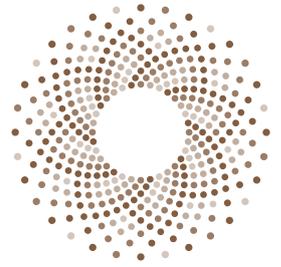
The NIA leads the Federal effort supporting and conducting research on the biological, clinical, behavioral and social aspects of aging. Dr. Hodes has devoted his tenure to the development of a strong, diverse and balanced research program. This has led to new and innovative ways to conduct research, share data and translate findings into practice. Basic biologic research is examining genetic and other factors influencing aging, how they affect longevity and the development of age related diseases. Research in geriatrics is uncovering new ways to combat frailty and improve function with age. Behavioral and social research is deepening understanding of the individual behaviors and societal decisions that affect well-being. Dr. Hodes also directs the Federal effort to find effective ways to treat or prevent Alzheimer's disease, as the NIA is the lead NIH institute for this mission. Cutting edge research conducted and supported by the NIA, often in collaboration across institutes at the NIH, has helped to revolutionize the way we think about Alzheimer's disease and related dementias. Studies in genetics, basic mechanisms, imaging and biomarkers have spurred the development of potential therapies aimed at a variety of targets and the testing of interventions at the earliest signs of disease.

Dr. Hodes' research laboratory in the National Cancer Institute focuses on the cellular and molecular mechanisms that regulate the immune response. A graduate of Yale University, Dr. Hodes received his M.D. from Harvard Medical School. He is a Diplomate of the American Board of Internal Medicine, a member of The Dana Alliance for Brain Initiatives, a Fellow of the American Association for the Advancement of Science and a member of the National Academy of Medicine at the National Academies of Sciences, Engineering and Medicine.



Professor Mary Sano

Dr. Mary Sano is Professor of Psychiatry and the Director of the Alzheimer's Disease Research at Mount Sinai School of Medicine. She is also the Director of Research and Development at the Bronx Veterans Administration Hospital. Currently she is the director of a national multi-center study known as CLASP (Cholesterol Lowering in Alzheimer's Disease to Slow Progression). Dr. Sano is a neuropsychologist by training and has been involved in designing and conducting clinical trials for Alzheimer's disease, Parkinson's disease, and mild cognitive impairment of aging. In 1989 she received the Florence and Herbert Irving Clinical Research Career Award to develop methodologies for the assessment of therapeutic agents in Alzheimer's disease. She directed the first ADCS multicenter trial of vitamin E and Selegiline, treatments which delayed the clinical progression of Alzheimer's disease and in 1998 she received the Veris Award for this study. In this study minority participation was more than double that of any other clinical trial for this disease. Her research interests are in clinical trial design and the impact of pharmacological treatments on the functional abilities of individuals with cognitive impairment. At present she is the director of a new clinical study to determine if home based assessments can be used assess treatments for the prevention of cognitive loss and dementia. She has also developed tools to assess the economic impact of subtle cognitive changes in elderly subjects. Other areas of interest include the role of depression in cognitive impairment and dementia, womens' attitudes about prevention of memory loss, and measuring quality of life in diseases of aging. She is also the recipient of the Alzheimer Association grant to study Resveritrol, one of the active ingredients in red wine. Dr. Sano has also conducted work characterizing the cognitive impact of head injury, Sickle Cell disease, and mitochondrial disorders.



Dr Paul Stoffels

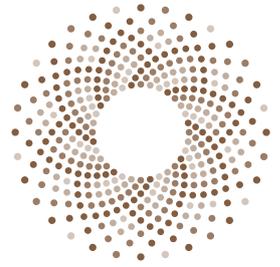
Paul Stoffels is a visionary leader who inspires and drives transformational innovation to bring years of life and quality of life to millions of people around the world. Paul spearheads the Johnson & Johnson research and product pipeline by leading teams across all our sectors to set the companywide innovation agenda, discovering and developing transformational healthcare solutions. He also is responsible for the safety of all products of the Johnson & Johnson Family of Companies worldwide, and steers the company's global public health strategy to make innovative medicines and technologies accessible in the world's most vulnerable communities and resource-poor settings. Paul's commitment to fueling innovation and finding the best science, wherever it exists, is the driving force behind the launch of Johnson & Johnson Innovation in 2013, which he now leads to foster science and technology through strategic partnerships, licensing and acquisitions. Paul also oversees JJDC, the oldest corporate venture fund in the life science industry.



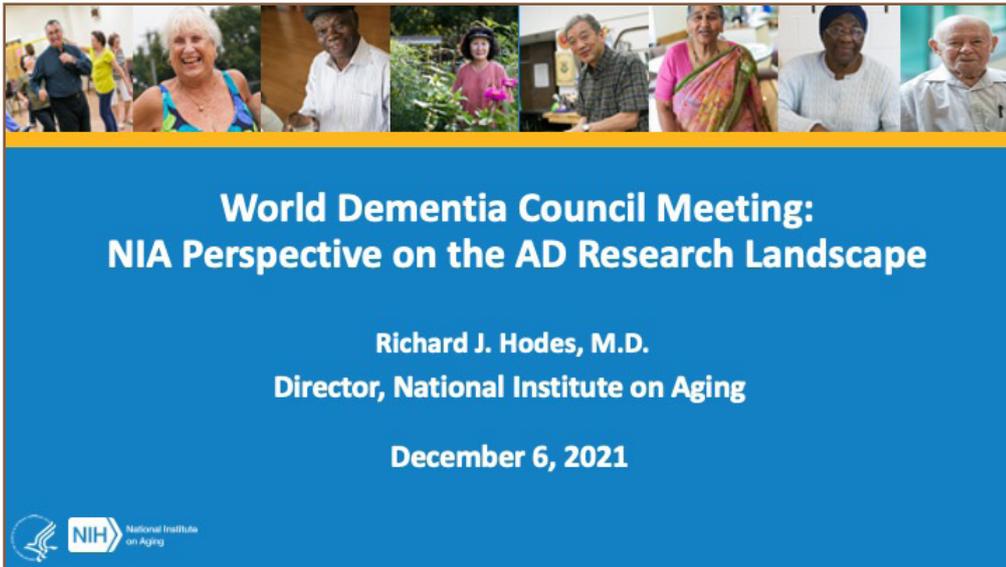
Professor Julie Williams

Julie Williams is Professor of Neuropsychological Genetics at Cardiff University and the Chief Scientific Adviser for Wales since 2013. She is one of the world's leading contributors to Alzheimer's research. Williams is Professor of Neuropsychological Genetics and Head of the Neurodegeneration section of the Medical Research Council Centre for Neuropsychiatric Genetics and Genomics at Cardiff University. She is a former Chief Scientific Adviser to the Alzheimer's Research Trust, and in 2012 was appointed a CBE for her contribution to Alzheimer's research. She is a Fellow of the Learned Society of Wales. Professor Julie Williams was Chief Scientific Adviser for Wales from September 2013 to September 2017, the second person to hold the post. Edwina Hart, Minister for the Economy, Science and Transport, said "She is a great role model for women in science ...Her networks of national and international scientists will be crucial in opening the doors for Wales". Williams' research aims to identify and characterise genes which confer a risk of developing psychological and neurodegenerative disorders such as Alzheimer's disease, developmental dyslexia, and schizophrenia. She has received funding from the Wellcome Trust, MRC and the Health Foundation

Discussion transcript



Dr Richard Hodes
Director, National Institute on Ageing (NIA)



Thank you for opportunity to speak briefly about state of Alzheimer’s research in the United States particularly with NIA support and the prospects for the future. This is a particularly exciting time.

Chat function

The chat function was available throughout the session for participants to ask questions of panellists and to hold discussion amongst each other. It began just under 10 minutes into the session and is displayed below. It does not necessarily correspond with the adjacent transcript in this document.

Growth of AD and ADRD Research Spending at NIH

NIH Funding History for AD/ADRD Research (Dollars in millions)

Research/Disease Areas	FY 2015	FY 2016	FY 2017	FY 2018	FY 2019	FY 2020	Difference – FY 2015 to FY 2020
AD/ADRD	\$631	\$986	\$1,423	\$1,911	\$2,398	\$2,869	4.5-fold increase
Alzheimer’s Disease	\$589	\$929	\$1,361	\$1,789	\$2,240	\$2,683	4.6-fold increase
Alzheimer’s Disease Related Dementias¹	\$120	\$175	\$249	\$387	\$515	\$600	5.0-fold increase
Lewy Body Dementia	\$15	\$22	\$31	\$38	\$66	\$84	5.6-fold increase
Frontotemporal Dementia	\$36	\$65	\$91	\$94	\$158	\$166	4.6-fold increase
Vascular Cognitive Impairment/Dementia	\$72	\$89	\$130	\$259	\$299	\$362	5.0-fold increase

¹ The ADRD row reflects the sum of the three existing RCDC categories: Frontotemporal Dementia, Lewy Body Dementia, and Vascular Cognitive Impairment/Dementia—where duplicates are removed.

https://report.nih.gov/categorical_spending.aspx

George Vradenburg

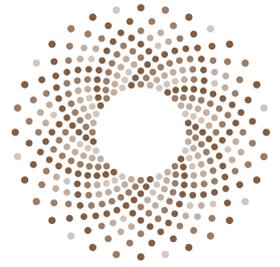
Dr. Hodes, what is your personal assessment of the prospect of our achieving the goal of ‘preventing and effectively treating Alzheimer’s’ by 2025 set by the US government in 2012?



