World Dementia Council
Leading the Global Action Against Dementia

Virtual Dialogue

Virtual Dialogue: Biomarker Implementation

Transcript

9 April 2026

Supported by

Alzheimer's Society

Virtual Dialogue: Biomarker Implementation

Meeting transcript

Lenny Shallcross, *Executive Director, World Dementia Council*

Good morning, good afternoon, depending where you are in the world. I'm sorry, I can literally feel the sun starting to shine through. I am unexpectedly in Wales and it is unexpectedly sunny, so I think I'm disappearing into the background. But I know most of you already. I'm Lenny Shallcross, I'm Executive Director of the World Dementia Council. As I think most of you know, the World Dementia Council was set up by the UK government to network international leaders in the field and to share thinking. What we do is a number of these dialogues and meetings in person, which a lot of you have participated in.

As you will have seen, we just pressed record. We publish a transcript, but what we do beforehand is check with you any comments that you make. So you can say whatever you want here, and subsequently edit it at leisure. That's the purpose of the recording; we don't actually publish the recording.

Today's meeting on biomarker implementation is being chaired by Fiona Carragher, who is Chief Research and Policy Officer at Alzheimer's Society here in the UK. I will leave it to her to introduce each of the speakers, but I just want to say thanks to Fiona and to all of them for taking part in this meeting, and also to Alzheimer's Society, who are sponsoring this overall programme of activity, looking at advocacy as it evolves in the era of diagnostics and treatments.

Today's meeting is really touching on two themes that we are looking at over this year, which are how we move from innovation to implementation, and the questions around science, policy and political pressure that are going to move us from the innovations that we are seeing into implementation in a health system. The idea of the set-up of this meeting is to have opening remarks, and then it's very much the intention to have a roundtable discussion. So feel free to share your thoughts, agree or disagree, ask questions, and enjoy it. And with that, I will ask Fiona to take it away.

Fiona Carragher, *Chief Research and Policy Officer, Alzheimer's Society*

Thanks, Lenny, and good afternoon from the UK, good evening and good morning to you from across the world. As Lenny says, I'm Fiona, I'm the Chief Policy and Research Officer at Alzheimer's Society, which is the UK's largest dementia charity. We provide help and support today through dementia advisers who hold the hand and really help families navigate through the real complexity and often crisis that they face with dementia. But also, because we really understand dementia, we are fighting for a different future, really driving hope through research and innovation, and policy and advocacy.

I'm absolutely delighted to be here today. This is an absolutely important discussion around implementation, around biomarkers, and something that's really close to my heart. I would describe myself as a diagnostician. I trained as a clinical biochemist in the NHS and spent 30 years focused almost entirely on diagnostics, in the latter years at very senior levels of policy and strategy. And I would reflect that in those three decades I've seen extraordinary scientific breakthroughs, as I'm sure many of us on this call will have done. But the consistent lesson in all of that has been that innovation alone does not change outcomes. Implementation does.

Think about other clinical pathways. We're at this era of biomarkers, real change we're seeing in dementia, but we're not the first clinical community that has been there, whether it's in cancer or infectious diseases; imagine what happened through COVID. All of that is about

system change. So today the question is not, do these biomarkers work? It's about whether we are ready, and our systems are ready, to implement them.

We all know that we're at this inflection point, and these last five years have been quite extraordinary in the dementia field. We can think about the biomarkers, particularly blood-based biomarkers, which are now becoming clinically viable. We have disease-modifying therapies emerging. And the possibility of earlier, more precise detection feels within reach in a way that it hasn't done before. All of this is a fundamental shift. And I would encourage us as a community not just to think about biomarkers as a new shiny tool, but as something that can be a system disruptor: something that can make us think profoundly differently about the pathways that individuals who are concerned about their memory, or who are showing signs and symptoms of Alzheimer's and dementia, have to go through.

Certainly when I look from the UK, our current pathway is just not fit for purpose at all. It takes on average three and a half years to get a diagnosis, so people are diagnosed at a late stage. Around two thirds get a diagnosis. That means a third of people do not get anything at all. But we also know that access to an accurate diagnosis remains limited, so we're not really even using the tools we have currently, let alone the tools that we'll discuss today.

So if we simply add biomarkers into the system, I don't believe we will unlock their value. What we really need to think about is pathway transformation. Where do biomarkers properly sit, or best sit? Is it in primary care? Is it in the specialist system? How do they trigger further follow-up, whether it's treatments or further diagnosis? And how do we really ensure that a better, earlier and accurate diagnosis actually improves outcomes? So this is not just about adoption; it's about redesigning the system for the best for patients.

And I really would encourage us to think about what other conditions have done. In cardiovascular disease, think about cholesterol. Implementation succeeded because you had guidelines and incentives and public understanding, all moving together. And in cancer, huge opportunities came when there was investment across the whole pathway, with the diagnostics as the catalyst for that. And again, think back to that COVID example and see how rapidly a system can change when it needs to scale up. It can be done.

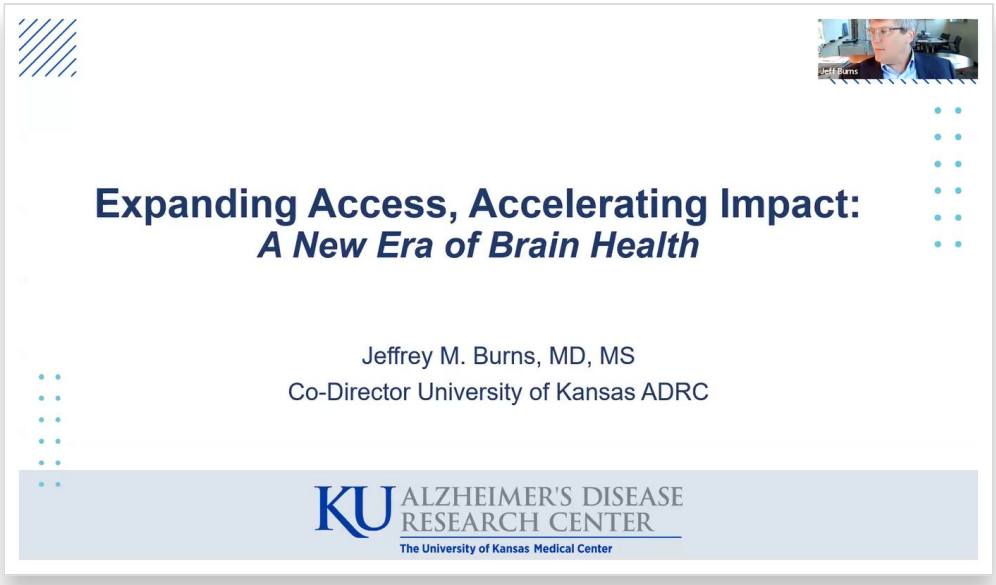
So I think the lessons are consistent and clear. We need to be deliberate, we need to be system-wide, and we need to be equitable from the start. So this is today's conversation: how do we move these biomarkers from that brilliant scientific promise into reality, so that we see, as I'm sure other advocacy organisations would want to see, that real-world impact on families and individuals?

We've got four brilliant speakers today who are going to set the theme, to set some provocation, to make us think about this challenge. Please feel free to put comments in the chat box as we go along, but what I'll be doing at the end of the four speakers is asking you to comment or ask questions, or to bring your thoughts to the discussion, and I'll do that by asking you to raise your virtual hand in this room.

So with no further ado, I'm absolutely delighted to introduce our first speaker, who I'm sure is known to so many of us: Jeff Burns, who is Professor of Medicine and Co-Director of the University of Kansas Alzheimer's Disease Research Center. Jeff, over to you. Thank you.

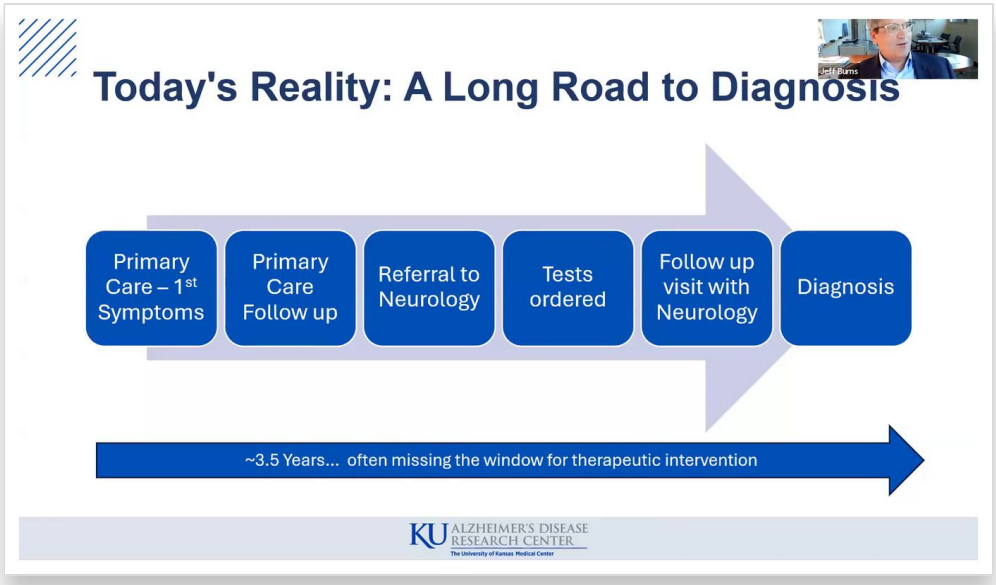
Professor Jeff Burns, *Professor of Medicine and Co-Director, Alzheimer's Disease Research Center, University of Kansas*

All right, great. Thank you, it's great to be here. And that was the perfect set-up, I think, with your comments. I'm going to give a quick tour of what we've been doing for the last couple of years and where we are with system change, because I think absolutely we must have system change to deal with what we have on our hands. This isn't as simple as dropping a biomarker into the system; we have to build a lot around it to make the biomarker useful. I think you nailed it, Fiona, that was perfect.

