Innovation and incentives

Transcript of a session from the World Dementia Council virtual summit
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Dr Peggy 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.
Dr Husseini Manji

Husseini K Manji, MD, FRCPC is Global Head, J&J Science for Minds, and immediate past Therapeutic Head for Neuroscience at Janssen Research & Development, one of the Johnson & Johnson pharmaceutical companies. His research has investigated disease- and treatment-induced changes in gene and protein networks that regulate synaptic and neural plasticity in neuropsychiatric disorders. This has led to the FDA approval of the first novel antidepressant mechanism (NMDA-antagonism) in decades and has been actively involved in developing biomarkers to help refine these diseases. Dr Manji has been inducted into the National Academy of Medicine, the World Economic Forum Global Future Councils and is a member of Harvard/MIT’s Stanley Center SAB, amongst other appointments. He has received a number of awards including the NIMH Director’s Career Award for Significant Scientific Achievement, and has published extensively on the molecular and cellular neurobiology of severe neuropsychiatric disorders and development of novel therapeutics with over 300 publications in peer-reviewed journals, including Science and Nature Neuroscience. He is an Honorary Fellow at Oxford University and Visiting Professor at Duke University, and previously served as Chief of the Laboratory of Molecular Pathophysiology at the NIH as well as Director of the NIH Mood and Anxiety Disorders Program, the largest program of its kind in the world.
Dr Gregory Moore

Dr. Gregory J. Moore, MD, PhD is corporate vice president for Microsoft, leading global health and life sciences. He is responsible for research and development collaborations, strategy, AI and machine learning engineering teams, and cloud and data product development teams to positively transform health. Prior to Microsoft, Dr. Moore served as vice president at Google, leading Google Cloud Health and Life Sciences globally. Dr. Moore is an industry thought leader, driving innovation to enable access to care and digital transformation toward a more transparent, interoperable and AI-driven foundation for health care delivery. Dr. Moore is an engineer, practicing physician, and experienced educator. He is board certified in Diagnostic Radiology, Neuroradiology, and Clinical Informatics. Prior to his leadership roles at Microsoft and Google, Dr. Moore served as the chief emerging technology and informatics officer at Geisinger Health System, where he was also Director of the Institute of Advanced Application. His prior academic and clinical appointments include Stanford University School of Medicine, Penn State University College of Medicine, and Wayne State University School of Medicine. He currently serves as a director on the boards of Hill-Rom (NYSE:HRC) and Davita (NYSE:DVA).

Professor Fiona Watt

Fiona Watt, FRS FMedSci is a British scientist who is internationally known for her contributions to the field of stem cell biology. In the 1980s, when the field was in its infancy, she highlighted key characteristics of stem cells and their environment that laid the foundation for much present day research. She is currently director of the Centre for Stem Cells & Regenerative Medicine at King’s College London, and Executive Chair of the Medical Research Council (United Kingdom) (MRC), the first woman to lead the MRC since its foundation in 1913. On 13 July 2021 she has been appointed as the new Director of the European Molecular Biology Organization (EMBO).
I want to begin by thanking Philip both for his leadership of the World Dementia Council and also this meeting today. And for inviting me to chair this important session. I also think great thanks go out to Lenny, Josh and the team for first putting together what was going to be a fantastic in person meeting and then, on very little notice, reformulating it into this virtual discussion. I think that we have been able to interact very well so far!

I want to just add one thing in terms of how this session will be undertaken. It would help me, if you really want to make an intervention into the discussion, if you can use the raise your hand function so I know to actually call on you. I’ll be monitoring the chat, but I’m not so good at monitoring the chat, moderating the session, and listening to the participants! So, if you really want to make a discussion intervention, please try to raise your hand using the zoom reactions icon. I think you just click on that and then the raise your hand option. I hope we can have time for discussion and engagement.

Let me briefly introduce and thank the speakers in this session. We have some outstanding presenters. First Professor Fiona Watt, who’s the chair of the Medical Research Council, then Dr. Husseini Manji, Global Head of Johnson and Johnson Science for Minds and Dr Gregory Moore who is Corporate Vice President at Microsoft.

The focus of this session, as you know, is on innovation and incentives and it will pick up on many of the themes put forward this morning. Importantly, we want to think about the ecosystem; the set of players and partners needed to advance critical innovation in the neurodegenerative disease space. We need to work across disciplines, we need to work across sectors, and we, of course, need to work on a global basis, in order to really advance the science and the understanding of neurodegenerative disease and dementia. But also, to harness that science in order to make a difference in the lives of people as we study the development of new therapeutics and other interventions. Importantly, this is a question not just of how we incentivise the proper scientific engagement to undertake those tasks and how we make sure that we not only have the scientific engine running in the most efficient and sophisticated ways possible. But also one of how we can actually deliver these products into the real world to make a difference.