Mathew Varghese

Also possible is looking at genes. We

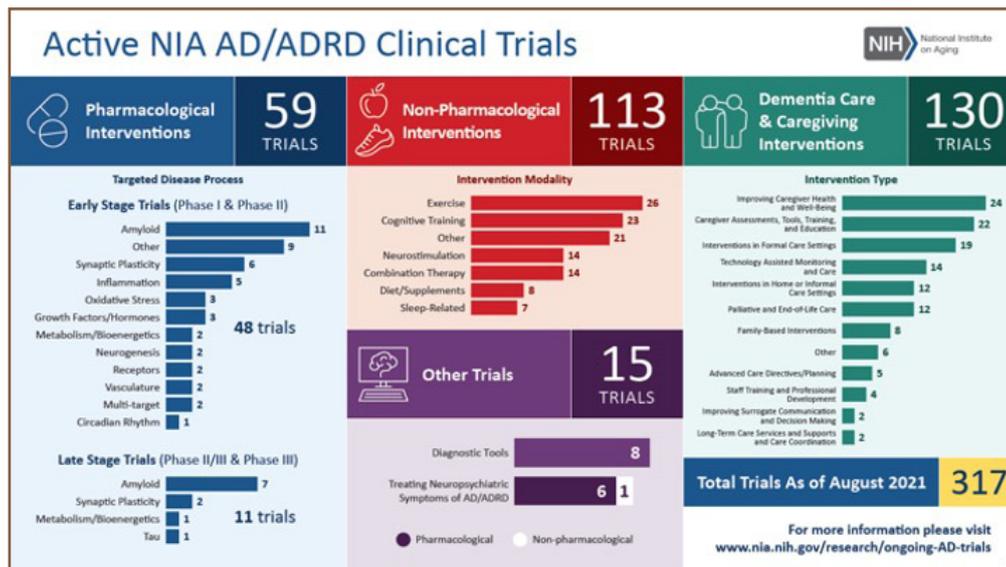
I will start with an outline, to give you a sense of the remarkable trajectory of support at NIH, National Institute of Health in the United States, over the past few years for Alzheimer’s and related dementia research.



You can see from the top line which is the total for research in the AD and related dementias that from 2015 through 2020 fiscal years the increase has been from \$631 million to \$2.9 billion.

Fiscal year 2021 of course has been recently completed but the final data is not here. When that is complete the total will rise to well over \$3 billion dollars. And if we look at as a fold increase, through fiscal year 2015 through to 20/21 that is greater than a 5-fold increase for Alzheimer's disease, for the related dementias, and for each of the dementia's categorised in our national plan. Lewy body disease, frontotemporal dementia, and vascular cognitive impairment all saw similar rates of increase.

have fairly advanced ipsc and cell culture research which is very much possible as it is not too expensive.



Jacqueline Hoogendam

Global funding of research is not easy. At JPND we try to increase the number of participating countries worldwide. To engage as many countries in a common research strategy and joint funding of international research.

As one way of summarising a compound of the progress that has been made, I would just show you this summary slide which illustrates the current ongoing clinical trials supported by NIA. There are some total of 317 trials as of past summer. And there's a diversity of topics. As you'll see some 39 pharmacologic interventions, 113 non-pharmacologic, and there's a large number 130 trials of dementia care and caregiving interventions as well.

George Vradenburg

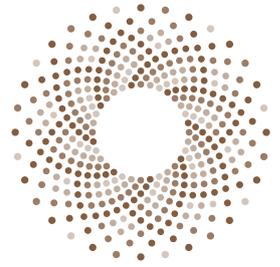
@Jacqueline, Is PEPFAR a good model? Or the Global Fund?

I would just point out the level of the diversity of targets engaged in the pharmacologic interventions for example. If you look at the early-stage trials, phase one or phase two. providing the newest targets, the newest approaches, translating ultimately to more definitive trials, of the 48 trials in that category being supported just 11 are in the amyloid targeting group. The diversity of targets illustrated here from synaptic plasticity to inflammation shows the richness of targets that are being discovered and put into clinical trials. For the later stage trials still Alzheimer's disease and amyloid predominates but this will be evolving as the early-stage trials and new targets come to fruition.

Cornelia van Duijn

Agree with Julie - the path of genetics building upon cohorts world wide and infrastructures but above all work together by solving data harmonization and analysis. And interpret and validate findings

You can see for the non-pharmacologic interventions there's also a great deal of diversity as there are for dementia care and caregiving interventions. This is as important as we deal with the large number of people living with dementia and those who care for them, even as we attempt to provide better interventions to treat and prevent.



Importance of Diversity

- Nationally, risk for AD/ADRD compared to non-Hispanic white Americans is
 - **2x** for Black/African Americans
 - **1.5x** for Hispanics/Latinos
- NIA recognizes the importance of and strives to ensure diversity in study participants and in the research workforce.



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Diversity is important across all of NIH, across all our efforts, and certainly in ADAR research it is clearly important. To illustrate it here, the well-established increases in risk for Alzheimer’s disease and related dementias in black African Americans and Hispanics compared to non-Hispanic and whites. To recognise this we’re taking efforts, as yet not adequately successful I think, to increase the participation of diverse populations across all our studies including in clinical trials.

before publication.



Peggy Hamburg

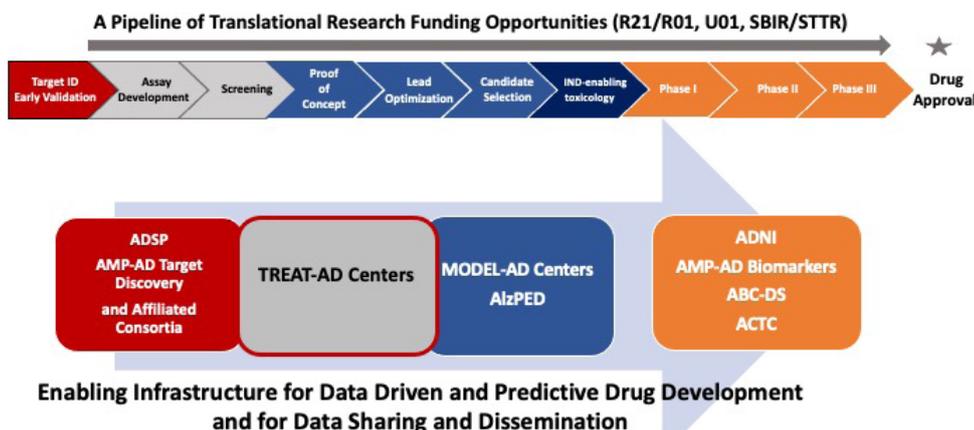
Aren’t both PEPFAR and Globl Fund, more about making medical products available where needed than collaborative research? I am sure there are important lessons to be learned from them bout how to successfully develop and run such programs however



Howard Bergman

Is there a place for open science in this discovery process? Or for at least part of the discovery process?