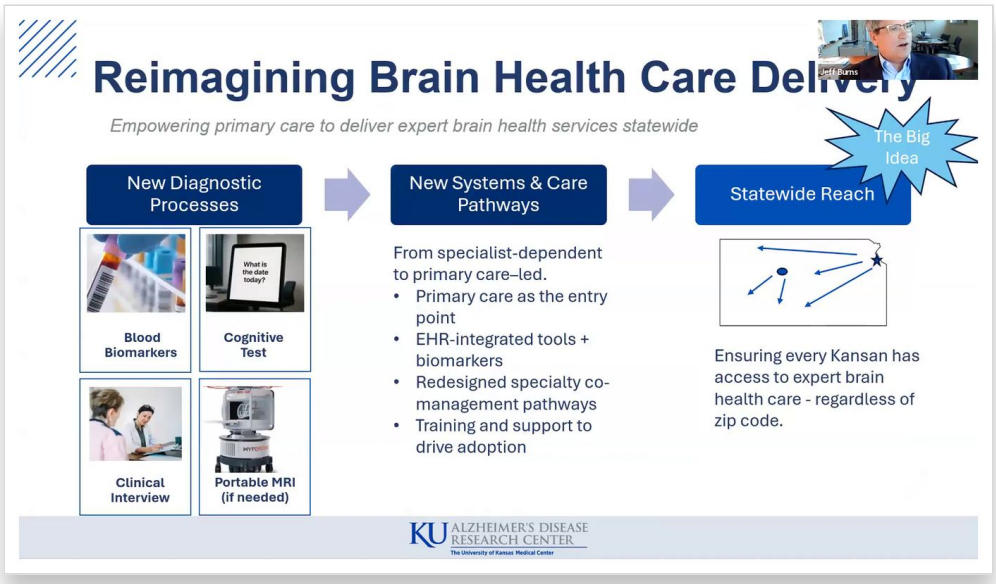


Let me get started here. I'm going to give a quick tour of what we've been doing to really drive access and impact, and use this new biomarker as a place to start and drive that change.

Help is here: we've got blood-based biomarkers, we have new treatments, but we need new care models. We can't just scale up memory clinics to make the change we need.



Fiona, you laid this out well: it takes a long time to get diagnosed right now. The reality is, on average, it's estimated to be three and a half years before someone's diagnosed. That's too long, especially if we have drugs that work best in the earliest stages, now, and more coming, hopefully. This is the reality, this is what we must contend with, and we must drive system change.



This is the overview of what we've been doing. I'll give the big-picture overview of how we're doing this on basically three different levels, really reimagining how we drive brain health care here at the University of Kansas Health System, at the University of Kansas in Kansas City. We're right in the middle of the country. If you imagine the United States and put a dot right in the middle, that's us. Our metropolitan area is about 2 million, and our state is big and broad and very rural, 400 miles across, and we're basically it for memory care in the state. That's our challenge.

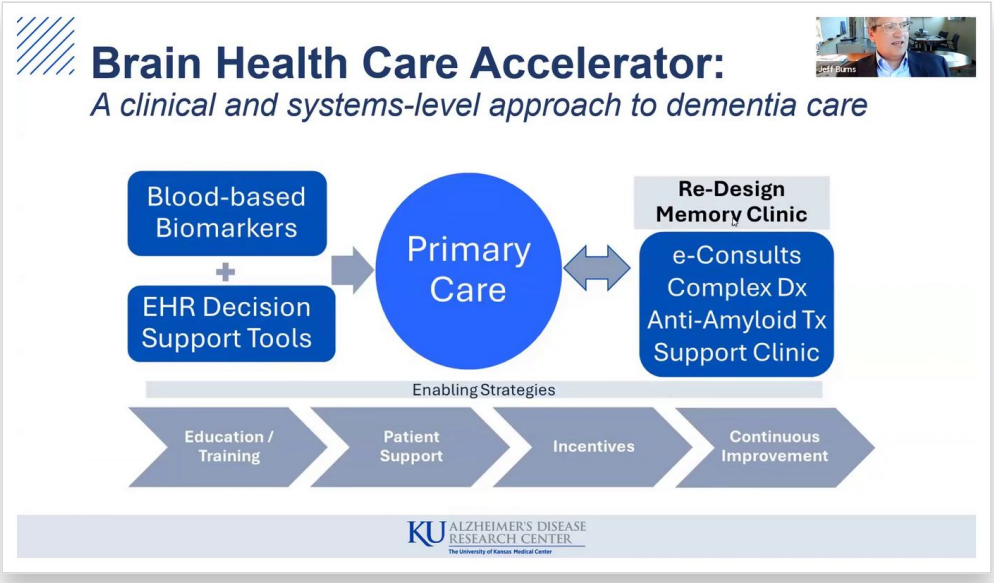
The way we're approaching this is, on the left, thinking about the diagnostic process itself. If we zoom in on what happens in the clinic, you can really break it down to these four things, and instead of taking years or many months to get these things done, we're developing processes to get it done with nurses in just a couple of hours. We're really thinking hard about the actual diagnostic process and the steps that it takes: the interview, the cognitive testing,

the blood biomarker, and we're experimenting with portable MRIs, to really try to make this packageable and portable.

But we're zooming out as well, and this is what I'll primarily talk about: working across our whole health system, which is a big system with a lot of primary care, spreading across the metropolitan area and across the state. We're thinking very hard about what we can do to bring primary care to the centre of this, and making a lot of progress on that front. Primary care is the entry point for dementia care, we believe, and dementia diagnosis. So we built tools in our electronic health record to help primary care do the right things, including interviewing the patient and collecting the right information, and then to support the next steps in terms of what orders to put in and how to think about the diagnosis.

But we're thinking very hard about what we call the "now what" question. Once there is a diagnosis in primary care, they need to know what to do, and this is the question we get all the time: I made a diagnosis, what do I do now? That's where we need more memory care, but we need to rethink the memory clinic and the purposes for which patients are referred to it. And then we drive a lot of training and support around that. So that's taking a bigger-picture, health-system-wide approach.

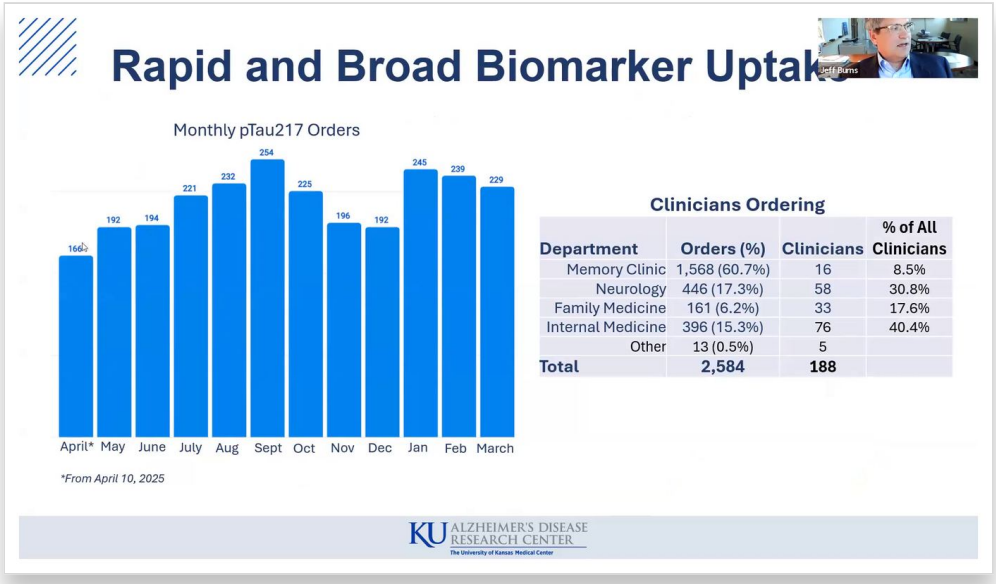
And then we're thinking now about how we move these things, how we port them, how we bottle this approach and move it out across the state, in various ways. We're working with our state legislature to try to get support in the annual budget to do this as well.



So this is the big picture. If you zoom in on our health system approach, it's primary care. We are making the blood-based biomarkers accessible, as I'll talk about in a second. We're supporting primary care in the electronic health record, and then we have the memory clinic. We don't want every patient coming to us; we want primary care making the diagnosis and working with us through e-consults, electronic consults. We have our complex diagnostic clinic, our anti-amyloid treatment clinic, if they want a quicker decision about whether or not somebody's a candidate, and then our long-term support clinic. So we're breaking up and redesigning the memory clinic. And then there are the supportive, enabling strategies: education, patient support, working on incentives around primary care, like the payment models, and we're always trying to improve.

About a year ago, actually a year ago tomorrow, we rolled out the blood-based biomarkers in our system. We spent a year getting them up and running so that a primary care doctor, or any clinician in the health system, could put an order in and get a result back within 24 hours, through our research lab, which we got CLIA certified. That took a year. So a year ago we turned it on, so that they could get a very easy, frictionless order of a blood-based biomarker.

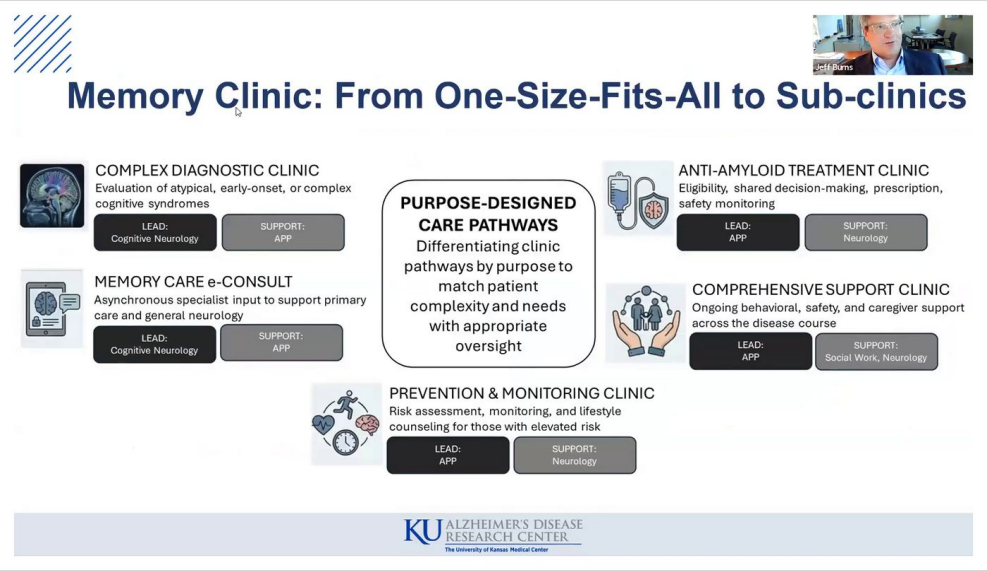
And we supported that with education and tried to create a supportive ecosystem around primary care to use those.