So, with that, why don’t we start off with our session, and I’m going to turn to Fiona first to get us going. As probably most of you know, but not all of you, the MRC works to improve the health of people in the UK and around the world by supporting excellent science and training future generations of scientists. It’s really at the very core of the UK scientific research infrastructure, and it is also vitally important at this time in helping to shape the research agenda and its implementation in critical domains of science and research necessary to advance our understanding and treatment in care of neurodegenerative disease.
Professor Watt is currently the chair of the MRC, but she will, as I understand it, be leaving soon to take up a new role as director of the European Molecular Biology Organisation, where she will clearly continue to provide important leadership. She’s played a leading role in helping to nurture the research establishment in the UK and is also the first female leader of the MRC, in its more than 100-year history! So, hats off to Fiona for that! We need more female models of her calibre and most importantly, we need her leadership and vision in this important area of endeavour. So, I want to invite Professor Watt to start us off by talking about the work of the MRC in terms of the dementia research landscape in the UK and beyond and to help us think about how research institutions like MRC can help guide and incentivise critical research. Over to you Fiona.

Great, thank you very much Peggy. I’m going to share four slides really just to put the UK funding landscape for dementia into some sort of context. So let me just make sure that I am sharing, I hope you can see that is that.

As Peggy said the Medical Research Council is an organisation which receives UK Government funding and our mission for over 100 years really has been to improve human health through world class research. Some features to note: we are disease agnostic; we fund everything from discovery science through to clinical trials; and also we fund individuals which could be, for example, PhDs right through to institutes like the Francis Crick Institute.

We are part of UK Research and Innovation (UKRI). Last year we did a quick tally of how much money is UK taxpayers’ money within UKRI is devoted to research on health and innovation, and it’s an impressive £1.3 billion.
However, even this number pales into significance if you zoom out and look more broadly at funding for health research in the UK. And here on this slide you can see UKRI funding alongside other research funders. We have a vibrant, very important, charity sector, including some really important dementia focused charities, and they invest a lot in this sector as you can see on the slide. This is people making donations or private foundations. Another important part of the ecosystem is government funding through the National Institute for Health Research. All of this really is dwarfed I would argue by the investment from the pharmaceutical industry. This funding should be good news for dementia research.

And here I’ve tried to summarise what we would describe as the dementia research ecosystem. Not surprisingly, with so many different routes into funding and so many entities involved it is complex, but I would argue that it is strong.

Just to pull out not all of the things on this slide but a few examples. We’ve got their Dementia Research Institute. This has core funding from MRC and also has funding was submitted to the High Level panel on Internal Displacement at the UN.

Professor James Rowe
We have not heard much yet on innovative trials designs - how can these non-traditional designs gain traction with regulators to move faster from experimental medicine to licenced agents.

Professor Jane Rookams
Peggy - I could not agree more. If there is a silver lining to this pandemic, it is in showing how we can create safe routes for shared data, procedures, analytics and modeling for an acute global crisis. COVID has accelerated the production of roadmaps and dig health (real world ev) approaches that could dramatically
from Alzheimer’s Research UK and the Alzheimer’s Society. This now constitutes a network of over 600 researchers across 6 different university sites with an effort in understanding disease mechanisms, early stage development of diagnostics and treatments, and innovative technologies for assisted living.

You’ve heard from my colleague John Gallagher earlier on. Dementia Platforms UK is a really innovative public private partnership. This involves investment from MRC, industry, and of course Gates Ventures. And I won’t say anymore about what DPUK is up to, but I think you’ll be impressed at the efforts in a data coordination.

You can also see on the slide the National Institute for Health Research. A really great collaboration which is forging partnerships in clinically based dementia research and academic and commercial clinical trials. And last but by no means least, a very important part of the system is the Dementia Discovery Fund. This is an international venture capital programme which invests in and creates new biotech companies that are relevant to this area.

So as if all of this were not, if you like, rich enough, I was really pleased that this summer the government released its life sciences vision. One of the government seven healthcare challenges is improving translational capabilities in neurodegeneration and dementia.

The overarching ambition is to build on those different elements, which I showed you in the previous slide to accelerate the pace of translational studies leading to novel treatments. I’m not going to rehearse all of the priorities, but I think that you would agree that these are all important for moving the goals of the World Dementia Council forward. So, with that, I’ll stop sharing and I’m really looking forward to participating in the discussion.
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 appreciate your laying out the UK dementia research landscape for us. Obviously, as you say, it is quite rich and complex, and it also does acknowledge the many different disciplines and the need for partnership amongst different sectors.

And so now I’d like to turn to Husseini Manji, who, of course, is in that private sector domain you spoke about. He has had the opportunity to work in many different roles that help inform how we should be thinking about incentives for advancing science and innovation in this area and how to foster successful partnerships.

Dr Husseini Manji is currently, as I mentioned, the Global Head of J&J Science for Minds and he’s the immediate past Therapeutic Head for neuroscience at Jansson Research and Development. In his own research he has investigated disease- and treatment-induced changes in gene and protein networks that regulate synaptic and neuroplasticity in neuropsychiatric disorders. He also has thought quite deeply about how to structure important research in order to advance knowledge and has worked in areas that previously have been very challenging in terms of research models and strategies. I’m very grateful that he also sits on the World Dementia Council. So let me turn it over to you, Husseini, and I know that you have some slides that you want to present.