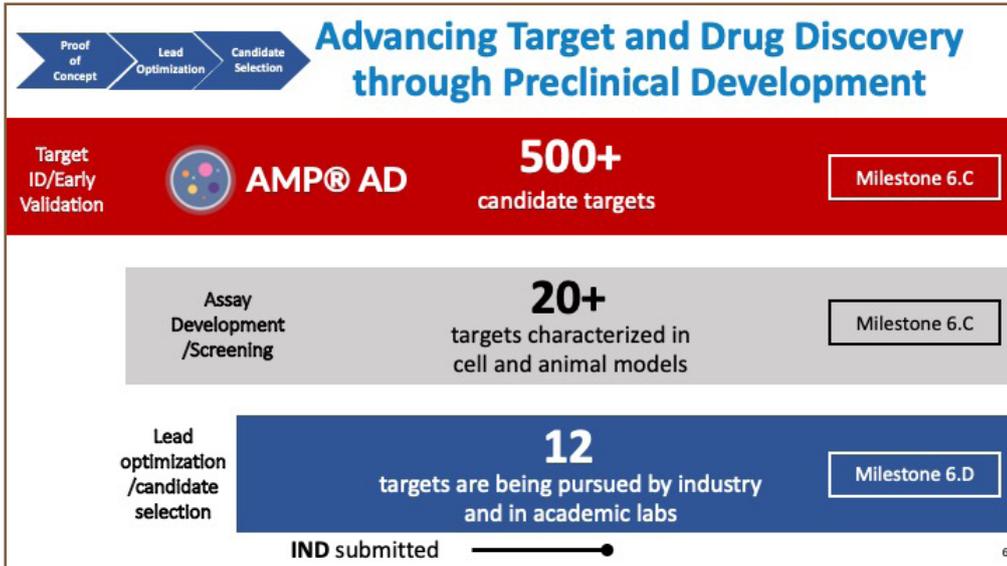
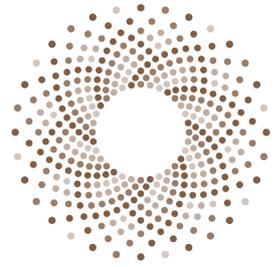
Diversifying the Therapeutic Pipeline and Enabling a Precision Medicine Approach to Drug Development



An illustration of the spectrum that we’re engaged in, ranging from early target identification through to validation into clinical trials is illustrated here. This is a continuum. But to draw your attention to the bottom portion of this slide, we have made every attempt to put together an infrastructure to minimise the barriers, to minimise the gaps, at each stage and level, from the earliest target identification through to clinical trials. It’s been critically important to do that in order to enhance the pace at which we translate early discovery into progress.

Susan Kohlhaas

I think there is value in global funders working together to understand the research gaps. At the very least, more coordination across funders means that we’re able to prompt thinking on data sharing, diversity and reproducibility.



As an example of this kind of progress, the funnel from early discovery onwards, I'll show you this slide showing the outcome of one of our efforts the accelerated medicines partnership for Alzheimer's disease. This is a remarkable partnership really of public and private sector, federal agencies, academia, philanthropies and importantly private sector and pharma, biotech as well. And one of our goals was to identify early targets, some 500 targets identified. By consensus of experts from all spectrums looking at the most promising of those and further develop them, now up to 20 have passed through the early stages of characterisation in cell and animal models leading to some 12 now at the stage of optimisation in industry and academic labs for target identification and selection.



Miia Kivipelto

Thank you Mary for highlighting the importance of various targets and involvning patients.



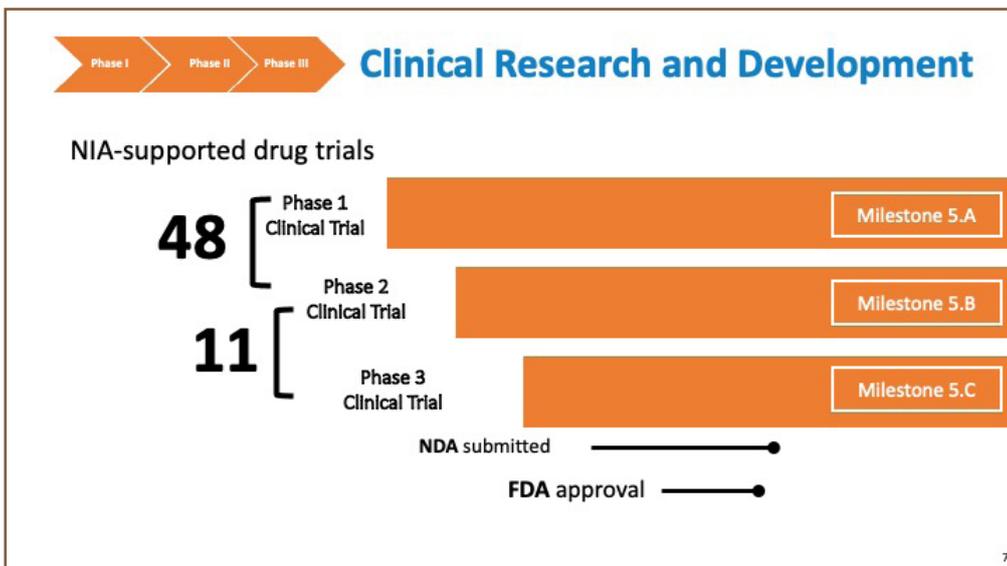
Jacqueline Hoogendam

The NL government looked into a comparison with HIV/AIDS initiatives. It wasn't the right moment 2 years ago. And now all MOH's have their focus on COVID. Perhaps more possibilities in the near future. As JPND vice-chair I will focus on bilateral discussions for the moment. Let's hope for better days!

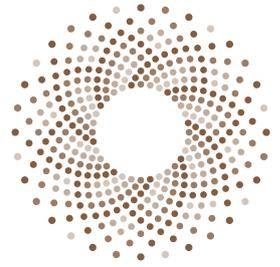


Carol Brayne

Dr Hodes, you need to incorporate what this means - multiple targets following regular diagnostics applied to asymptomatic populations, with polypharmacy added to the large number of medications folks



The NIA supported drugs trials just illustrated here. There are 48 phase one clinical trial, 11 phase 2/3. And as we work through this funnel there will be increasing numbers that are under submission for NDA and ultimately, we hope, for FDA approval.



Recent Advances in Biomarkers for Alzheimer’s

- The **first commercial blood test of AD**, PrecivityAD, became available to doctors for use with patients in 2020. NIA supported this work from early foundational research through test development.
- In 2020, the FDA approved the **first PET tracer for tau imaging**. NIA supported a key study used to validate this biomarker.
- In 2021, an NIA-funded study identified **ptau-217 as the more accurate marker of AD in diverse study participants**. (Brickman, A.M. et al. (2021). *Alzheimers Dement.* 17(8):1353-1364.)



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In terms of biomarkers, I want to point out this has been critical to progress in understanding the disease and to tracking the effectiveness of interventions. There have been some important discoveries over this past year and 2020. The first commercial test for Alzheimer’s disease became available, on the basis of research supported by NIA across NIH. In fiscal year 2020, FDA approved the first PET tracer an important breakthrough as well. And in 2021, the current year, NIA funded studies comparing multiple candidate markers show that one very promising marker was ptau217 specifically as an accurate marker of AD, in diverse importantly, study populations.

are already taking. This is why it is so very important to think about the implications (for people, for societies, for the climate) at this stage of excitement being expressed here. This needs to run alongside the work described at this meeting.



Maria Tome

Maria , very good point. With need cohorts to compare the current natural progress nowadays



Caleb Webber

Given the range of potential underlying pathologies and the benefits of power, is it time for greater globally aligned brain banking efforts with lifetime data linkage?

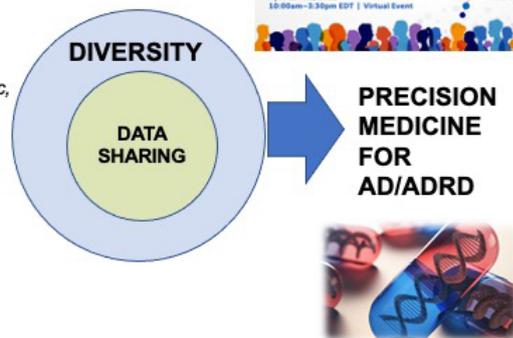


Maria Tome

We just qualify in EU a register for Hungtintong disease that collect information from pregnancy , consent,

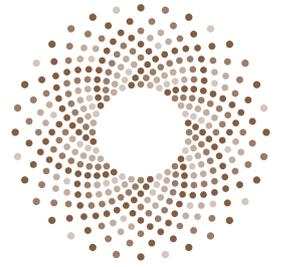
2021 NIH AD Summit- Summary of Gaps and Opportunities

- Expand multi-omic data to **globally representative and diverse populations**.
- Use **AI and deep learning** to improve personalized diagnosis, subtyping, prognosis and interventions.
- Combine clinical **endo- phenotyping, multi-omic and mechanistic research** aimed at deeper understanding of resilience, sex differences, metabolic, vascular, immune.
- Support **systematic evaluation of A/T(N)** and other emerging **biomarkers** (including omics biomarkers)
- Develop dynamic digital indices as the next generation of **digital biomarkers**



And then finally, just to illustrate the ongoing process that involves summits, all of you, the academic, research and advocacy communities.

Some of the overarching recommendations that came from the Alzheimer’s Disease Research Summit earlier this year included the expansion of multi-omic data on importantly globally representative and diverse populations. We’re making exceptional



progress, I think, in this area, moving to more and more international global studies with diverse populations. Other recommendations included use of AI and deep learning to improve the ability to diagnose, analyse, the increasingly complex data. To combine endo-phenotyping and multi-omic data research and mechanistic researcher. Looking importantly at sex individual differences and resilience. Looking at systemic markers of disease and developing digital biomarkers.



This then is a brief summary. I hope that illustrates the pace of progress, still frustrated by the fact that we don't have as definitive interventions, diagnostics, treatments and support as we would like. But I think we're enormously well on the way thanks to collaborative efforts across the country and across the world. I hope this provides a component to this conversation and we're happy to be an important part of this session.