Here's what's happened in the last year. This shows month-to-month orders across our health system, and we have seen, right from the start, really rapid and broad uptake. In the first month we had 160-ish orders, and that rose to about 220 to 250. We had some changes to our system and we dropped off a little here, primarily because the clinicians were worried that patients were going to have to start paying out of pocket for the tests. That led to a hit here, and then we're back to a stable 220 to 250 orders.

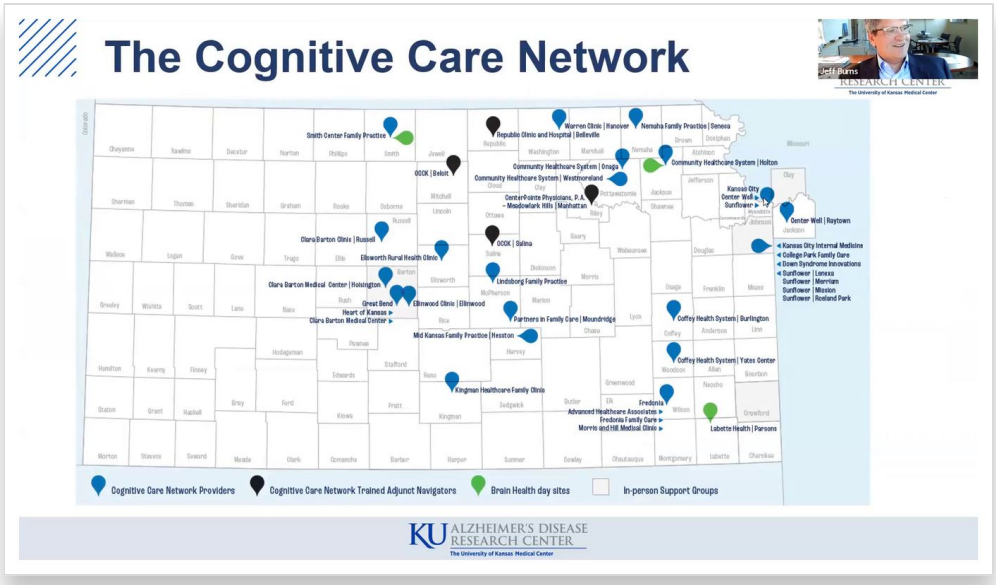
But the important thing is that in one year across our health system we've had 188 different clinicians from all different disciplines order blood biomarkers: over 2,500 tests in a year from 188 clinicians. And over half those clinicians (not half the tests, but over half the clinicians) were primary care. So I think this is clear evidence that primary care can use them. We're also studying whether they are ordering these tests appropriately, on the right patients, and what they are doing with the information. How are they using it? We don't have data yet, visibility yet, on that. But our early look is that they're using it appropriately 95% of the time, and they're doing good things with their patients.

So the message we've got is that primary care wants these. They want to be empowered, they want to use these tests, and they want to take better care of their patients. This is one of those issues where they haven't felt adequate, but we can get them there, we believe, with training and these tools. That's the early message: broad uptake.

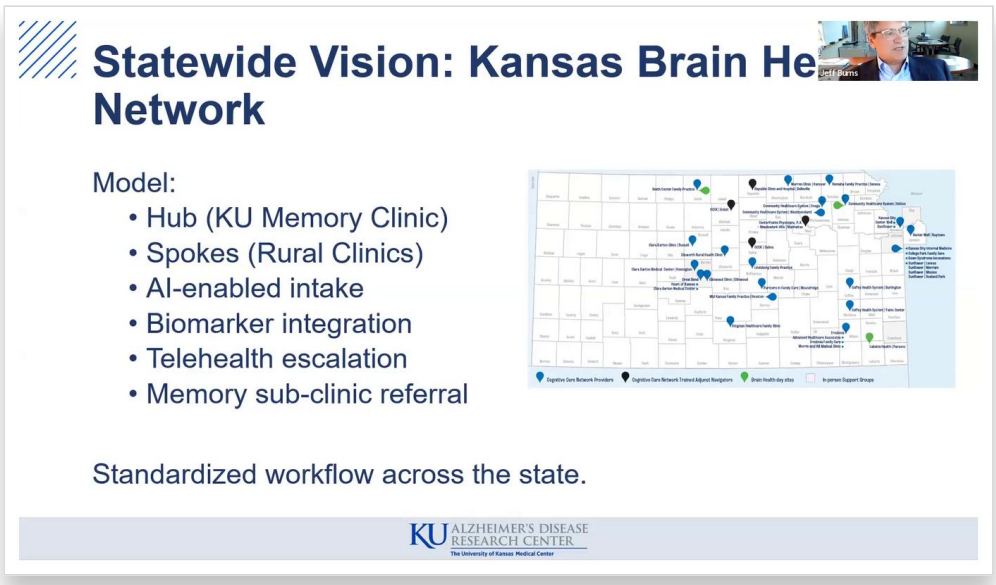


I'll finish by saying that we're really trying to make our memory clinic more supportive. We can't take every patient. We get about 400 referrals a month, and we can only see about 100 new patients a month. So we're thinking very hard. We don't think the model of getting in line at the memory clinic for every cognitive concern is the right approach, one size fits all, and so we've broken it into sub-clinics. It's a little noisy, but we have our complex diagnostic clinic, which is the traditional clinic. We have our anti-amyloid treatment clinic for much quicker decision-making, as I mentioned. We have our long-term support clinic for the journey. And then we're hoping to build out a prevention and monitoring clinic, because a lot of what we do for many patients is just keep an eye on things.

And then we're really experimenting with e-consults, electronic consults: if primary care works patients up the way we have trained them to, they can send us that note and we can give them quick feedback electronically without seeing the patient. The key thing about organising in this way is that we can have different leads; we can really rely on nurse practitioners and physician assistants for some of these sub-clinics. Doing this has allowed us to increase our throughput by about 50% within our clinic without additional staff or clinicians. So we think it's smarter organisation, and then matching the right clinicians with the right level of care that the patient's looking for. This helps with the "now what". It's not the ultimate answer. We need to keep scaling this up, but we're making progress in terms of what's at the back end, in terms of memory clinic and specialty care.



I'll wrap up with this. We've also spent 10 years building a care network across our state. We're here on the far right side, the eastern side of the state, but this is our state, and we're really trying to impact everyone across it and make these things accessible.



You can see, hopefully, that our strategy is to really get better at these diagnoses and take our approach (AI-enabled intake, nurses doing these intakes, the biomarkers) and build these spokes out across our state, and escalate to the sub-clinics as needed, but build a more standard approach across the state and empower primary care all across the state.

And I'll say it is built around biomarkers. Biomarkers do provide great confidence to the clinicians. They can get a good history, especially if we train them up on that, but if they take that biomarker in the context of a good history, their confidence goes up and they feel more empowered to make a good diagnosis. Then we need to help them with the next steps. But they're good at this, and they can get good at it. We need to support them as specialists in certain strategic areas, but they can do a lot here, and so we're really trying to empower and optimise that kind of care across our state. So, built around biomarkers. That's it.

Fiona Carragher, *Chief Research and Policy Officer, Alzheimer's Society*

Thank you. That's so good, and I think it really gives you an understanding if you think system-wide, particularly when you had that last statewide view of things, of how you're implementing certain principles that mean it all aligns together. And of course that's a US view of things, but there are definitely themes that can be brought across to the rest of the world. So thank you so much, Jeff. I'm sure there'll be comments and questions later.

We're bringing you across to the other side of the Atlantic now, to Vanessa Raymont, who I know will be known to many of you as well. She is Associate Professor at the University of Oxford, and lead for one of the UK's Blood Biomarker Challenge programmes, READ-OUT. Vanessa, I'm sure many people will be really interested in hearing the experience from the UK and how we're going about this.

Dr Vanessa Raymont, *Associate Professor, University of Oxford, and Director, Dementias Platform UK*

Thank you, Fiona, and again, I'm also delighted to be with you today. This is a really important topic that we're discussing, and yet very challenging. As you said, Fiona, and Jeff also, it's one thing to have these biomarkers, which are a massive opportunity in terms of how we provide diagnoses and better management for all of our patients. It's a completely other thing to think about how they sit within existing healthcare systems, because I think it's such a massive change for dementia healthcare systems compared to where we have been over past decades.

I think that's particularly true in publicly funded healthcare systems, as we have in the UK. Having worked in the UK and the US, I think there are some huge advantages to the system here in terms of the data we have on patients coming through and the continuity of care. The challenge, I think, is that our healthcare systems, when they're publicly funded, move very slowly. They're like a big tanker: trying to change direction is not a simple thing to do.

Having said that, as Jeff has pointed out very eloquently, we're already here. Diagnoses are now biomarker-led. The Alzheimer's Association published guidelines two years ago now about how we should be thinking about using biomarkers as really the basis of how we're making clinical diagnosis. And of course we have disease-modifying treatments. Whether or not they are available in all healthcare systems, they are with us now. The other thing that's really changed over the last few years is what we know about risks for progression of memory disorders and how those could be managed.

And the final thing, as a clinician, is that patient and public expectations are shifting. I did my first memory clinic back in 1994, and when I think about how people would talk about dementia, or the possibility of developing dementia, then compared to now, it's just a world away. But in comparison, what we do with those patients when they are referred to our clinics is not. If I'm frank, I still do exactly the same thing in my memory clinic as I did in my first clinic in 1994, which obviously has to change given where we are now.

There are some innovations in the UK. We have some brain health clinics, a little similar, Jeff, to your model. But I think one of the issues, particularly in these publicly funded systems, is how we get the evidence that we need for wider rollout. A lot of this ultimately does come down to health economics. One of the things that has shaped systems like the UK is that we have historically been dealing with illnesses that are chronic, where we haven't had good disease-modifying treatments, and they have been managed as such. With most of the pressures on healthcare systems, the emphasis has very much been on making a diagnosis, with differing levels of accuracy, but not a lot of emphasis on long-term support. That now tends to be provided by third-sector infrastructure, charities and so on.