Dr Husseini Manji  
Global Head, J&J Science for Minds

Thank you very much Peggy and thanks to the organisers for the kind invitation. It really is a pleasure to follow up on Fiona’s outstanding comments. As you can see, I think we’re both really trying to highlight, certainly some of the many challenges in neurodegeneration, but also the tremendous progress we are making to increase our need for inexpensive and widely accessible diagnostic tools integrated into primary clinical practice as well as practical RWE platforms to assess the clinical benefit of narrow ‘precision’ products in messy real world populations. Otherwise, we will have to have many many ‘precision’ medicines to address the heterogeneity of real world populations.

Dr Ruth McKernan  
For a platform of frequent remote digital assessments with remote EEG - check out DDF-funded Cumulusneuro.com

Professor Carol Brayne  
We will need a robust ethical research programme running in parallel with all the potential work and hopes being expressed in this meeting. There needs to be...
This slide doesn’t need really recounting to this audience. We all know that dementia is a tremendous health care problem. And one that’s getting worse. As this slide highlights, both in the UK and globally, population are aging, and with this comes huge financial costs. And obviously, the pain and suffering for individuals and families is immeasurable.

Now I think as this slide shows, if you look on the left you can see that we absolutely need new approaches! I think it’s fair to say that the situation we currently find ourselves in is certainly not from a lack of trying. So, for example, it’s been estimated that in the last 20 years the pharmaceutical industry has invested over $40 billion into R&D to develop new dementia therapeutics. And of course, we’ve made some progress. But, to date we have only four symptom relieving therapies globally and a fifth one i.e a disease modifier approved in the US only.
So why is this the case? We all hear about the tremendous breakthroughs in biomedical research things like on you know immuno-oncology, [indistinct] therapies, and the recent COVID vaccines. As you can see on the left of this slide, the R&D challenges and dementia are formidable.

For example, while we’re making tremendous progress in genetics and basic biology, we don’t yet have the same degree of understanding about the underlying pathophysiology as we do with some other illnesses. Similarly, although we’re making lots of advances in neuroimaging, there’s still the relative inaccessibility of the brain, and furthermore, until relatively recently, our endpoints have been somewhat insensitive.

As you can see in the middle panel, these barriers to dementia R&D research, have led to a very low success rates in terms of new treatment development currently estimated at 0.4%. And because of current lack of sensitive outcome measures and other barriers, the trials are riskier, they take longer and cost more. And because we traditionally don’t really know if something is going to work until several hundred million dollars have been invested, the cost of development of a drug for dementia is also considerably higher than for other disease areas.

So, one can see why despite the tremendous unmet need several pharmaceutical companies have pulled away from dementia R&D and are focusing on other areas, certainly important areas, like oncology and immunology instead.

But despite his numerous challenges, I truly believe that there’s a reason for optimism.

Some of the reasons for the optimism should be first and foremost the scientific advances we are making. Our understanding about the underlying biology of neurodegenerative diseases, great work from academia and institutions like Dementia Research Institute. As you heard from Miia, in our understanding of the potential modifiable risk factors. And importantly, we are developing very accessible and low-cost biomarkers, including blood based biomarkers and digital biomarkers.

But I think another major reason for optimism is because of advances in what I call the
culture of science. As we heard from the data sharing group in the morning, there's a growing recognition that to make major progress we need to more comprehensively work together. And as we heard a moment ago from Fiona, recognising the need to do things differently dementia has recently been called out as a priority area for public private partnerships by the UK Government.

In this regard, I was delighted to join Fiona and many stakeholders at the round table discussion that was convened by Will Warr at 10 Downing Street in September. This roundtable assembled a unique team of dementia leaders from different societal sectors to think about innovative ways to markedly accelerate the development of new treatments and solutions for patients. As you can see on this slide on the left, this roundtable involved nearly every major UK government stakeholder. It involved leading charities. It involved leading patient advocacy groups. And it involved leading industry partners. And I think it’s really important to point out that the industry partners included not only leading pharmaceutical companies, but also leading digital, tech and data sciences companies. Because it’s very clear all of our collective efforts are undoubtedly going to be a big part of the solution. The objective of this round table was to discuss a transformation new initiative designed to really make a difference for patients.

### Major barriers identified to advancing dementia and neurodegeneration R&D with data science as a key enabler

- **Drug pipeline**
  - Target validation
  - Lead generation
  - Early optimisation
  - Preclinical development
  - Phase I
  - Phase II
  - Phase III

**Validation in neurodegenerative research**

*Source: Mauricio et al. (2017)*

**Without surrogate markers, ineffective drug candidates advance to the largest, the longest, and the most expensive (Phase III) clinical trials when they otherwise would not**

*Source: Scott et al. (2016)*
I think we all recognise that there are many unmet needs in dementia treatment development, but this group identified three major specific roadblocks to transformational progress.

- First, there was inadequate human based translational research at the standard required to initiate the very large investment necessary for late stage clinical trials. By reducing failure and increasing sensitivity to efficacy, shorter, less expensive clinical trials will be enabled at reduced costs and most importantly, increased the delivery of new medicines to patients.

- Second, there was a recognition that there's a lack of novel tools and technologies for experimental medicine studies. The right tools can really enable better patient stratification, more sensitive endpoints and effective outcome measures. Once again, this would result in decreasing trial size and duration.

- And finally, the need to implement innovative clinical trials and to overcome operational challenges in trial execution. And in this regard delighted that the body that Fiona mentioned the NIHR is also part of this initiative to think about how we can streamline the clinical trial process.