Professor Philip Scheltens

Professor of Cognitive Neurology, Amsterdam University Medical Centers and Chair, World Dementia Council

Thank you very much Dr Hodes, this was a really excellent and very exciting overview and there's so much progress as you can see. Thanks to all the initiatives and the increase in the budget, which is extremely important, I would say!

I would now like to invite Professor Julie Williams from the Dementia Research Institute in the UK to share her perspective. Professor Williams is also the director of the DRI in Cardiff. Welcome and the floor is yours.

from 18 years old. Blood plasma biomarkers has improved are reliable and validated by csF or imaging



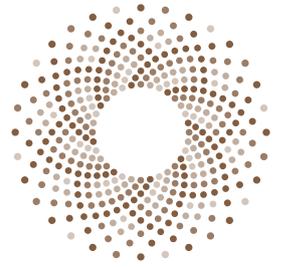
Adam Smith

Back to the earlier point.....A key element of improving diversity in trials and public participation will be to start with improving the diversity of researchers undertaking the work - better careers support. We know that the public are more likely to agree to participate in research when the researchers come from the same background - and equally those researchers are better able to understand the needs of their communities.



Susan Kohlhaas

I think registries can be a great tool for collecting longitudinal data,



Professor Julie Williams
Director, UK Dementia Research Institute

UK Dementia Research Institute

**DEMENTIA RESEARCH:
WHERE ARE WE NOW?**

Julie Williams CBE
Director UK Dementia Research Institute
Cardiff University

measuring clinical practice and helping monitor progression both with and without therapies. Doing something about this now, before we have a range of DMTs available would be timely.



Gloria Wong

we need parallel development in phenotype (not just diagnosis but symptoms, behaviours, cognition) research to maximise the usefulness of biomarker research

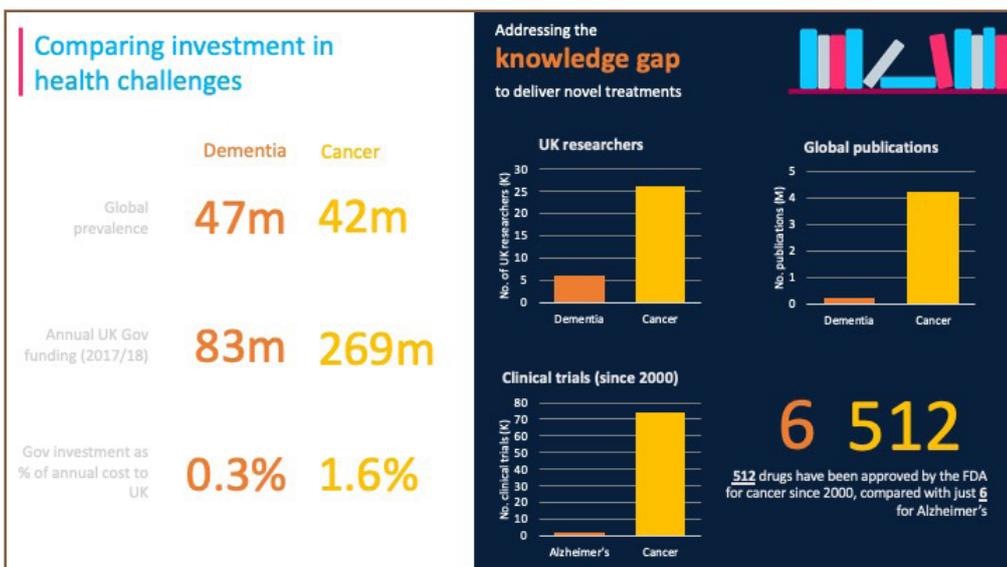
Thank you. Can I just say I've been involved in in this area of research for the last 25 years and I applaud the funders for their increase in in funding and some of the successes that we have seen in the last few years, especially in epidemiology, environmental impacts, genetics, biomarkers and remote care and assessment to name but a few.

But I think it's important for us to be realistic, to look across the piste and see where our success stories are and ask can we emulate them.

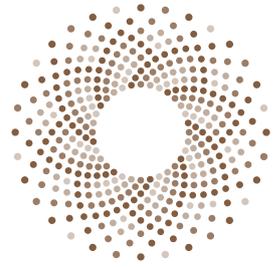


Allison Sekuler

Agree with @adam - very critical point. We also need to recognize the importance of building trust and relationships in diverse communities, and - as much as possible bring research into the communities instead of bringing community members into labs.



Cancer is an obvious success story. 50% of people now live with cancer and this is to a large part due to the fantastic research that's gone on in this area.



It's sort of comparative in terms of numbers to dementia as you see on the slide. But when you look at what has been achieved in cancer, with the investment they've had over a sustained period, I think we need to be a little more ambitious in the investments that we are making and continue to make in this area.

I've just given on some examples of the contrast because of that level of investment on the right of the slide. We probably need more researchers, this will result in more global publications, and something we're all aiming at in some way, more treatments and more clinical trials going forward.

Challenges and Barriers

- The dementias are complex diseases with multiple components and we don't understand enough about the causes/mechanisms
- Relatively few fully validated therapeutic targets
- Paucity of disease relevant models of common forms of dementia
- Poor knowledge of early stage disease
- Smart clinical trials with surrogate end points, extensively phenotyped subject pools to precision select on biomarkers (disease pathways, stage and predisposition).
- Replication of findings
- Global funding structure for global disease

So, what are the challenges? I think the dementias are complex diseases. We've heard this mentioned a number of times already today. It is multiple components and really we still don't understand enough about the causes and mechanisms, and if I had to put a number on it, I would say for the knowledge to take us to treatments we understand perhaps 40% of what's going on in Alzheimer's disease, perhaps 20% in Lewy body disorder, and perhaps 30% in vascular dementia to name but a few. And that results in, I think we can all agree, relatively few validated therapeutic targets to go forward. There's a lot of work in this area, but we're still way off where I think we should be aiming at for the future.

We have a paucity of disease relevant models for common forms of dementia. It's easy to model in various animals, etc, or induced pluripotent stem cells, the single gene variants. But the common forms of dementia are multicomponent and complex, and how can we model those? We are attempting some with the human models of extreme risk in in the Dementia Research Institute currently, and we'll see how those come off.

Another area that we know very little about is the poor knowledge of early-stage disease and really that's where we want to aim at. If we're going to prevent or delay these diseases, we really need to understand what is going on at the early stage and that's a big area for us to research into.



Nina Silverberg

Caleb, what are the impediments to implementing this suggestion?



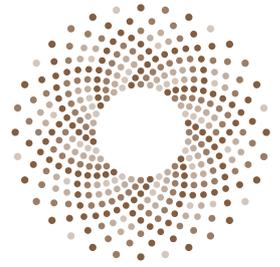
Jane Roskams

Julie Williams (and all!): Global collaboration of defined expert groups in dementia, EeG, biomarker physiology and cognitive testing from different countries Is exactly what the Global Brain Consortium is trying to do. We have begun with having a data platform that will support and enable the open sharing of data protocols and streams that will drive analytics.



James Rowe

Agree with @Susan. Registries linked to longitudinal data can facilitate in silico trials - optimising the design and stratification of



We've talked about clinical trials already. We do need to think about smarter clinical trials looking at surrogate endpoints. We know that there are different components and pathways, so we should be designing those endpoints for those pathways and not necessarily for disease as an endpoint. For this we need extensively phenotyped subject pools so we can precision select on biomarkers. And I don't think, even with all the work that is being done throughout the world, we don't have enough of those at the moment that are fully phenotyped that we can use to look at different stages of the disease and look at different aspects of predisposition, including a genetic risk, and we can also look at ethnicity, which Dr Hodes rightly mentioned earlier on.

A big issue I think going forward is replication of findings and a global funding structure for global disease. I think those are sort of entwined and I'll tell you a little bit about my experience. I work in the genetics of Alzheimer's disease. In our early days we thought we could find things with 1000 samples, and we worked individually. We realised we had to collaborate. It was difficult to collaborate across different countries, different funding systems. Many of our colleagues fell by the wayside because their grants were not funded because other people were doing it. But actually, we needed loads of people doing similar things. And I think the same can be said for other areas of research going forward from molecular biology to epidemiology, we need to be working together. I'm not arguing for one global research fund but a fund that can help fund those collaborations across different countries so that we can set up research beforehand where we can replicate. It's very difficult to do that across different countries and different funding structures, but I think it could be solved. And with that I'm going to stop and hand back to the chair. Thank you.

future in vivo 'real' trials.



Carol Brayne

@Nina - funding for long term cohort studies that are contemporary. MRC could have funded brain donation from our CFAS II studies and we applied multiple times for longitudinal follow up to try to understand the biology that underpinned the reduction in dementia prevalence we observed. It was rejected every time.