Again, if I reflect on what I'm doing in my memory clinic: 30 years ago I used to follow everybody up on an annual basis. Now I follow nobody up, basically, unless there's a case for why I need to do that to make a better diagnosis. So there does need to be a huge shift, but we also need to be able to demonstrate how biomarkers add value to a system that, frankly, is already very cheap.

And yet the biomarkers are here. They're available direct to consumer in a lot of settings, and I'm emphasising, as I speak to people who are thinking about how we manage systems, that they're already here. We're going to see more and more people coming forward saying, "I've got my biomarker status", so we have to be adapting now. There is good evidence that they reduce costs, both in terms of people going into trials and in terms of providing more accurate diagnosis without needing additional assessments that we've traditionally done, like neuropsychology.

There are obviously huge advantages to these. They have the possibility, I think, to really revolutionise clinical pathways. Obviously better diagnosis is what we all want. But, Fiona, you made a good point: so what, if the system can't deliver those effectively? The reality is that all of us are managing systems where there's only so much resource in the pot, and these have the possibility of triaging and optimising the use of those resources in a way that we've never been able to before in this disease area.

And then, of course, there's a big question about how far to the left we go, if you like, in terms of the disease curves. At what point do we think about using these to triage people in primary care, whether they have an objective memory impairment already, whether it's about case-finding people who are at risk, or whether ultimately this is about population screening? That is a huge step, but I think it's ultimately where we're all going, and where we would probably like to be able to go.

But we also have to think, if we're going to use biomarkers for earlier and earlier detection, what we are going to do with people when we provide them with a biomarker status. Again, I think most healthcare systems are not set up to support people at risk, or people with varying degrees of risk identified by their biomarkers. And not everybody will get the drugs. Certainly in the near future they won't be eligible, they won't be suitable for the drugs, and, because of financial and infrastructure restrictions, they may not be able to access the bloods.

And yet blood biomarkers are obviously massively acceptable, much easier to have than a lumbar puncture or a PET scan. With things like dried blood spots (there's increasing evidence about assays being able to be carried out on dried blood spots) and remote blood collection devices, we really have an opportunity to make these biomarkers truly accessible to people who can't get into clinics to even have a blood test. And this means they are also affordable in their own right.

But there are challenges. Validation is still a big one, in terms of different areas of the population: certain ethnic groups, people with medical comorbidities, the very elderly, people on certain medications. As I said, the cost-benefit of integrating these in services, and where they should sit, is still a challenge. There's obviously a potential benefit in using AI and biomarker data to identify people more accurately. Also, in the UK, where most people are, as I said, discharged very quickly back to primary care, how are we going to find those people again when drugs are available to give them? We're going to have to detect people more efficiently, and AI provides a solution, but also a challenge in terms of where that data sits, who oversees it and how it's protected. And then, finally, the regulatory approval of biomarkers and how we standardise the use of assays nationally and internationally is a huge issue.

Now, as Fiona mentioned, I'm one of the co-leads of a project called READ-OUT. This is one of two studies supported by the Blood Biomarker Challenge and a range of funders in the UK. James Rowe, one of my co-leads, is also on this call, I see, which is great. This project is looking at the clinical utility of a range of blood biomarkers in secondary care to identify Alzheimer's dementia and other causes of dementia. We're working with 28 sites currently across the UK, with a real emphasis on recruiting people that we don't usually get into trials, whether for biomarkers or drugs: particular ethnic groups, people with comorbidities, and people who aren't engaged and don't turn up to memory clinic appointments.

We're then going to establish a panel of biomarkers, based on an initial observational study that's running now, and that will feed into a randomised controlled trial to look at the outcomes of disclosing biomarkers to the person and their physician. I think studies like these

have the potential to provide some of that data around health economic benefit, but also: what do the public want? What are they willing to live with, in terms of how we disclose this information, and how far their data is used to detect their risk in the future and their suitability for future drugs? And how are we going to integrate this with services moving forward?

As I've been doing this project, I've been really aware that in the UK, historically, most memory clinics sit in mental health settings. It's just the history of how we've set up our healthcare system in the UK. Trying to get a blood test done in a lot of mental health memory clinics is still a challenge. They don't have access to a freezer; they maybe don't have access to a centrifuge to process the blood. Solving that for sites sounds like a small step, but actually it's a really important step, so that we have the sustainability to keep delivering this in a healthcare system that is already very stretched and is actively having to keep making cuts just to continue doing what it's doing now.

The other challenge we have is that there is huge promise in terms of detecting people more accurately and earlier, but people are still going to continue to develop dementia, and our healthcare systems need to be able to support and manage those people, frankly, much better than we are now, alongside thinking about that earlier detection.

So, just to finish off, I think there are huge opportunities. I'm immensely grateful as a clinician that I'm working in this period, when we have these incredibly exciting drugs and incredibly exciting, accessible biomarkers. But our systems need to change dramatically. We particularly need to think, for publicly funded healthcare systems, about how we work with our sites to develop business cases, to move data from research to service development, and how much of this should come from the bottom up, with individual sites developing new services, versus top down from our governments, with restricted budgets.

I think we need to speak to the public much more, because we can't boil the ocean in all of our healthcare systems. What do the public want, and when do they want these changes, reflecting on the challenges we face? And finally, as you said, Fiona, we need to learn from each other much more, from the experiences of other countries that are already doing much more of this. Thank you.

Fiona Carragher, *Chief Research and Policy Officer, Alzheimer's Society*

Vanessa, thank you so much. You covered so much there, from the real practical side of how we actually do this when our memory assessment clinics are not set up for it, right through to the more philosophical piece, which might even be around ethical and moral debates, if you think about moving to early detection where not everybody will have access to potentially disease-modifying therapies. So a lot there to discuss. But your point at the end is really important: not just learning from each other, in this global virtual room that we are in, but also learning from other clinical conditions that have gone down this path. There are certainly things from other clinical conditions, like cancer or cardiovascular disease, that we can learn from. So thank you so much, Vanessa.

We're staying in Europe for our next speaker, and I'm absolutely delighted that we have Argonde van Harten from the Alzheimer Center Amsterdam, who's going to speak to us about the experience in the Netherlands.

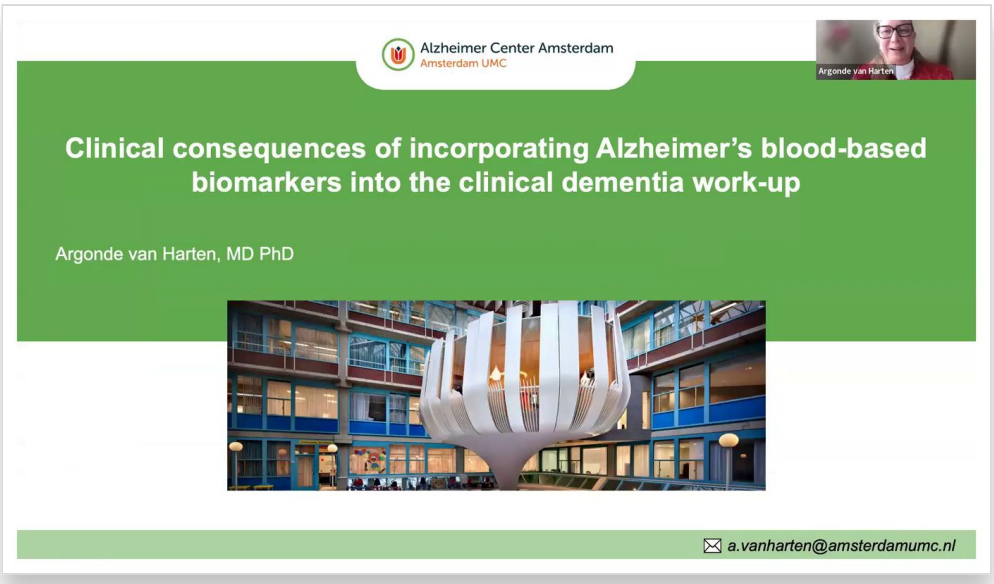
Dr Argonde van Harten, *Neurologist, Alzheimer Center Amsterdam*

Thank you, Fiona. Oh, one moment, I have to share. Hopefully you're now seeing my presentation.

Fiona Carragher, *Chief Research and Policy Officer, Alzheimer's Society*

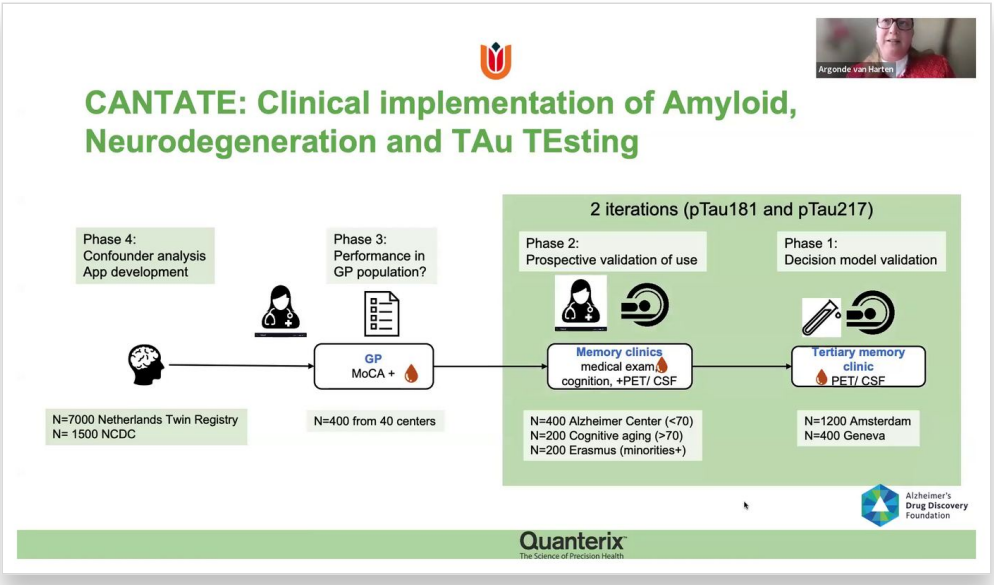
Yes, that's brilliant, thank you.