So, to address these challenges, a model has been proposed that will bring together the rigor and experience in human-based translational research and experimental medicine that exists in industry together with the tremendous innovation of academia, truly innovative clinical trial design thinking and the input of regulators in a major new initiative. This initiative will be built on a strong foundation of data science, so we’re delighted that the major data science and digital tech companies are part of this initiative.

We truly believe that several factors make the proposed initiative quite different from previous initiatives and sets us up for success.

First and foremost, it really focuses on the core unmet needs and bottlenecks in neurodegeneration treatment development. The focus is completely about accelerating implications of the research approach if successful in implementation into clinical populations) to mitigation of Climate Change or the opposite. How do the panellists see this challenge.

Paola Barbarino
Jeff you are so right!

Dr Chris Fox
Automation could help?

Sarah Lock
Mary Sano -- could not agree more -- patients are the authorities in determining outcome efficacy that matter most

John Dwyer
Jeff’s call to action is exactly right; to catalyze change regulators need to inquire whether labels should be narrowed if they lack diverse study populations and governmental
Summit 2021

Innovation and incentives bringing treatments and solutions to patients. And I think a very important consideration, you know I think one of the main themes of this discussion today, is that this initiative pool significant monetary and other resource contributions from academia, government, industry, and charity stakeholders to tackle what we have to recognise are expensive scientific roadblocks.

So as I said I think we have a lot of reasons to be optimistic and thanks to tremendous leadership of the MRC, the Office of Life Sciences, the NHS, NIHR, and many other stakeholders, many of you who are in the virtual audience today. We have been making a lot of progress and hopefully will be able to move forward with this initiative soon. And of course, once we launch this initiative, the intent is completely 100% to work with many of the other global initiatives, including what we heard from Pierre Meulien, including what I’m sure we’ll hear from Richard Hodes and the NIA/NIH, including with the Alzheimer’s Collaborative so that we can really make a difference for patients. Thank you for the time and I will hand back over to Peggy.

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

Great. Thank you and what an exciting presentation in terms of this really essential collaborative work that you’re doing. This effort you just described has really found its birth and its home within the UK, but it’s the kind of model that has much broader implications and hopefully, over time, much broader participation in terms of the opportunity that it represents and the recognition of how all of these different components of the research landscape and the biomedical innovation ecosystem can and must come together.

And earlier this morning, we had a very rich discussion about data and data sharing. Now we have a chance to continue some of the themes of that discussion, but in this somewhat broader context. And we’re very fortunate to have Dr Gregory Moore with us her to help lead us through some of that thinking and discussion. He’s the Corporate Vice President for Microsoft, who’s responsible for leading global health and life sciences. He now is going to, as I said, build on the earlier themes of data sharing and offer his perspective on how cloud computing, data sharing infrastructure and tech collaborations are helping drive innovation in dementia research. He will also address how this work can be integrated into the kind of collaborative that we were just hearing about. So, I will turn to you, Gregory. I understand you’re going to take the controls and actually present your own slides, so let’s hope that technology works.

funders must insist on more diversity as part of their granting process.

Professor Brian Lawlor
Lack of diversity in clinical trials reflects one of the many inequities in brain health that we urgently need to address.

Dr Inez Jabalpurwala
Agreed with Husseini; digital technologies will be a game changer in enabling remote assessments--reaching people wherever they are, and also contributing to living labs with feedback loops.

Dr Andrea Slachevsky
Totally agree with Dr Sano. Efficacy also need to consider intra and inter-countries differences

Hilary Doxford
Absolutely right Chris
Thank you. Real pleasure to be here. Thanks to the organisers. It is a pleasure to follow up on Fiona and Husseini’s comments as well as the prior panel chaired by Bose that I think really highlighted some of the broader issues. I’m really thrilled to share a technology perspective here.

So, I want to start about two variables that are growing. One that we’ve heard about already. And that’s really the urgency and the increase in the number of dementia cases that are happening around the world. And the vast burden of that is, as has been highlighted before, is in low-and-middle income countries.

The second variable, and as someone who is an engineer, a neuroscientist, and a neuroradiologists, that I want to talk about is the data. And it’s one of the reasons that I actually at a technology company is because of those data challenges. So there’s tremendous growth in the data. Really historic growth in healthcare data. By some estimates, healthcare data around the globe now is exceeding over 2000 exabytes and growing, doubling by some estimates every 6 to 12 months. Having come just come from a largest imaging conference, the RSNA we now have spectral CT scanners that are putting out hundreds of petabytes of information per scan, so this is only going to grow as we go forward. So, we’re witnessing this incredible influx and growth of data.

So, as was highlighted in the in the prior sections and as is set out on this slide, we have a variety of barriers, but I would present as actually opportunities for us as we go forward. But these barrier are delaying research discoveries. I have been really heartened to see the progress and the ecosystem leaning into these challenges as we go forward, but I would also challenge us all that we can do better. To mention some barriers. The vast majority of real world data that would result in real world evidence is still siloed in in various forms, particularly clinical data that is out there. We have restrictions in data sharing. Varying governance and security policies. All of these represent challenges.