Professor Philip Scheltens

Professor of Cognitive Neurology, Amsterdam University Medical Centers and Chair, World Dementia Council

Thank you Julie, this was really important to identify the funding and knowledge gaps and also a look at the challenges. And there are many. It's worthwhile to consider them. Thank you for pointing them out.

We'll move on now and will go and listen to Professor Mary Sano from Mount Sinai to offer her thoughts. Mary the floor is yours.



Cornelia van Duijn

We need to understand the relationship between the genetic and epidemiological risk factors with blood based biomarkers - that will help us to dissect the complexity of disease discussed by Julie. We can do this most efficiently is stored blood samples in epidemiological cohorts with long-

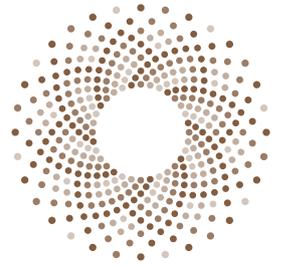


Professor Mary Sano

Professor of Psychiatry Ichan Mt Sinai, New York

I want to thank everyone for the invitation, and I want to address this question of are we on the right track?

Are we really diversifying our targets and our populations? It's exciting to see NIA point out that only 57% of funding is exclusively on Alzheimer's disease, however, an even higher percentage as shown is specifically targeting amyloid in their trials, as shown



on this slide. The question is how many more funded projects require amyloid, tau, and neurodegeneration as part of the diagnosis? It may be an inadvertent movement to not having the full diversity that we were hoping for.

I wanted to mention also the IDEAS study which was an incredible collaboration of the CMS, the only public health system in US that serves exclusively older adults, and the Alzheimer's Association. We were able to get dementia experts to tell us who would receive value from these important biomarkers. I think what's really interesting is even with all of this strength and influence of the experts, about 29% of those who registered never made it to the scanning and informing aspects telling us there's so much more work to be done.

Also, our current biological models are created on really homogeneous and exclusive populations. How can we really ask diverse populations to participate in research specifically designed without them in mind?

Another observation about how we can stay on the right track is to ask ourselves have we abandoned the scientific method in testing our hypothesis? The best science requires that we state our hypothesis and test it. And in so many trials, not only clinical trials but observational studies that include pharmacological as well as non-pharmacological interventions, we've seen midstream changes in almost every aspect of the design to favour a positive outcome, abandoning the principle of testing our hypothesis. I think these changes include variables such as the subject criteria and the dose outcome measures, etc. So, I think it's really important that we use the principles we have to be sure we collect the right information and use it.

I also want to ask ourselves the questions, are we really following the true leads? I'm just showing you on this slide a little smattering of studies that tell us that we may have targets that were not fully engaging. For example, in this community-based study from Mayo Clinic, what you're seeing is a very high level of neurodegeneration among those who are symptomatic and yet amyloid tends to be a target way more often than specifically neurodegeneration. And on the other side of my slide, I'm showing you some data that has indicated the real interaction between what we know how to measure are apolipoprotein E4 and outcomes in clinical trials that target amyloid. Are we really following that lead? Have we done enough to be sure we're engaging that information as we move forward with our research?

I just want to offer some considerations that might help us be more effective in staying on track. I think I really want to applaud the early presentations in this day's seminar for talking about the importance of sharing and harmonising data. But it's really not enough. We really need to include in sharing what we've learned: publication of negative results, identification of key modifiers and exclusions that may not be so transparent. We could legislate, or at least mandate this, from our colleagues and scientists.

I think another place where we need to be careful is the concept of targets. They're really helpful and have moved us forward, telling us very much about the ones that we can now measure. But they're possibly restricting if they are created from highly homogeneous and exclusive populations. Pathology agnostic approaches may be needed to truly engage these diverse populations.

term follow-up. This will be cost and time efficient.



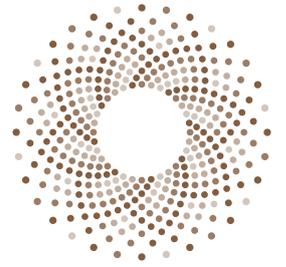
Allison Sekuler

Agree with @george: The remote and virtual based assessments would help tremendously in enhancing global research. Baycrest is leading a collaboration across the Toronto Academic Health Sciences Network creating mobile testing labs to do community based assessments (including neuroimaging and blood draws, etc). Would be terrific if we had a globally networked of mobile labs. We also are developing methods for low cost, in home neuroimaging, which could be done worldwide.



Miia Kivipelto

I think also the repurposed drug approach can help in finding the solutions. It is great



Finally, I think it's important to realise that we are now engaging people at earlier and earlier stages, and so it's really important to ask what do they care about, who do they trust, and can one really provide anticipatory consent? Do I know how I will think in 10 years about my care?

In summary, let me just say, are we on the right track? I think we're on a great track and it has had many, many successes, but I think we may need to provide more resources to ensure the best track for the largest community. With that I'm going to stop and turn it back over to you.



Professor Philip Scheltens

Professor of Cognitive Neurology, Amsterdam University Medical Centers and Chair, World Dementia Council

Thank you very much Mary that was really insightful and I agree completely with your concluding point. I think we all here today would agree with that. We're on the right track, but that track can be better and can be speed up with a little with more resources.

We're now moving from academia to the perspective of industry and to Paul Stoffels who is for a few more weeks, the Chief Scientific Officer at Johnson and Johnson. I say for a few more weeks because I'm sure that everybody knows he's retiring at the end of the year. And Paul, is also notable because he was very much involved in setting up the Council after the G8 dementia summit hosted in London back then in 2013, when David Cameron led the initiative and he has been a really, really great support ever since. So, thank you again, Paul for that, and also for all your hard work over the years, I'm going to invite you to give your perspective.



Dr Paul Stoffels

Chief Scientific Officer Johnson & Johnson

Thank you. A great symposium today with a lot of very productive discussion, on innovations and data and everything which is happening, and the progress made. I have a lot of respect for all of you of what you have done in the last 10 years, more than 10 years since the Dementia Council was started. I was part of it initially as an industry representative, we have gone a fairly long way since those first meetings in London, with the establishment of the Dementia Discovery Fund, with many clinical trial initiatives, biomarkers initiative, regulatory initiatives.

I wanted to just reflect for a few minutes on what happened in the last twenty months with Covid and how an emergency declaration and a global pandemic could move the acceleration of development of new products so much faster. It was definitely based on a very strong foundation which was in place before because many governments have been funding a pandemic preparedness, based on the 9/11 bioterror thinking.

It took industry, government and academia expertise and innovation, along with the regulators, all working together, and with government funding, to make this

that Part the Cloud is supporting also this approach (and several targets). And digital tools can really help,



Mathew Varghese

Registries are also expensive and difficult to get funds committed for 10 or 20 years. In addition due to migration and domiciliary transitions it is difficult to hold participants in these registries.



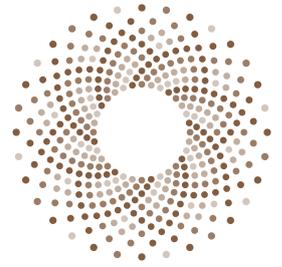
Allison Sekuler

We can also do much more to partner with companies that have commercially available sensing technologies to advance data collection. But we need mechanisms to integrate those data into shared databases



Hilary Doxford

My question does not relate directly to this session, but a few of the comments



covid response happen. But what was very important was that it was at a global level considered as a global crisis. And it still is. And suddenly, because of this, there was a completely different level of collaboration happening between all of the different partners and that was like quite remarkable.

If you look at what you had in place from investment pre-covid in platforms, BARDA had strong investments in viral platform, we had an mRNA investments from the Gates Foundation, but also SEPII was founded including investments from Gates, Wellcome, governments and supported by several industry companies. Suddenly you get Covid and then it all got on steroids!

Specific governments took rules on driving progress. For example, in the UK with Astra Zeneca in Oxford. We took the collaboration with the NIH, BARDA and J&J on a vaccine. And then what was very important is that industry, academic, NIH and regulators worked very quickly together on setting up initiatives for clinical trials both on the on the European side on the WHO side but also on the NHS, US government and industry side.

I happen to co-chair the ACTIVE program with Francis Collins which was an extreme experience in fact! You had all the agencies in US including the heads of the regulatory bodies, FDA, the CDC, BARDA, NIH, everyone you can imagine. And all the heads of industry R&D. We set up six platform studies in different areas, antivirals, antibodies and support medicines. 30,000 patients were enrolled. 614 clinical sites. 700 agents. Different medicines were evaluated. 26 went into platform studies. 15 were already fully enrolled and reagents already proven efficacious to covid. Of course, Covid is totally different than dementia. But what you see is that an accelerated in-depth collaboration, when something is declared a global challenge, you can do something different from what we have been doing over the last 20 to 30 years. In addition to that, there was an exceptional data sharing between industry, academics and regulators where there was like no inhibition on sharing data, as we discussed earlier this morning on how that is absolutely essential. And all of that in 18 months.