Dr Argonde van Harten, *Neurologist, Alzheimer Center Amsterdam*



Perfect. Well, it's such an honour to be here, and it's already been a great discussion. I think the major points have already been made about the challenge of getting these new diagnostic opportunities into the clinic. First, we need a very good diagnostic test that is accessible, but we really do need to show that such tests have clinical consequences, especially in publicly funded healthcare systems, which the Netherlands also has.

What I wanted to do is to show you some data from the CANTATE project. I'm working on multiple projects around implementation of blood-based biomarkers, but this is the one that already has some results, so I thought I would share those with you.

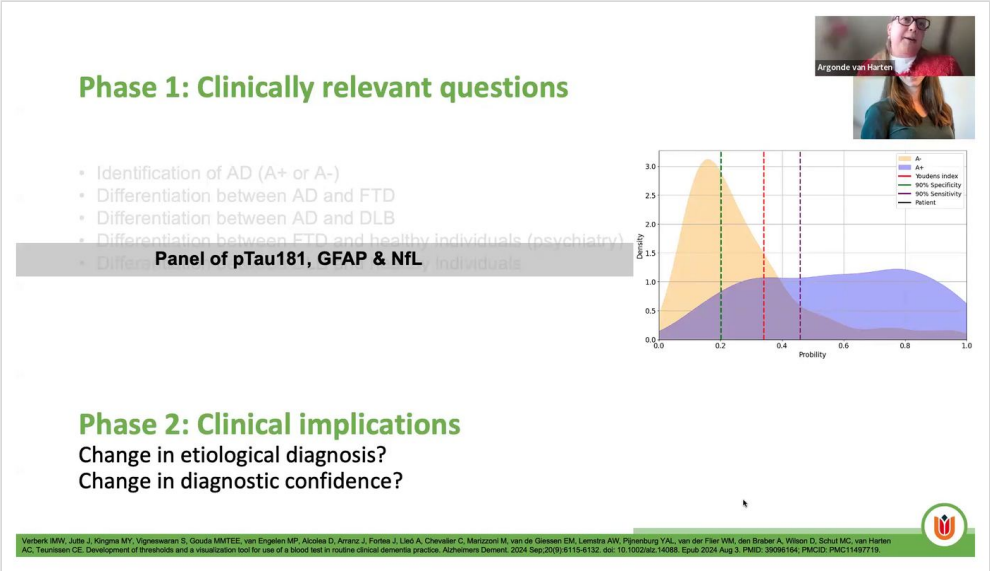


This is an overview of the CANTATE project. You have to imagine that the Alzheimer Center Amsterdam is a tertiary memory clinic in the Netherlands, in a landscape of about 18 million inhabitants and around 80 memory clinics. That's quite different, I think, from many countries. And we are a tertiary memory clinic mainly focused on dementia with an early onset.

What we tried to do was to develop a decision model that would help us decide what to do with those blood-based biomarkers. Then we prospectively evaluated it in three different memory clinics in the Netherlands. Two were academic, ourselves and an academic centre in Rotterdam, and the third was an elderly care memory clinic, so that it would also be representative for those other patients.

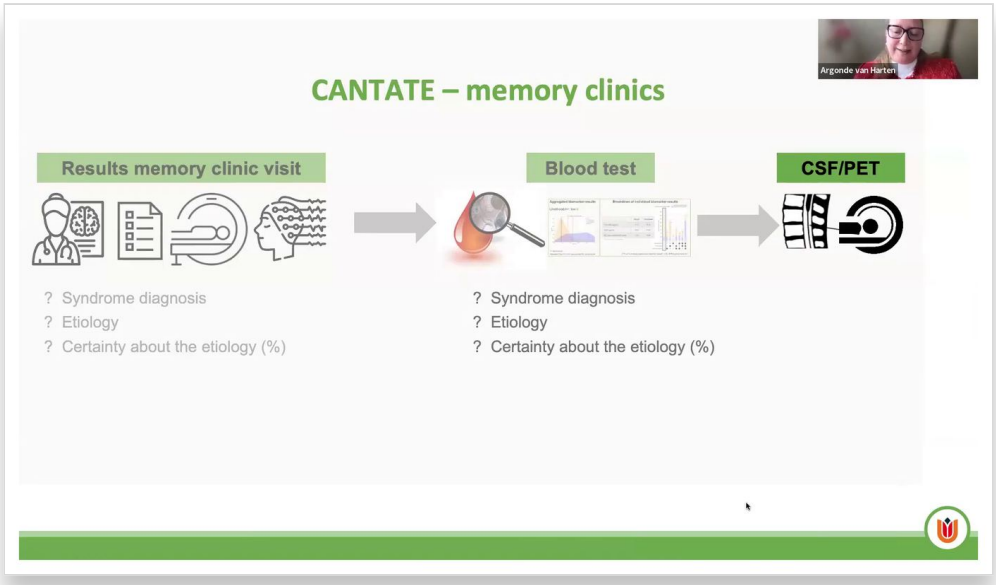
What I'm not talking about, but what is a major challenge in my experience, and maybe something to discuss later on, is the performance in the primary care setting. I'm also experiencing quite some resistance to change in that setting, so that's important to think about, I think.

We actually had two iterations of this process, in which we developed a decision model and then prospectively evaluated the model. The first had p-tau181, and the second included p-tau217 instead of p-tau181. I'll take you quickly through what happened.

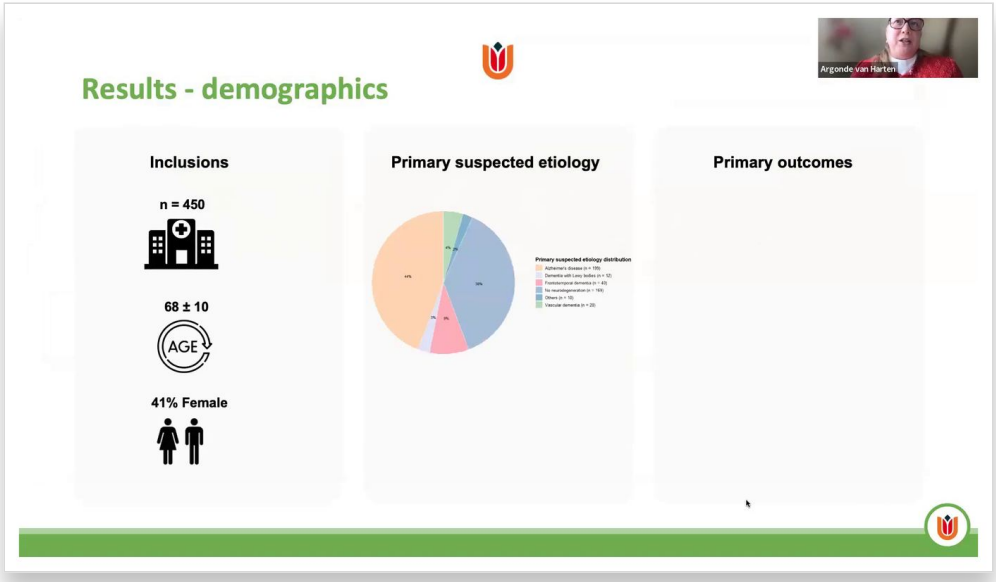


We started out with the clinically relevant questions. We wanted to identify Alzheimer's disease, but also to differentiate between different types of dementia, and to differentiate all those types of dementia from healthy individuals. In the first iteration we ended up with a panel of p-tau181, GFAP and NfL. The results looked like this. It was a probability score: left of the green line you had a low likelihood of Alzheimer's disease, between the green and the purple line an intermediate likelihood, and past the purple line a high likelihood of having Alzheimer's disease. The same was done for all those other diagnostic questions.

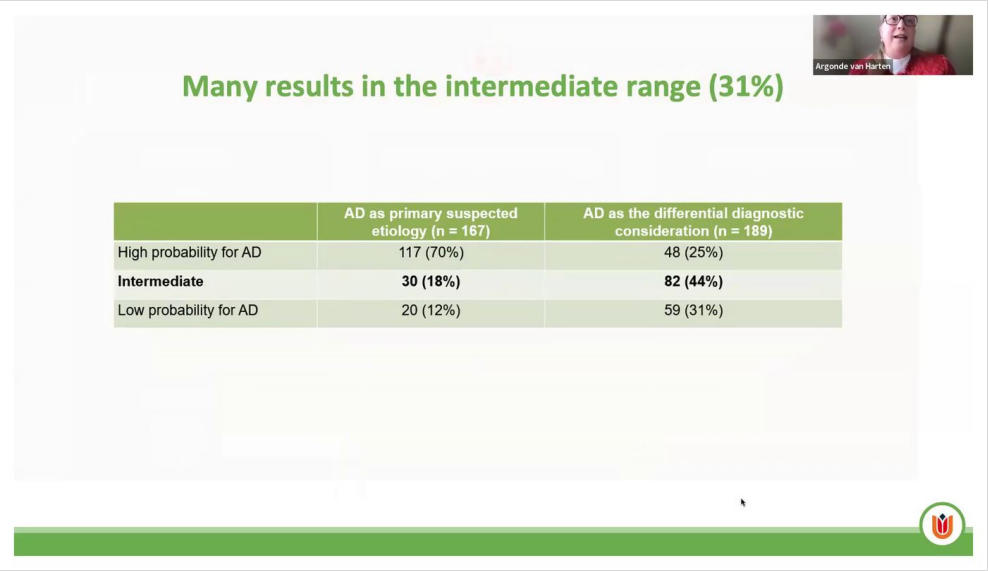
What we asked ourselves is: does this have clinical implications? Is there a change in aetiological diagnosis? Is there a change in diagnostic confidence?