But we’re making incredible progress here as we go forward. There are initiatives, like you’ve heard about today already, that are allowing discovery to proceed and accelerate. And this is where technology companies like Microsoft, and others as well as Husseini mentioned, are really coming together to bring to create platforms to allow and facilitate this data sharing, including enabling governance, privacy and security to allow that that sharing across different platforms.

But I will say, unlocking this full potential of data, that’s been created now in vast quantities, to deepen our ability to understand disease, accelerate biomedical research discovery, and develop new treatments, is going to require a whole new set of technology capabilities applied to the domain.

As listed on the right of the slide this includes technologies that will create data liquidity. New forms of computing, including quantum computing will be important here as we go forward. We’ve talked about interoperability, advanced analytics. And probably
the most important it’s been highlighted already is, you know, healthcare data is some of our most private information that’s out there, so ensuring trust, security, compliance on these data sharing platforms could not be more important for this ecosystem to accelerate research as we go forward.

As an neuroradiologist I can’t help but to lean in here and say that imaging in this vast quantities of data that I mentioned now represent over 80% in terms of the volume of data as we go forward. So, it’ll be really important that we lean in here and create and link this data, not only mentally imaging, but with the omics the phenotypic data and I’ll say the internet of things as well as we create new digital biomarkers. We know that multimodal learning models, multiple datasets are becoming very powerful in other domains and certainly will become more powerful as we go forward in this domain as well.

Finally, I’ll say that partnering is key, and I’m really gratified to be a part of this session today to accelerate biomedical research and discovery. I think this is this the key opportunity for us as we go forward.

We and other technology companies have been leaning into sharing. Open data sets but also controlled access datasets with a platform approach for NIH for Terra and across the NHS. And I think that these will be really important for us as has been articulated to make progress.

I did make a comment in the chat window earlier, but I do think federated learning models and new technology around confidential compute will be incredibly important for this ecosystem, and I think getting the entire global ecosystem access and actually up to speed with these new technologies will be an important responsibility for technology companies as we lean in here. So, with that, I’ll stop sharing and turn it back over to Peggy.

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

Greg, thank you. And thanks to the three of you for great presentations to start us off. I do want to just add one additional component to our ecosystem discussion and that is to underscore what Husseini had mentioned in passing about the importance of bringing in the regulatory perspective as well. We hoped to have an official card-carrying regulator as part of this session, but having served as the FDA Commissioner for six years, in the United States, I will step in to emphasise that one of the things that’s very exciting about the way we are now thinking about accelerating innovation in this space is really the early and continuing engagement of regulatory authorities.

Someone in the chat earlier mentioned the importance of regulatory science. It is crucial-- whether you're in academia, whether you're in industry, whether you are working in terms of basic research or translational research or in the data science area-- to really understand the regulatory context. To understand what it takes to actually move a good idea and important discovery into a real world product. And what kinds of trials, including in low resource settings, may require lower cost imaging or moving entirely away from imaging to blood and digital tools for pathological and clinical assessments.

Professor Cornelia Van Duijn
Agree with George - we must trial blood based biomarkers and Digital tools in future trials along side the standard PET and classical cognition.

Dr Mathew Verghese
Absolutely George! Inequity will remain in LMIC unless costs and cheap tech is addressed. PET and CSF and other bio markers are far away in LMIC

Phyllis Barkman Ferrell
Not surprised to see Brazilian leaders taking such a role in this meeting, they have been leading the way in the
critical questions are going to need to be asked and answered. This is so important in this area where the science is moving fast, where there are new opportunities to advance this critical work, and where we're talking about bringing in new kinds of technologies to help us with our data collection and our ability to assess both product development, product impact and take advantage of data sets in new ways.

Getting the regulatory perspective very, very early on, really working together, not as individuals in stove piped areas, but as scientists and subject matter experts working together to figure out what's the best way to both advance research and provide the appropriate oversight. This is vital so that we can really be sure about what works and for whom, understanding and harnessing the science in the most powerful ways. It hasn't always happened in the past, but it seems very much to be a part of this new UK collaborative enterprise and importantly, of many other activities in the neurodegenerative disease R&D space. But more broadly, certainly it was an essential feature of our ability to accelerate, so successfully, the creation of a COVID vaccine, and I think we really need to use this model to address the critical unmet public health and medical care needs in the neurodegenerative and dementia arena.

So enough of my thoughts on that topic, but let me use that as a transition to get the insights of a couple of our panellists now and some of you that are in the participating audience on one of those important areas of collaborative research that's so crucial to where we are now and what we need in the future, and that is clinical trials research.

I think that we all know that one of the great challenges in this area has been being able to structure and undertake the appropriate clinical trials. Clinical trials add a great deal of time and cost to the R&D process. But we are also seeing important innovations that will enable us to do clinical trials in new ways; for example the use of biomarkers of various types to help accelerate the process and offer early insights into how products are working. And, as we've been hearing, there is the opportunity to integrate digital tools and data collection methodologies, including real-world evidence, in new ways.

So, you know perhaps first I could turn to Fiona, and then Husseini and then Greg if you want to comment on this as well. Perhaps you can briefly reflect on where you think we are in reimagining our clinical trials approach, including some learnings from COVID, but also from experience in this area of work, and what might we aspire to going forward? Fiona?