I think we have made good progress with dementia with Dementia Discovery Fund, the collaborations with IMI, NIA, AMP, all of the different programmes, and with the regulators. Lots of money was invested. \$40 billion since 2000. And we made absolutely not enough progress. It's partly industry. It's partly collaboration. More needs to happen, and happy to hear the work with the UK on the dementia initiative.

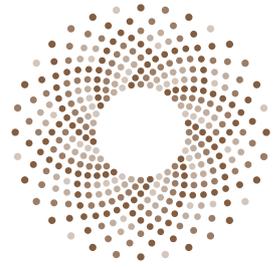
But I wanted to just bring the message let's learn, diagnose what we learn from all these initiatives and best practices to see how we can accelerate progress and let's bring that information together and happy to share more on different platforms and publications and others. But I learned that if we can get the support that this is a crisis, that dementia is a real crisis, the world could act much faster than we do today. I offer this thought as a contribution before I leave my job, but I won't leave the field and the world. I will continue to support dementia, as well as other initiatives, and the pandemic initiatives I have supported before. Thank you for listening to me.

reminded me of it. As understanding of the disease(s) has improved, and the high level of misdiagnoses of patients participating in trials (myself included) is now apparent. Is there any utility for those who have run trials following up to see how many of their participants had been misdiagnosed? And if so how it affects the results. It would be tragic if a treatment that could help some patients has been missed because of misdiagnoses of a significant number of participants, especially with the improving diagnostic tools now available.



Christopher Chen

As covid and other factors compel us to take up digital assessments, will regulators accept these as outcomes? Similarly if we use fluid biomarkers as surrogate outcomes



Dr Maria Carrillo
Chief Scientific Officer, Alzheimer's Association

Thank you so much and I'll pick up from here with my colleague Dr Scheltens but thank you very much Dr Hodes, Dr Williams, Dr Sano and Dr Stoffel for starting us off. We do have a little under 30 minutes to really try to tie this up, and we've heard several themes not only over the course of the few hours we've been together, but even just this half hour, about are we on track. There are more people on the call than, on multiple screens, than I can scroll through. It will be hard to see who's ready to ask questions. One thing I would like to ask is if you could use your raise hand button. Under reactions you can raise your hand and lower your hand that way, that would make things a lot easier. But in order to start this discussion, I did see a question for Dr Hodes specifically on your thoughts on whether we are on track. There certainly is more money available, and I know that the Alzheimer's Impact Movement has had a tremendous contribution to ensuring that that money has continued. And we hope even more this year.

That said, it takes time for that money to get invested, to get invested in the right way. Richard, you did a fantastic overview of all of the initiatives that are being launched and the different types of work that the National Institute on Aging is funding. But let me ask you in terms of are we on track, how much do we work with international funders in order to understand what the gaps are on a global scale? I know you represent a US-based organisation, but what are your thoughts about that international goal?



Dr Richard Hodes
Director, National Institute on Ageing (NIA)

It's a great question. If I take the question as whether we are optimally collaborating, crossing, forming globally and across nations, I think that that is the short answer is we're doing a lot and clearly not enough.

At the level of individual scientists and investigators, individual research programs, I think we're doing quite well. I think over this past year's field has made great advances along the lines that Paul Stoffels was commenting on. A change in what's acceptable in terms of data sharing and openness. So, I think across studies the data sharing and the methodologies to deal with complex data have improved enormously. I think in terms of some global efforts that have been necessary to look at diverse populations, some of those that both of our organisations have been much involved in, like DIAN and ADNI and HRS where we are looking more and more globally, we're doing well. I think then the area of genetics, which is prime for it, but only recently really lived up to its capacity to explore data, as Mary was commenting on, and make it possible to truly analyse across studies we are doing better and better.

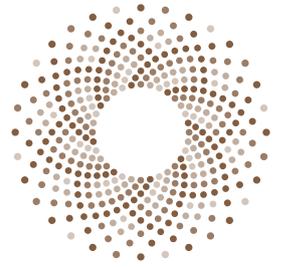
Clinical trials, coordinating platforms, this has been an area that has been much slower to happen. I think it is not just a matter of the global participation. It's been

in addition to for diagnosis, will regulators accept that these replace clinical outcomes?



Caleb Webber

Hi Nina, For a start, brain donation numbers are not as high as we would like. Obviously, this takes time but global efforts would accelerate. We need numbers to deliver sufficient power for GWAS associated with neuropathological biomarkers. Secondly, storage approaches vary which significantly limits downstream analyses. There is a huge demand for tissue. The demand illustrates how many parties could benefit from a systematic analyses. Spatial Omics approaches have arrived but it's the coupling with genetics and longitudinal health data that would deliver fantastic insights into picking apart distinct



a great frustration to all of us the difficulty and challenge in recruiting people into clinical trials and studies despite all of our efforts to establish appropriate platforms, funnels and so on. It's been complicated by the fact that, as other people have commented, we have moved more towards looking at early-stage interventions, which means we're looking for people who are at risk, may or may not know they're at risk, and may not yet have access to biomarkers and know that these are candidates for studies. And trying to develop through various registries, platforms and means with a lot of collaboration, public/private sector, but not yet sufficient, ways in which we can bring people in for screening in more efficient ways. I think some of the progress, for example in fluid and digital biomarkers, will allow screening of large numbers of people more efficiently than before, this will make a difference, and I think this should happen effectively.

I think in terms of regulation or regulators globally, you know we are having our first experience around, dare we speak the name, aducanumab, with FDA and now other agencies looking which point to the complexities at a regulatory level. We much more now talk about regulation but it's the right balance of regulation being sufficiently permissive to let promising agents go forward while being sufficiently rigorous to maintain a faith and confidence in the system. To have promising results quickly subject to the right kind of confirmation on all parts of the regulatory of profile. This is something which has become more and more compelling over this past year in particular.

Happy to have you push for more details, there's a first go. I also have a comment on what went into the chat from George and the question which all of us are increasingly are bound to be asked: are we going to make it by 2025? The stated goals of the US national plan that have been rather broadly embraced.

And I'll say the answer in in ways that are rather obvious. Yes, it is possible we will succeed by having one or more effective interventions by 2025. If that's to occur, since we're now approaching 2022, that means this will occur from some of the studies that are in progress and then are powered and designed and have the capacity to show whether or not they have success. And there are some both pharmacological and non-pharmacological. So yes, it is possible.

But I think what we've learned, even from the time we first articulated those goals, is that it is very unlikely there's going to be a single intervention, a single target, that is going to be appropriate for addressing the diversity of individuals who are affected with the clinical syndromes around Alzheimer's and related dementias.

And for that very reason, even if we are, as we hope, successful by 2025 or soon thereafter in having one or more effective interventions, that's not an end game. It will lead us to doing what we're doing now, continuing to look for more and more targets at early stage, developing them with the best information we have in improving technologies, and constantly adding individual and likely combinational approaches that are going to be necessary to address real world complexity of the heterogeneous disease. So let me stop there, it's quite a general statement, but one we all better get used to practicing and implementing because it's coming upon us.

and overlapping etiological contributions.



Andrea Slachevsky

Totally agree with @gloriawong . Phenotype also need to include how valuable or meaningful are for people in daily life.



John Dwyer

Great points Mary.



Maree McCabe

thank you all a fantastic summit



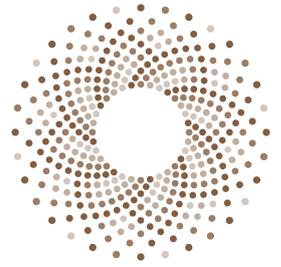
Nina Silverberg

Caleb and Carol B please reach out to discuss further.



Jane Roskams

Thanks to the WDC team (esp Lenny and Josh) for giving me a reason to get up in the middle of the night and engage in something so critically important in our world.



Dr Maria Carrillo
Chief Scientific Officer, Alzheimer’s Association

Thank you Richard I think that there is no doubt that we are seeing the low hanging fruit, really mature now with the programmes across monoclonal antibodies to amyloid beta maybe to tau in the near future. But we all recognise that across dementia, we've talked about many times, there are so many other proteins going wrong in the aging brain, associated with broader degenerative disease that we must actually do more. We are all trying to push for that. I know the programs that you outlined are, and certainly the Alzheimer's Association Part the Cloud program, with 59 therapeutic trials, only two of them are actually amyloid and tau based, is also.

I think at the same time something that Dr Sano mentioned is very important to bring to the table. That is even with this broad, diverse approach that we have in the pipeline, are there are going to be people left behind? And there are some participants here, in this meeting, from low- and middle-income countries that can share their thoughts about that.