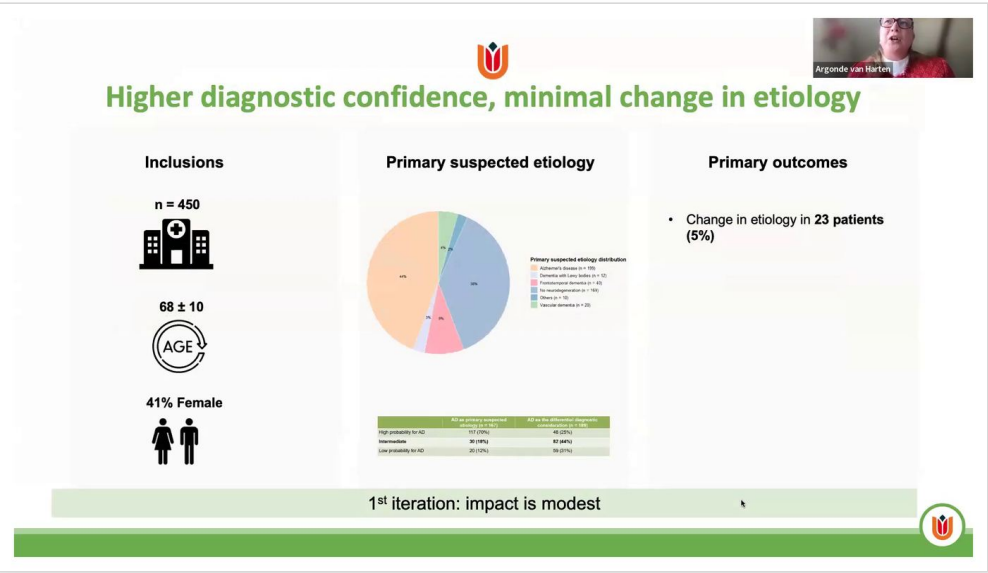
In our memory clinic we currently have a standardised protocol for seeing patients, something that I think really also needs to change, in line with what Jeff spoke about. But currently the patient sees a physician, we have an MRI, they have a neuropsychological evaluation and an EEG, and often also a lumbar puncture. During our multidisciplinary meeting, in which we talked about these results, we would add the blood test prior to reviewing the CSF or PET results.



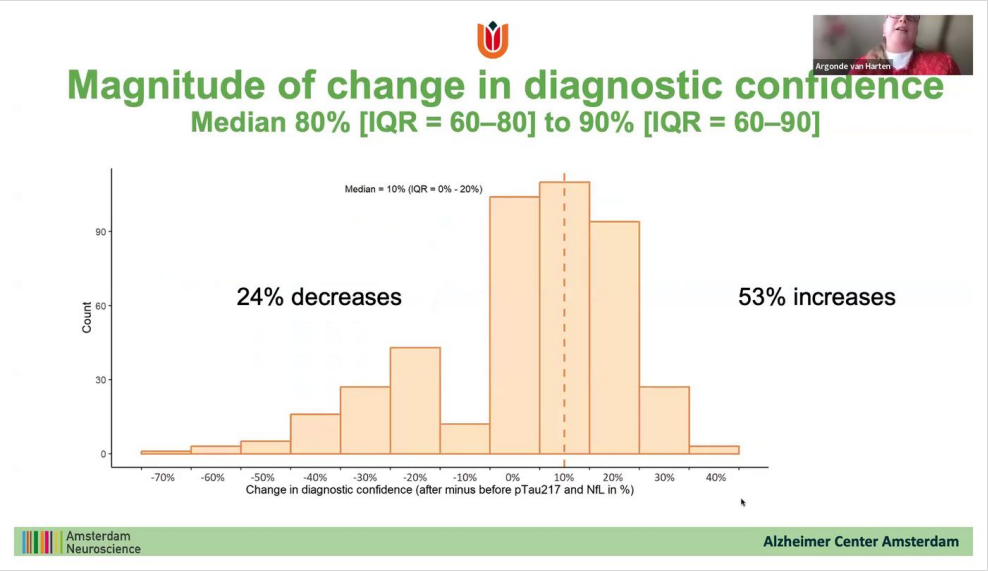
We included 450 participants, all consecutive participants visiting our memory clinic. The most suspected aetiology was Alzheimer's disease, or no neurodegeneration. We see a lot of people with subjective cognitive decline, which goes, I think, to Vanessa's point that we need brain health clinics to serve these people better.



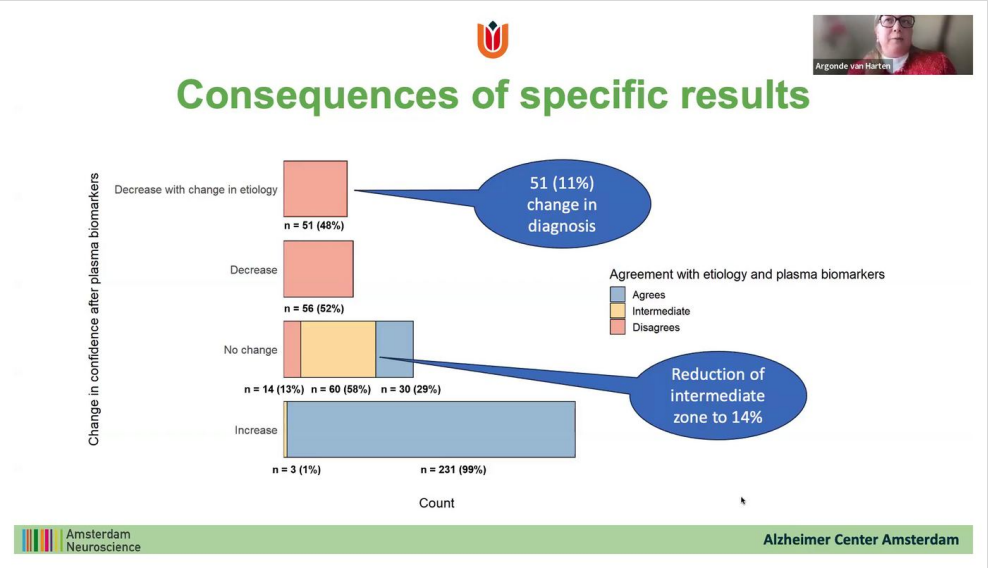
A major point is that we had a lot of results in the intermediate range in that first iteration: 31% of results. That also led to a lot of remaining uncertainty, or less added value.



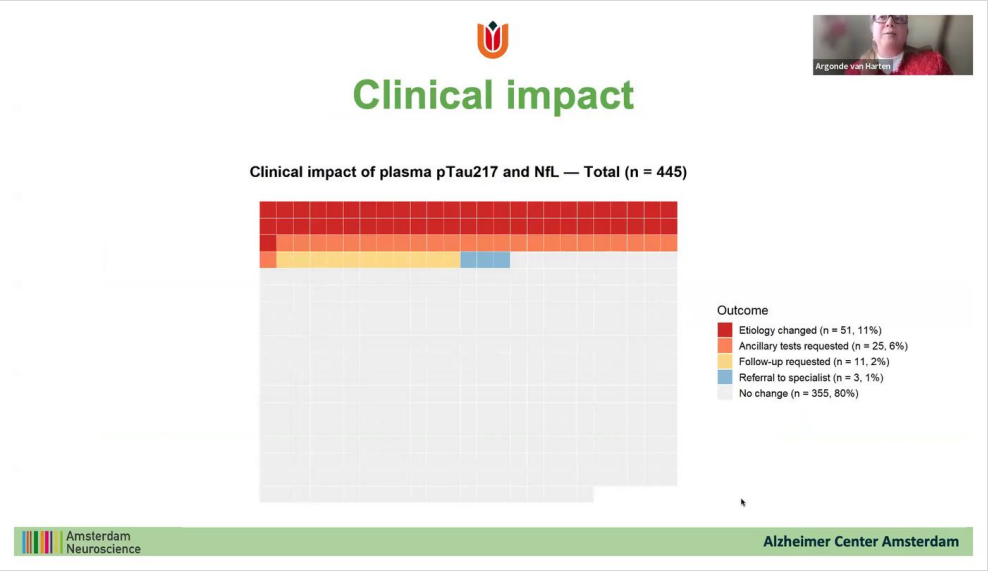
So the change in aetiology was modest: only in 5% of patients did we change our suspected aetiology. The median diagnostic certainty increased from 80% to 90%, with a lot of variation. But in that first iteration the impact was quite modest, actually.



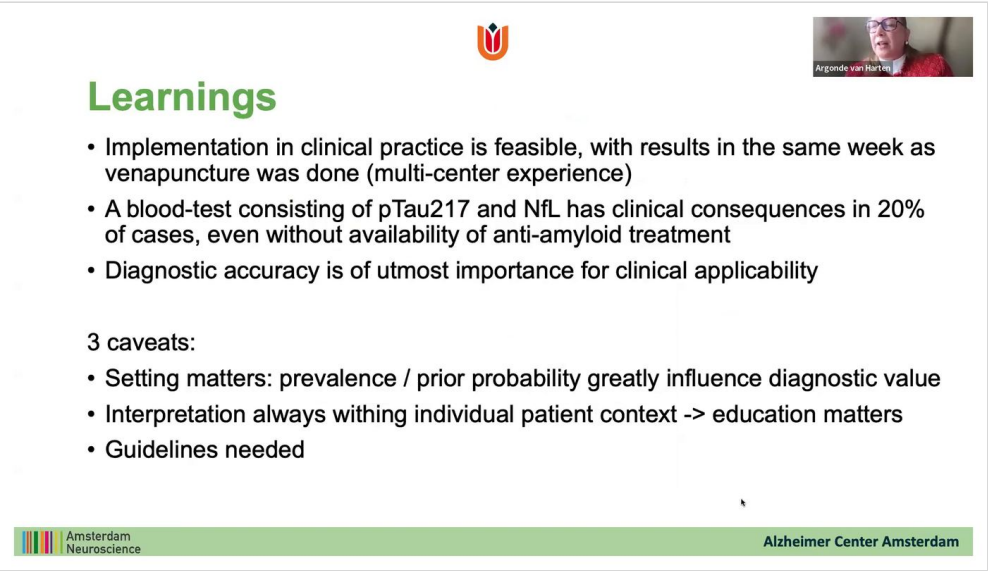
Then we did the second iteration, based on NfL and p-tau217, again in 445 participants from those three memory clinics. I'm showing you the change in diagnostic confidence a little differently here. In that sense the result didn't change much: still from 80% to 90% certainty. But there was a lot of variation. We even saw decreases of up to 70% in confidence in the first diagnosis, and most confidence still increased.