Professor Fiona Watt
Executive Chair, Medical Research Council

Yeah, thanks I'm happy to kick off on this. At first sight saying what have you learned from COVID clinical trials that would apply to dementia seems mad! Because we're talking about an acute infection versus something which is much manifests over a much longer time. But, actually, there are things that we learnt which we can apply.
One thing is that I think is really reducing greatly the obstacles to participate in trials, both for the clinicians and for the patients. So, simple protocols, data sharing, and a way of coordinating clinical trials.

You mentioned the regulators and certainly in terms of the approval for trials of drug repurposing the relationship as you said should happen between the investigators and our regulator MHRA was incredibly tight. And so instead of MHRA receiving a surprise package of data, there was this dialogue saying we will need to know this, we will need to know. And that was really helpful. So, I think making sure that we coordinate the clinical trials rather than having individual investigators or hospitals trying to own them will make a huge difference. And I think there’s a big appetite for that now.

Great. Thank you. Husseini, I know that this has been an area of focus and some considerable passion for you, so we’d love to hear your thoughts.

Thank you Peggie and I’d really echo and amplify everything Fiona just said.

I think that many of the challenges we faced in neurodegenerative clinical trials, I think, can and are being overcome by the development of more sensitive tools for patient identification for stratification and for diagnosis and will make sure we can roll the right patient for the right trial. I think what’s also very important that you know with the data scientists we are able to apply advanced analytics. And I think, what you touched on, the technological advances that have been made over the past few years. And certainly the implementation of this accelerated during the pandemic, it has really brought digital technologies to the fore.

I think digital technologies actually could be game changer and they could have many benefits in terms of their clinical trial space. One is that you know, as you know, many of our readouts have traditionally been subjective. Almost paper and pencil! But now with digital technologies, both efficacy and safety endpoints might even be more sensitive than traditional readouts are. Not only do you have more sensitivity, but they can reduce the size and the duration of the trial.

I think, something that Fiona also touched on, there could be a reduction in patient burden, since remote assessments can minimise the need for as many in-clinic visits. Although we’re moving earlier and earlier in the treatment population, in terms of ages, we recognise that many of our patients still are elderly patients and people who may have mobility issues, so reducing patient burden is important.
I think another thing that is really front and centre on everyone’s minds is diversity. And I think in principle doing remote digital assessments can include the increase the diversity of participants because it’s easier to have graphically delocalised trials so you can reach representative populations wherever they are, not just because they happen to be near Harvard or happen to be near Oxford, etc.

And in opinion one of the most important things, and you know this well from your FDA time Peggy, I think we really want to really know that our interventions make a difference in the real world. And using some of these digital technologies you can basically capture information that is ecologically relevant. So you’re getting it while people are going about their daily lives rather than coming to the clinic.

You know, I hate to use the term silver lining with respect to COVID, but I think it’s true. I think COVID-19 has altered the conduct of clinical trials for the better.

So again, thanks to the regulator throughout the world we are seeing different models of trial execution including assessment at home, digitally enabled primary care trials, we see more in the way of use of electronic medical records and real world data for recruitment. The use of what we call you know digital twins and external control arms. I think once again coming back to what Fiona said with have seen more platform trials and ready to go protocols and shared receivables.

And I’d also like to note that we delighted that Martin Landry, who along with Rory Collins had headed up the transformational UK COVID recovery trials which helped us understand whether things like dexamethasone or hydroxychloroquine work, is a part of the neurodegenerative initiative I outlined earlier.

And so I do think that actually, you know things are aligning so that we can bring technology, we can bring data science can bring new ways of working together, we can bring regulators to streamline the clinical trial process without sacrificing quality so we can reach better outcomes so I do think that’s something for us to be hopeful about.

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

Well, thank you and you certainly underscored some of the potential applications of data systems and digital tools in strengthening our ability to do clinical trials closer to where the patients are and in ways that will also add real value collecting different kinds of information to enhance our understandings. And Greg, you may have some important perspectives on where we are in terms of our capabilities to do that and how best to integrate those kind of somewhat more novel approaches into our clinical trial system.
Yes, certainly and I agree with both the comments that were made earlier by Husseini and Fiona.

It's been amazing to me one of the key trends that we've seen with COVID has been this rise in virtual care. What was a fraction of a percentage of all visits before the COVID pandemic, peaked at over 50% of all healthcare encounters. What’s important now, 19 to 20 months into this, is that’s perpetuated. It is holding steady. About 25% to 28% of all healthcare encounters are virtual. If you really dig into what's happening virtually, 70% of all of those virtual encounters are either in behavioural health or neurology. So, 70% are neuro-based consults so that creates an incredible opportunity that I think this entire community needs to be careful to lean in and perpetuate. This creates access not just to care, but for clinical trials. And a more equitable access. So, as was said earlier, you don't need to live next to an NHS Trust or MGH or Stanford to participate in a clinical trial but this creates access. My hope, and I think for many here, is it really creates global access for those 4 billion people on this planet without meaningful access to care and not having an ability to participate in the trial.