To start, I know that Dr Sano you are on the scientific Advisory Board for US POINTER study, which is trying to make an effort to ensure that risk reduction and the science behind it can be strengthened, shored up, so that we can create programmes that reach even those that might not obtain in the US the ability to have aducanumab or other future treatments. In cancer, as Dr Williams very well pointed out, we have made huge investments and progress, but there are treatments that are also very costly. And we are still in the US leaving people out of life saving cancer treatments. So, we are still going to be living with this!

But Dr Sano maybe you could tell us a little bit more about your thoughts on that. And then I would invite folks from low-and-middle-income countries to tell us their thoughts. Who are we to say what they should need or have? So Dr Sano what are your thoughts about that and what do you think blood and serum might do for that future?



Professor Mary Sano
Professor of Psychiatry Ichan Mt Sinai, New York

So I think that you're highlighting something that several people have spoken of, and I think Julie mentioned it herself, and that to consider trials that are agnostic to the underlying biology, but are not agnostic to the risk, the concern, and the worry about cognition, about the aging brain.

I actually think these non-pharmacological trials offer us an incredible opportunity to identifying new biomarkers that are not dependent on pre-stated biology. I think that comparing cognition or examining cognition in these broad cohorts is really



Allison Sekuler

As @mary said, we should not underestimate the importance of cognitive tests. And sensory tests as well.



Elisabetta Vaudano

Thank you for a great summit



Hilary Doxford

Thank you everyone for all you are doing and for a great meeting



Allison Sekuler

Thanks Lenny, Josh and everyone for a great session. Here's to next March in person.



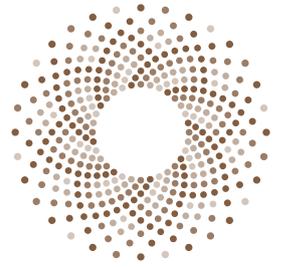
Mathew Varghese

And Prevention research can be possible. Absolutely needed is political and govt support and a National Strtegy



Maria Tome

Thank you



an important opportunity. And if we talk about low hanging fruit, the fact that we have people who are worried and who are interested is really the first place to begin. We then listen to the voice of the individual: I'm interested in this and I want to participate and I'm not being excluded for the reasons of the science that was built upon a very narrow population.

I think the targeted work that we do is very important, but it's very exclusive and I think these trials provide us with incredible promise to identify new biomarkers that are really relevant to the breadth of biologies that probably underlie cognitive changes in aging.



Jane Roskams

Lenny and Josh - we will be coming in march!



Angela Bradshaw

Cheers, Lenny, Josh and all @WDC! Thanks for excellent talks, chairing and discussions



Dr Maria Carrillo
Chief Scientific Officer, Alzheimer's Association

Dr Tome I see you have your hand up thank you for joining us.



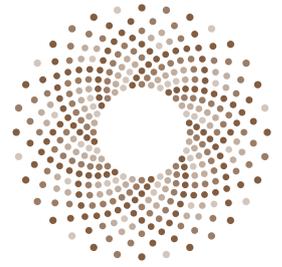
Dr Maria Tome
Senior Science Officer, European Medicines Agency

Hey, thank you so much Maria. You made an excellent point; we need a course the natural history. It will be far easier for regulators. Maria it's true as you say people don't get treatment. But the reality is we are living longer in this is driving cost. We are having treatments developed for other medical conditions. and as previous speaker has set out, this is changing and we're going to have treatments for AD. We talked before Maria with the data on treatments. It is really important to collect this information and will be really important for people like the EMA. It is because that is the way that we brought treatments for orphan diseases in. That is the way that we have brought in treatments for other diseases. You know we compare. Cancer is the same you compare with what will happen you don't interfere. How long this treatment will improve a person for? Is it for three months, if it improves for three months you can still be driving for six months or five years? It's a huge difference. But that information is fundamental and thank you so much for letting me bring that point. Thank you.



Dr Maria Carrillo
Chief Scientific Officer, Alzheimer's Association

Thank you thank you Dr Tome appreciate your perspective especially from the regulatory perspective which is so important. I think it was mentioned in a previous conversations here, I think by Derek Hill if he's still on, that it is very important to collect all the data and it is very important to join it across countries across the globe. We have the technology now, so we should be able to do this and I think there are great efforts that are working towards that.



But one of the things we should think about is how we might want to ensure that some of that data is rigorous enough to actually help regulatory decision making. And certainly, there are in US and in Europe, there are examples of those registries that have regulatory grade data. I think that was something that was already mentioned. It's going to be an important part of the conversation. And as we collect blood throughout registries, certainly like the one the Alzheimer's Association has just announced, it's going to be important.

But I think one of the other comparisons that we might want to make is how did heart and HIV also, which are prevalent in all countries across the world, penetrate with cheaper and cheaper medications, that can reach countries and all levels of social economic strata, which still we have a difficult time actually penetrating. Even in the United States, we continue to have deaths of heart disease, deaths of high cholesterol leading to heart disease and stroke. I think this is something that we should all be thinking about in terms of a grand plan and that's something perhaps the World Dementia Council can help us in terms of road maps, because it can't be done just by one country alone it really has to be a collaborative effort of thinking group like this.

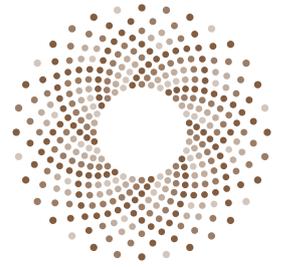
But you know, blood can potentially change a lot! We've talked a lot about biomarkers and how expensive they might be. We talk about imaging and MRI's and I saw some of that information, some of that in the chat. How do we think that blood might actually change the horizon? What can plasma measurements tell us? This is not just about Alzheimer's, because there is there promise that it can tell us a little bit more about neurodegeneration broadly speaking. How might that change our landscape in the future? Not only our clinical trial landscape but for our ability to deliver medications and make assessments in individuals in a way we really can't reach today with a PET imaging or maybe even cerebral spinal fluid. Does anybody want to comment on that in particular? I see Julie you want might want to respond.



Professor Julie Williams
Director, UK Dementia Research Institute

I think that the we are now learning so much about both biomarkers and predisposition in terms of genetics, that putting those things together you may be able to identify people with some accuracy in the very early stages of disease. That I think that is only just beginning to be able to happen. It's a new way forward. We're certainly looking. We can identify people at high risk of developing Alzheimer's disease, and we're looking at Parkinson's disease, in their 30s and 40s. We can see differences in their brain imaging at the age of 30. It's a slightly smaller hippocampi.

There's something happening from a very early stage in these diseases and understanding that is one of the big gaps. So, I think there are things coming out of research on blood, plasma biomarkers and the genetics, putting those things together will help us identify people at a very early stage. There's a lot going on here.



I think the point that I'm trying to make is we need more investment. We're doing really well in relative terms to where we were. We really are improving. But don't stop there. There's a lot more to be done and I just like to come back to this global funding structure. I really think an extra layer where people can collaborate across the world. We collaborate in areas across Europe and in the States, but actually collaborating across the world is extremely difficult for individual research groups. And this body could do something about that, and I'd like to throw that out there



Dr Maria Carrillo
Chief Scientific Officer, Alzheimer's Association

I agree and I saw I think Caleb Webber had something similar I don't know Caleb if you'd like to make that comment here and amplify.



Professor Caleb Webber
Chair, Informatics Steering Committee, UK Dementia Research Institute

Thank you Maria. So basically, there are benefits to power. Ultimately, we see brains have a range of pathologies that we see. You know it's not just people have cleanly one particular pathology. There's not one particular protein biomarker but a mixture. So it seems to me that we're all joining smaller numbers together of brains to really understand the pathology.

And so global brain banking efforts, where we could actually describe the brains in a very similar aligned way. We have the genetics, so we can understand really what the drivers are behind this pathology, connected to a longitudinal lifetime collection of data and health records. Where we have data linkage could really help us to pick apart these different drivers rather than going to this extant clinical diagnosis because ultimately, it's what's going inside the brain that really will take us to that treatment.



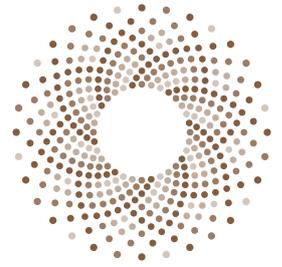
Dr Maria Carrillo
Chief Scientific Officer, Alzheimer's Association

Thank you, Caleb, appreciating your point. I think George you have your hand up?



George Vradenburg
Co-Chair, Davos Alzheimer's Collaborative

I think that we have to begin to work with health systems around the world to understand what the protocols are that they need to collect blood, to make



digital assessments, and potentially to have home based collection kits for the microbine. And then have mechanisms for the consolidation of genetics for risk, blood for detection and diagnosis, digital assessment for clinical evaluation and then the microbiome and the omics associated with that material, will give us an opportunity, I think, to do research at a global scale in low resource countries and low resource settings.