Jeff was saying that he had the impression that people were actually doing wise things with these biomarkers. Here I'm showing you what happens when the biomarker agrees, disagrees or falls in the intermediate zone compared to the initially suspected aetiology. When the biomarker disagrees, confidence will logically decrease, and in this case there was an 11% decrease with a change in aetiology. In the intermediate zone there was usually no change, and an increase was seen when the plasma biomarkers and the suspected aetiology agreed. So in that sense, people act logically based on these biomarkers. And importantly, where we first had a 33% intermediate zone, we were now left with a 14% intermediate zone, so that helped a lot in terms of diagnosis.



This is the clinical impact that we saw. You had the 11% of changed aetiology, but there were also sometimes fewer ancillary tests requested: either follow-up was not done when it was first suspected, or it was requested because of increased uncertainty. We had some additional referrals. So in about 20% of patients we had a clinical impact from these biomarkers.



This was all done in a one-week scenario: venepuncture was done Monday to Wednesday, and results were back by Friday. Now, the Netherlands is a small country, and logistics are fairly easy. But I do think it's clinically feasible to implement these biomarkers, and there are clinical consequences. What we learned from that first iteration is that diagnostic accuracy is key for clinical applicability.

Then some things that I think the others have also already mentioned: setting really matters. Prior probability influences the diagnostic value, and thereby the potential value of these tests. And education really matters. It's always interpreting a blood-based biomarker within the individual patient, which may be harder with less experience and less education, so that's key. And I think for the Netherlands there will be no change unless we change guidelines. We really need scientific evidence to inform those guidelines for us to move ahead with implementation. Thank you.

Fiona Carragher, *Chief Research and Policy Officer, Alzheimer's Society*

Thank you. I'm sure there were lots of comments coming in the chat on this. And your final point about guidance is really, really important. What's interesting, though, in the UK, is that if a drug gets approved, it's a must-do for the system. If a diagnostic goes into guidance, it doesn't have the same must-do for the system. Speaking as somebody who tried to, or did, lead adoption in the NHS of heart failure diagnostics that were in guidance: James Rowe's point about every single hospital having to make its own business case for investment is something that really stands in the way of scalability and sustainability at pace, which we all know is something that we would look for in this field. Thank you so much.

So I'm going to move to our final speaker, who I'm sure will have much to say and reflect on this: Mark McClellan, who is Professor of Practice at Duke University. We'd love to hear your views. We're back to the US now.

Dr Mark McClellan, *Professor of Business, Medicine and Health, Duke University*

Right, Fiona. I want to take you up on your offer of lessons that can be learned from population-level scaling of new care models to prevent and move upstream the care for major chronic disease risks. I'm going to use cardio-kidney-metabolic disease, because that's an area that's had a lot of attention and where we're seeing changes at scale. It will also hit on things that I think can make this cross-Atlantic.

I am in the US, and we do have a different healthcare system here, as you all know. But harking back to some of the comments that have been made before, it is also not one that's easy to change. There is a lot of friction in moving care upstream, because of capacity reasons, as you have all talked about, and because of payment reasons. Even if there is coverage for specific biomarker tests or for specific drugs, that doesn't automatically translate into large-scale, sustainable access. So the kinds of reforms that we've heard about from all of the other speakers today are, I think, highly relevant to this work.

The institute that I lead, the Duke-Margolis Institute for Health Policy, is a university-wide programme at Duke, and we also have a lot of our researchers and staff based in Washington, DC. This is a reflection of my prior experience, first in academia and clinical medicine, and then having the privilege of leading a couple of US agencies, FDA and CMS, and finding, exactly as you have all said, that just having the scientific evidence, while critical, and the treatments approved does not automatically or easily translate into large-scale care transformation and population health impact.

The focus of our work at Duke-Margolis is not particularly on Alzheimer's early diagnosis or, even better, prevention, although that is a key priority for us. It's really on how to do the kinds of things that you're talking about here more broadly in health systems. We've had opportunities to work with NHS leaders and others on this.

What I'd say is that the progress on biomarkers and the progress on disease-modifying treatments have been really important. But if we're going to get to scalable models, everything that we've seen in successful examples in other diseases suggests you have to move in the direction that Jeff was describing earlier. Doing this kind of population impact through specialty clinics is very hard to scale. Integrating it into what could be a routine part of prevention-oriented, enhanced primary care, where there is already a lot of effort under way on chronic disease health risks like cardio-kidney-metabolic disease, is a good model to build on.

Further biomarker progress is absolutely critical for making these models work. It helps you identify where exactly you want to target specific interventions, and as biomarkers are validated for monitoring progress on slowing risk progression towards further complications of disease, that provides a very effective way of motivating patients, supporting clinical care models and developing better evidence.

But I also want to emphasise that there are a lot of prevention opportunities as well that align with cardio-kidney-metabolic disease: things like nutrition, lifestyle, and steps to reduce

cardiovascular risk factors that also affect cardiometabolic disease risk. That's an opportunity to leverage patient engagement and, with the biomarkers and the kinds of tracking that you have already described, give patients a much better picture of their own risks and of how the activities that they are undertaking, alongside the clinical interventions, can make a difference.

Just a couple of other things from the cardio-kidney-metabolic experience. What the US has started to do is to try to support these longitudinal care models, like Jeff was describing (I appreciate Jeff's efforts in the centre of the US). This is hard work, because our payment systems and policies are not designed to make it easy to do longitudinal, effective care from the standpoint of what really matters to a patient, their family, their caregivers and the like. They're designed to provide specific services: covering a drug, paying for those downstream complications, the nursing care and so on that go along with more advanced disease. So this is a fundamental change.

The US has implemented some pilot models in our Medicare programme to help support better-coordinated care, especially at later stages of disease, through a team like Jeff was describing that can help coordinate a patient's needs and make sure that those needs are being addressed as efficiently and effectively as possible. We have a model called GUIDE that provides a per-person payment, not tied to delivering a specific service but to meeting the needs of an Alzheimer's patient and their family that are not being met through the specific coverages and services that are part of the fragmented, less patient-centred care pathways. That's so important as you think about transforming Alzheimer's disease care. It is not yet available for early-stage diagnosis and treatment, or prevention, but it could be.

This is where I'd like to go to the cardio-kidney-metabolic examples. We do have models in the US, including the Diabetes Prevention Program, the Million Hearts model, and now some technology-enabled care models for cardio-kidney-metabolic disease, that make that shift. They are essentially a payment to a provider, or a team of providers, that takes on some accountability for making that person-level pathway work for particular patients.

What matters for that? The payments in these models depend on measuring the risk factors, including biomarkers. In the case of cardiometabolic disease, it's things like BMI and lipid levels, and if patients have progressed to diabetes already, haemoglobin A1c control: identifying people who have those risk factors, or predictors of those risk factors, maybe just BMI and prediabetes, and then payments that are linked to changing the trajectory of those patients' outcomes over time. So it's a per-person payment.

For those of you who are interested, the latest US effort to try to scale up these activities in Medicare is a programme called ACCESS, which is setting up a new category of person-focused Medicare providers that are essentially digitally forward teams. Why digital and AI-focused? Well, these are very hard programmes to scale, to reach patients in rural areas. We don't have the primary care physician workforce, and we're still working on scaling up team-based approaches like Jeff was describing. So these payments are intended to encourage the incorporation of digital tools and resources to help pull a patient's data together and monitor progress over time.

I do think that there is a lot of potential for doing something similar for Alzheimer's disease and related dementias. At this early stage, you may not know which dementia it is until you do the diagnostic testing. But these broad-based approaches are important for getting an infrastructure in place that can really shift disease progression.

Just a couple of other things about how these models typically work. Fiona, I think you mentioned that usually the expansion in these kinds of care models comes first for individuals who can be identified as at higher risk. Biomarkers can help with that. Other risk factors, like family history, social history and socioeconomic conditions, can all lead to predictable risk. If you can put that data together on a patient, that can help you as a care team, like what Jeff is doing, to identify the patients who are most likely to respond to the care model capabilities that you have.

And then a big part of the evidence development in these programmes is showing that these reproducible, scalable interventions do have an impact on clinical care, as Professor van Harten was talking about: that you change clinical outcomes or clinical care decisions, which leads to an impact on biomarkers (a lot easier to measure than waiting for the heart attacks or strokes that are downstream) and potentially predictable implications for other healthcare costs, such as specialty care referrals, which can be expensive, further complications, hospital admissions and the like.

It really is important, I think, for these models to work, to take these different pieces and build them into measurable, reproducible impacts in longitudinal care models like Jeff is describing, with those models paid not for doing specific services but for putting this together as efficiently as possible: using digital and AI technologies, team-based approaches to care, and tools to help empower individuals and families to take better steps to change their Alzheimer's risk and trajectory. That's what can get to the evidence of sustainability on costs, and that can make these programmes much easier to scale.

So a lot of our work in this space is focusing on whether we can take some of the steps that are being implemented now in areas like cardio-kidney-metabolic disease or musculoskeletal disease. I appreciate the analogy to cancer care too, where, as you get to earlier stages, there's a behavioural and large-scale population risk. I think that's relevant as well. But probably the better examples for where we are with Alzheimer's and related dementias are going to come from some of these other very broad-based, very high-risk chronic disease burdens in all of our developed countries, where we need a stronger, more person-focused, primary-care-based system to be able to implement effectively at scale. And we really need a lot more evidence on how to do that effectively.

Fiona Carragher, *Chief Research and Policy Officer, Alzheimer's Society*

Mark, that was a tour de force. I think it shows why we need both the real scientific rigour of the opportunity that biomarkers bring, to really catalyse a different approach, and the deep, hard-graft policy thinking that needs to be done to change the system. I think this is where countries across the world are beginning to grapple with this. But your analogy to the population approach around cardio-renal-metabolic disease is something for us to really think about, because there are many of the same patients who will end up in the memory assessment clinic further down the line. So that real risk approach in primary care is, I think, a real provocation for us as a field. Thank you, Mark.

There have been lots of comments and questions in the chat, but I would like to open up the discussion now. It's really important to hear from you on the call. Please put up your hands and I'll come to a number of you to get the conversation going. We've got just about 25 minutes before I have to hand back to Lenny in a very wet Wales. So, Ashton first, and then Diane.