So, as we think about virtual I think the question is how can we bring truth to virtual encounters? And as was mentioned by Husseini earlier, digital tools allow us the opportunity to do that, and I think there's some amazing research now, not only active but being published and validated. Voice biomarkers, video biomarkers, as we bring these together with imaging and our electronic health records or phenotype are and other data sets. I think incredible opportunity there.

There's a whole new field, at least for healthcare, that's being developed in the in the technology industry. So I think we've all asked a device to play a song for us or maybe you've ordered food with our voice? That's something called ambient intelligence. Now what we're seeing is there's something called in the area of health care ambient clinical intelligence. Applying these not only to virtual encounters but in-person encounters to actually capture that data that we see in the health care setting even as the digital exhaust of what we do in healthcare. And of course, wearable devices, helps us fill in all those blank spaces from someone who's with the provider less than 1% of the time. That is 99% of the time. It's incredible cloud connected opportunities there as we go forward.

So, just to conclude there, I think this whole area of ambient clinical intelligence is just getting started at the moment. But there's very powerful technologies that we've used in other industries that will lean in here pretty quickly.
Well thank you. I think it’s clear there are a lot of exciting opportunities and pressing needs. I want to pull out a few points from my monitoring of the chat.

There have been some important observations about how, as we move forward, we need more thinking about the kind of collaborative to advance innovation and to incentivise more research and more product development that will make a difference.

Another is that we really must make sure that the patient population and the caregiver population is engaged. So that we really can understand what works best for them as we move clinical trials out closer to where the patients are. And also as we think about how to assess what kinds of symptoms and patient capabilities must be priorities in our assessments.

And importantly thinking about the fact that we need to be developing products, not just for the UK, not just for the Western Hemisphere, but for settings that have very different healthcare systems, and very different human resource capabilities, but very urgent needs in terms of the growing problem of neurodegenerative disease and dementia.

I do want now to encourage people to raise their hands if you want to make an intervention by voice and face, but I also want to turn to Professor Jeff Cummings, who I understand is ready and willing to make a comment on this important topic, and I see that you have joined us Professor Cummings.

Hi Peggy thank you very much for inviting me to comment on your terrific talk. This has been a really exciting series of presentations. I want to add the tremendous importance of more minority participation in trials. Among the greatest challenge in terms of participation in clinical trials is more equitable representation of a diverse group of participants. With more equity in terms of clinical trial access we will have greater understanding of the impact of new therapies on minority communities. Inclusiveness and diversity must become cornerstones of clinical trial conduct.
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 I couldn’t agree with you more. I think that will be important as we think about how to restructure our clinical trial activities, at least in the United States but in so many other countries as well. Moving requirements of participation away from elite, often hard to access research institutions closer to where people actually are getting their care, whether in local facilities or in their homes, will make a real difference. But it also needs to start from the very beginning in terms of a commitment to ensuring appropriate diversity of patient population in our clinical trials.

I do want to engage some more of you in this conversation. I am going to turn to my colleague and friend, George Vradenburg, who’s never shy, because you posted an interesting thought on the chat. Would you be willing to introduce that into our conversation?

George Vradenburg  
Co-Chair, Davos Alzheimer’s Collaborative

Sure. We have talked a lot about precision medicine and about the need for tailoring very, very specific clinical trial populations to particular biomarkers, but the more that we slice and dice therapeutics for narrowly designed populations, the more drugs we are going to need to serve the broad real world population out there who have a wide variety of biomarker characteristics, or suites of biomarker characteristics.

So that requires that we will have to address two challenges. One is how do we get public and private insurers to pay for what may be multiple drugs for each person with mixed dementias. And the second is a health care system, hopefully primary care physicians, to be able to discern in the real world the right intervention at the right stage of disease for each patient at the level of detail that a precision medicine strategy implies. I say, hopefully, primary care physicians, because there aren’t enough neurologists in the world to be able to do this. So, we need inexpensive and widely-accessible precision diagnostics, into routine primary care practice. So that was the comment.

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

Thank you, Husseini?
I think as always George hit the nail on the head there. There’s going to be two critical things that we collectively need to address.

I think the first one also comes back to the regulators. We have been delighted that the regulators have also recognised that some of our definitions are a little bit broad. Most of the new treatments are probably going to target underlying pathophysiology say tau cascades or neuroimmune circuits etc. We may need to be thinking about how those things may work across our current diagnostic classifications. As George mentioned and as we all know, we have these sort of demarcations which aren’t as real. I do think that’s something we’re going to have to collectively do together. And make sure we get not treatments that sort of work a little bit but really treatments that treat some core aspect of disease well. And then you know potentially you can add on treatment as we do in other fields of medicine.

If I could just come back to the terrific points Jeff made I think that’s another very important considerations, and I think that’s what’s really being thought about as well. So, I do think that the centralised clinical trials which can reach people wherever they are, that will be very important. But then you need to engage certain communities where they get their information. So, for example, what we and others are doing is going to church leaders and other community leaders who can help educate people that this isn’t just a part of aging, or reduce the stigma, and help people start to early on, in the course of potential decline, seek the intervention and hopefully get the best intervention.