We talked a lot about the need to involve low-and-middle-income countries or low resource settings, whether it's in high resource countries or in low resource countries. But there are practical ways to do this at scale if we have the right mechanisms and the right funding to do it.

So, I would simply mention the Davos Alzheimer's Collaborative, which is aimed at this topic. We're only into our first year, but we are aiming to do that global collection of that data, and to built-in protocols in health systems to actually use that data to detect and diagnose and then to treat populations



Dr Maria Carrillo
Chief Scientific Officer, Alzheimer's Association

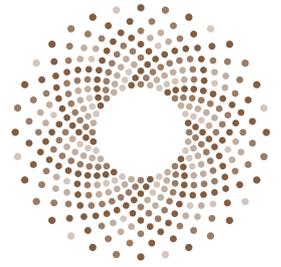
Thank you thank you George for that comment. Paul do you have a question?



Dr Paul Stoffels
Chief Scientific Officer Johnson & Johnson

I think with what is on-going over the last few years, more and more infrastructure is available for diagnostics. If you look now, worldwide PCR gets introduced with Covid and that will not disappear. But also clinical trial capabilities and collecting data. Today you shouldn't underestimate the digital status of low-and-middle income countries. Today we are doing a large scale Ebola study in Rwanda in the field and all people have now digital tools to measure their side effects, be called for us to come to the lab. We do a 400,000, 500,000 patient study now in South Africa with real world evidence, in Covid, all collected by digital systems. So, there is a way to start using the new technologies in order to get many more people in lower-and middle-income countries involved.

And one more point, I want to make. We used for our HIV vaccine trials a network of 200 clinical trial centres in the world which were then was available for Covid. So clinical trial training and capabilities also are being set up as we speak. And I think using those existing capabilities as an engine to get to new areas could well be of benefit here and I'm talking with MRCs around the world or governments that could really help. So just a comment and contribution. Thank you.



Dr Maria Carrillo
Chief Scientific Officer, Alzheimer's Association

Thank you Paul. I think that this body under the leadership of Philip, Lenny and others and the trustees are in an excellent position to be able to influence at that level, very good points, and I think they echo a lot of the thoughts going on in the chat and some of the conversations we've had. Thank you very much. Dr Tome I see you have your hand up again?



Dr Maria Tome
Senior Science Officer, European Medicines Agency

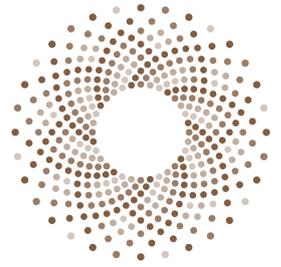
I'm thinking that there are a lot of issues here. We need to recognise those people that did the work before and that was the Commission. The European Commission and Council that started work a long while ago on how to do trial and training in low-and-middle-income countries. And WHO was very involved with that. So thanks to them we can do these trials now. And our colleagues mentioned about HIV. We are doing the vaccines but we also have even prevention in HIV. It's not easy. The statistics I agree with you, but low-and-middle income countries have been building capacity for years. South Africa is a good example but there are other countries that have put a lot of money in and WHO and the European Union definitely put a lot of money to train these countries to do trials. And the information that is coming is quite reliable. We can now do treatments and prevention in HIV. It is what we are doing now. And we could treat in in Alzheimer disease. We have the technology,

And related to the protocols, I agree. But then you can collect the information. We have registers. We are good in Huntingdon's. We are good in pregnancy women. We are in children with rare diseases. You know with genetics disease, they have the family history. They want to help, and people will use digital technologies. They will come forward. So, there is no excuse not to collect this information if they are happy to help you to collect the information. You know and we are in the same boat! I think covid is a lesson. We are in this war together!



Dr Maria Carrillo
Chief Scientific Officer, Alzheimer's Association

Thank you thank you very much. Yes so that there is no doubt we can learn from other diseases that have done this before in digital markers. Miia I think you have your hand up as well.



Professor Miia Kivipelto

Professor in Clinical Geriatrics, Karolinska Institutet

Yes, just a brief comment. Thank you Maria for highlighting the importance of different targets and even non-pharmacological interventions. I'm especially thinking of the Part the Cloud support for this kind of novel intervention that combines non-pharma and pharma interventions and even repurposes drugs. This design could be something also for low-and-middle-income countries.

I think in the Alzheimer treatment cocktail we probably need to have several targets and always that non-pharmacological intervention. It is really beneficial to have this approach included as well.



Dr Maria Carrillo

Chief Scientific Officer, Alzheimer's Association

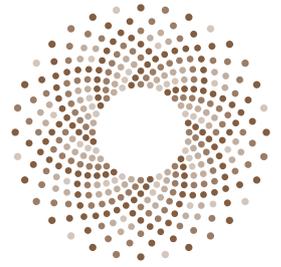
Thank you. No, I know that we have folks from Argentina and from India and from other countries. We would be happy to take your comments as well. Allison I see you have your hand up?



Dr Allison Sekuler

Vice President, Research, Baycrest Health Sciences Center

Yeah, just sort of on that last point from Canada, by the way. On that last point around technologies, we've been working quite closely with some companies that already have technologies out there that were not designed with a purpose in mind of advancing clinical trials or any of these kinds of things. But we've been able to repurpose the kind of data that they collect to be able to collect, to be able to collect for example, very inexpensive EEG data. And these are devices that are significantly cheaper. The EEG system in my lab is a \$250,000 system. This is a \$200 system. Canadian dollar, so it's even cheaper for the US! And what that means is that we could potentially be using these kinds of commercially available systems too. Be collecting data even on neuroimaging and other kinds of things around the world, that's really the goal. So, we have a project where we're working on that, trying to create a mechanism so that any researcher can really make use of these systems in this new way. And then the problem just becomes, and this is where I have a question really, how do we get these new kinds of methodologies integrated into the existing data sets? Because they weren't initially envisioning that you'd have EEG data on everyone because it's too labour intensive and you can't get it around the world. But when you have the new opportunities to integrate this kind of data, what can we do to make sure that it's going to be embedded in all of the different datasets and then also made accessible to everyone because we never know where the next innovation is going to come from.



Dr Maria Carrillo
Chief Scientific Officer, Alzheimer's Association

Thank you. Very good point. Dr Sano you might be the last comment I can take.



Professor Mary Sano
Professor of Psychiatry Ichan Mt Sinai, New York

I just want to highlight something commented on by Gloria Wong and that is we really need to acknowledge we have great ability to discriminate and diagnose with phenotyping that's just simply not done. It is true that we cannot always afford to give someone an expensive scan, but do we actually take 25 minutes to give them a cognitive test? It's so available and possible and as Rhoda Au has told us, there's also ways to use other kind of phenotyping, other kind of technologies, to make even greater precision with this.

But one of the most universal things is that individuals in this age group are thrilled to spend 20 minutes speaking to someone. So we actually have the capacity to do way more discriminating than we feel comfortable doing right now. I think raising confidence are about our ability to do that among practitioners, a broad group of practitioners, would make a very big difference.



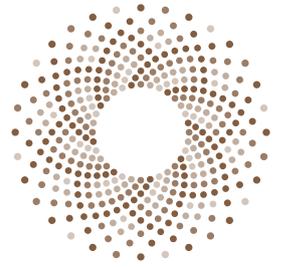
Dr Maria Carrillo
Chief Scientific Officer, Alzheimer's Association

Excellent I think that's an excellent point thank you very much. We have to remember that we are getting even better with those cognitive tools, though they are also improving. And they are being transferred to digital platforms as well so they can be delivered in that way for those areas, especially under Covid times. So I think that's a fantastic point to make. Mathew, I see you came off of your video, did you want to make a comment before we closed?



Professor Mathew Varghese
Professor of Psychiatry, National Institute of Mental Health & Neuro Sciences (NIMHANS)

Actually, I've said most of the things that I wanted to say in chat and I was saying that MRI scans, genes, iPSCs and cognitive tests, these are all things which are fairly cheap and easy to do. I think registries are expensive. There are other ways of picking up amyloid for example. We have tried to use retinal scans, for example to see if we can pick up amyloid. CSF is difficult. Autopsies and brain autopsies are difficult PET scans are difficult, not just for the cost. There are PET scans available



for cancer, but it's an issue of getting the amyloid, and that's difficult because you need to line up patients and get it done.

So those biomarkers are difficult, but I think we're making some progress in terms of the stuff that we're doing with the LASI study and various other projects that we have. So I think collaborations on this front is definitely something that's very much possible. And I think phenotypic evaluations as Mary said is something that's very easy to do. And there is a great deal of consensus as we've shown on different consensus websites. So I think that's there's a lot of stuff that we can do there. Thank you very much.



Dr Maria Carrillo

Chief Scientific Officer, Alzheimer's Association

Thank you, Mathew, appreciated and it's great to get insight from India really appreciate that. Thank you all very much for a fantastic discussion and great day.

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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