Similarly, coming back to something Greg said, I think we’ve also got to recognise that unfortunately there are disadvantaged populations. Sometimes the social, economic and minority population is sort of an overlap. And with some of these digital technologies we’re seeing if we can also do a lot of work on the device itself, so you don’t need to use your expensive precious data plan to be constantly uploading information you can be doing a lot of it really on your watch or your smartphone etc. and then periodically engage with the internet to upload things etc. So, I think coming back to what you said we need to recognise that this is a major societal problem should be about the haves and have nots and include people right off the get go. Thank you.

Well thank you and I understand that Dr Maria Tome from the EMA would like to have her hand raised and it’s great to have a fellow regulator joining this discussion now.
Hi, thank you so much and congratulations on the meeting. It’s a pity aren’t all together in London which is a wonderful city.

I really like the talks. I think when regulators will work with real world evidence. As you know very well we have digital department where you can come and validate your devices or clinical meaningful changes you want and of course we also have digital department at the EMA. We are very much involved in designing guidelines. It’s extremely important for us. What we called real world evidence. information in the future is basically increased. Trials you will not finish with phase three you will have phase four and I think, as in the recent FDA decision, you need to collect these patients that will need to be in trials for years.

I’m very optimistic also in the advantage of biomarkers. I think as our colleague has mentioned, we have very good and rapid developments here. You have blood biomarkers alongside CSF.

It is great we talk altogether. We need to discuss with regulators. Regulators are very keen nowadays in real world evidence. It will inform the payers. Very important there are biomarkers these can be blood or CSF and of course digital technologies. Clinical events nowadays are measured by digital data. That’s the reality. Covid moved things very quickly. As medics we see people online nowadays, particularly in London but all over Europe.

And thank you very much, but excellent meeting and keep looking forward and listening.

Thank you Peggy. Our time is unfortunately getting short, but I do want to turn to Chris Roberts who has put up his hand. He, of course, has been an important voice and long-standing advocate bringing the perspective of the patient community to these important efforts. So, Chris, the floor is yours.

Thank you Peggy. I’d like to thank you all. It’s been very interesting. Hearing it from your perspective has been even better. I think one of the things that we’re missing out on is yes, we’re getting better at engaging with people living with dementia.
themselves. You know that the experts by experience, as it were, but one thing we are missing is using the experts by experience to actually promote research. I think it’s going to come much better to the general public if they see someone that’s actually benefiting from it, or explaining what help that they can be. And you don’t know what you don’t know is the big problem.

When people mention research they think it’s going to be very invasive, it’s going to be time consuming and a lot of the time it isn’t. I think it would be great to do some promotional work from the patients themselves, explaining how it isn’t invasive. You know, people are scared when you mentioned research that they think they’re going to be operated on, they’re going to take a piece of their brain. I did, you know, I take lots. Yeah, I take part in lots of research projects now, and I realise how valuable they are. And it’s also to explain to people affected by dementia, especially in the earlier stages, that this research gives them the hope that that was missing from their lives. It goes a long way to help people and taking part in things then boosts their their confidence and gives them value and focus. The professionals are absolutely amazing, but we mustn’t forget about those living with the disease as well. They can be such a help.

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

Well thank you for those observations and I think I’m going to build on them as we end our session. We are almost out of time, but I do want to just quickly ask our three panellists for reflections about, where they think we’re going, and perhaps a reason for optimism. As I think you all know, one of the challenges at this time of great urgency to advance an exciting set of scientific and technology opportunities is how to make sure that people understand what research is all about, why it’s important to invest, the critical role of patients and caregivers, but also the critical role of policymakers and funders in terms of understanding, willingness to participate, and willingness to invest. Ultimately, progress depends on being able to really explain why this matters, why the moment to act is now, and how we’re going to make a real and enduring difference. So let me turn first to you Fiona very quick reflections and you know maybe you know a wish for the future.

Professor Fiona Watt  
Executive Chair, Medical Research Council

Well, that’s easy because I completely agree with what Chris said. If we could increase the proportion of people enrolled in clinical trials for any treatment or drug that would have huge benefits. It would help with the diversity agenda it would help with everything. So, I always emphasise that it’s a true partnership: there's the funders, the patients and there's the clinicians and the researchers. We must do that to help to help everybody.
Thank you, and now to Husseini

Dr Husseini Manji
Global Head, J&J Science for Minds

I think as HIV/AIDS and more recently Covid has shown, when we work together and come together, we can make big progress. We need to do that in dementia and neurodegeneration. I'm very optimistic. Research has led to so many advances in other fields like cardiovascular, oncology, immunology. We can do it in dementia. We just have to come together, work together. I'm very optimistic.

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

Greg?

Dr Gregory Moore
Corporate Vice President leading global health and life sciences, Microsoft

It's clear that digital technologies are a key accelerator and enabler here as we go forward. My reason for optimism is that those digital technologies and ambient clinical intelligence will allow us to create an ecosystem that we've all envisioned here, one that can be built by all. Built by many and accessed by all. So that's my that's my hope and my vision for the future. Let's build it together and let everyone access it.

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

Well, I think that's a great message to end on. I want to thank not just our three panellists but also all of you who've been participating through the chat or through your questions and importantly, through the work they are all doing every day to help advance a really important agenda. Once again I want to thank the organisers of this meeting for giving us this opportunity to focus on some of these critical issues. So, with that I apologise that I allowed our discussion to go 3 minutes overtime, but back to you, Philip.
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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