AH

Ashton Harper, *Head of Medical Affairs, Roche*

Thanks, Fiona, and great webinar. My question was to Jeff. I think primary care plays a pivotal role, or will play a pivotal role, in trying to achieve earlier diagnosis. There's understandably quite a bit of concern about using these biomarkers in primary care, and you mentioned the educational challenges. I just wanted to pick up on your mention that 95% of primary care physicians, in your experience, were using them appropriately. I wondered how you determined that, and whether you are looking to publish results. And also about the education there: over half of the doctors in the graph you showed were primary care. Did they all receive education, or was there a wider educational programme, and how did you implement that?

Professor Jeff Burns, *Professor of Medicine and Co-Director, Alzheimer's Disease Research Center, University of Kansas*

Great, thanks. Don't quote me too strongly yet on that 95%. That's our early look, and we haven't published it yet. But we're very serious about asking the question: are they ordering it on the right patients? We define the right patients as people with cognitive change documented by history, and with a cognitive test; at least, have they done a cognitive test? And our early look is that primary care is doing that.

Our education is built around that too, right now. We do have education that's online. Any time we see somebody order a test for the first time, we hit them with our educational material. But it's also something we're doing in the background, really trying to reach all of our primary care with basic information on diagnosis, but also on how you use blood biomarkers: when to use them, how to interpret them, how to communicate them to patients. That is a great trigger, an action point. Primary care is interested in this now. They've always been a little interested, because they have a lot of patients with dementia. Now they're really interested, because their patients are asking about these tests and about the new drugs, and so we're trying to capitalise on that.

AH

Ashton Harper, *Head of Medical Affairs, Roche*

So it's predominantly online? You're not having in-person seminars?

Professor Jeff Burns, *Professor of Medicine and Co-Director, Alzheimer's Disease Research Center, University of Kansas*

Primarily, although we do in-person live training. We have our tools as well, these electronic health record tools, on how to get a history and document it so that you can bill appropriately through Medicare. So we have other things built around it; it's not simply biomarkers. There are these other wedges that we use to drive behaviour change in the right direction. We are meeting with people one to one to train the champions in clinics on the tools, but for biomarkers it's primarily online: a short, 15-minute set of biomarker talks.

AH

Ashton Harper, *Head of Medical Affairs, Roche*

Sorry, last point on that. Do you have any figures on the uptake of that education?

Professor Jeff Burns, *Professor of Medicine and Co-Director, Alzheimer's Disease Research Center, University of Kansas*

That's harder to measure. Not yet.

AH

Ashton Harper, *Head of Medical Affairs, Roche*

Okay. Thank you so much.

Fiona Carragher, *Chief Research and Policy Officer, Alzheimer's Society*

Thank you so much. And obviously, Jeff, the model that you're using in Kansas is very much a primary care model, as part of the whole pathway. So if there are colleagues from primary care, or who have experience or thoughts, it would be great to hear them come through in the conversation as we go this afternoon as well. We might come back to you, Jeff, on the primary care point. Diane?

Dr Diane Bovenkamp, *Vice President of Scientific Affairs, BrightFocus Foundation*

Yes, hi. I have a couple of questions; maybe you can look at the chat later on. I think this is one of my first times on a live dialogue, so if you've already discussed this in prior meetings, just let me know. All of the speakers were amazing. I think non-profits, for-profits and academic institutions across the globe will want to try to put this in place.

As I asked in the chat, some countries are thinking of using the biomarkers pre-symptomatically. So, two questions. The first is just to be careful, and maybe account for the fact that, if we do want to use biomarkers in preclinical situations, sometimes people don't develop the disease, and then there are ethical, regulatory and access-to-care issues that can arise. I put a link in the chat to a recent commentary that was just published by Dr Rod Corriveau, with his suggestions for five ways, not just to call it Alzheimer's disease, but clinical AD, genetically determined AD, pathological plaque-defined AD, and AD as a broad category. As you said with communication, words matter. So maybe just incorporate that, so that there aren't implications. In the US, you could lose your insurance, or maybe not have care, if you have a head full of amyloid or tau and you never actually develop the disease. So that was my first question. Are there any reactions? And then, I guess, just in terms of choosing the right biomarkers…

Fiona Carragher, *Chief Research and Policy Officer, Alzheimer's Society*

I'm going to ask Jeff first, and then Vanessa, because you mentioned population screening, which really takes you into that very early preclinical detection space. So Jeff, and then maybe Vanessa.

Professor Jeff Burns, *Professor of Medicine and Co-Director, Alzheimer's Disease Research Center, University of Kansas*

I'll be super quick, but thanks for bringing that up. That's why we really are working hard to get our primary care to use the test in people with cognitive change, clear cognitive change. We don't want to use it yet for screening the preclinical population on the clinical side. We're doing that on the research side, but we've got a long way to go before we use it preclinically, or for risk stratification.

Fiona Carragher, *Chief Research and Policy Officer, Alzheimer's Society*

Vanessa?

Dr Vanessa Raymont, *Associate Professor, University of Oxford, and Director, Dementias Platform UK*

Yes, I think that's the thing, isn't it? We're all mindful as a group, having been talking about this for a while, that that's probably where we're heading. But I think the reality is that in implementation we're a way off that. And certainly for publicly funded healthcare systems, there's going to be a continued challenge in how biomarkers like this are managed in primary care, even if you're talking about symptomatic people. So I think the concept of us being able to push this in to identify people at risk is still quite a long way off.

But I also recognise that a lot of this is subject to increasing public pressure, rightly so. I think more and more people, as I said, will be going out to direct-to-consumer tests in the future and coming with those anyway, and that will have to be managed within the context of the system. I do think we're very aware, as clinicians, of where the barriers usually lie in terms of the data we have and what the systems can manage. What we have to be mindful of is that this is moving faster than we are, in terms of the data we have, but also, as I said, in terms of the public appetite for understanding risk.

I sit in lots of conversations where people still say, "I don't think most people want to know their biomarker status before they're symptomatic." But I would equally say that huge numbers of people, I think, do. It depends who you ask. And the more information comes out about new treatments… Again, in the UK this has been a little couched in the fact that the current drugs are not available on the NHS yet. But I think they will be very soon, and certainly drugs will be, and then I think we're going to be facing these questions anyway. So I think that's also a key thing: the ethics of how we handle the fact that people are going to be coming with this, whether or not we think the system is prepared for it. How do we manage that?

Dr Diane Bovenkamp, *Vice President of Scientific Affairs, BrightFocus Foundation*

Yes. And it could just be addressed by saying, to be able to get a systematic global system in place, maybe pre-symptomatic will be phase two. Anyway, something to think about.

Fiona Carragher, *Chief Research and Policy Officer, Alzheimer's Society*

I think the bottom line…

Dr Vanessa Raymont, *Associate Professor, University of Oxford, and Director, Dementias Platform UK*

…is it's driving service change, right? Which I think is what we all need and want. So actually, I think the public being interested in more case identification, or even screening, is not a bad thing. We just need to recognise, as you said, how we are going to respond to it.

Fiona Carragher, *Chief Research and Policy Officer, Alzheimer's Society*

Yes. I think there were maybe other members of the panel. Argonde, were you going to come in on that point as well, perhaps on the technical point around the actual biomarker tests?

Dr Argonde van Harten, *Neurologist, Alzheimer Center Amsterdam*

I was. I think most of it has already been said, but in terms of meeting the want or the need that exists in the public space, it's very important to realise that individualised prediction models aren't sufficiently there yet. In all honesty, I do quite a lot of biomarker tests in people with subjective cognitive decline, mostly. We have a lot of experience disclosing results, and it goes well, but what I tell them is that a normal result is good news, but an abnormal result means uncertainty. I think we really have to remember that, especially as we're moving from a memory clinic setting to a more population-based setting; that part will only increase. So I thought it was important to say that.

Fiona Carragher, *Chief Research and Policy Officer, Alzheimer's Society*

Really important points, thank you. James, I'll come to you next.

Professor James Rowe, *Professor of Cognitive Neurology, University of Cambridge*

Thank you. I'd like to pick up on some of the points that have been made, but I really want to thank all our speakers in this forum for being consistent in talking about the use of these blood biomarkers, these diagnostic tests, in the context of a proper assessment and a good history. In this forum that seems to be well understood, but much of the discourse (the public discourse, commercial discourse and non-clinical research discourse) really pushes the idea that these are screening tests, or that they are a cheap substitute for a proper brain health assessment. If we allow ourselves to go down that route, we will allow far more harm than good to come out of misusing and misinterpreting these tests. So I think there's a real risk that the people on this call are in a good position to defend against.

Fiona, you talked about lessons from cancer. Our colleagues in cancer had very bitter lessons in the 90s and 2000s, when they took very good diagnostic tests, mammography and PSA, diagnostic tests that were part of an assessment, and took them to the general public. That led to far more harm for many, many patients, and they had to retreat. It took another 20 years to come forward with more nuanced screening programmes, age-limited, for example, and with other screening factors. So we know from cancer that misusing diagnostic tests for population screening has huge risks, and we need to defend against that.

It's also not always cheap. For me, an accredited p-tau217 costs more than an MRI. That's fine; I'm happy to do both where needed, and I'm not worried about the cost. But it's not a cheap and cheerful substitute. It's part of a good assessment. I think all of our speakers today talked about it in that context, even in very different healthcare services, and I just want to really emphasise the need to defend the need for a proper assessment, augmented by p-tau217 or the other tests.

Fiona Carragher, *Chief Research and Policy Officer, Alzheimer's Society*

Really strong points, and very clear in this room, but there is the risk that that isn't the public narrative. Which is why a forum like this, and the role of advocacy organisations like ourselves, the Alzheimer's Association in the US and others around the world, is really important. Dementia is having its moment; it is coming out much more from behind closed doors, although we still have a long way to go. But these are debates and discussions that all of us need to be really aware of.

I'm wondering whether the panel has any comments to come back with. Perhaps Mark, on this point, because you talked a lot about the learning from cardio-renal-metabolic disease, and how that has potentially moved to a much more risk-based approach.

Dr Mark McClellan, *Professor of Business, Medicine and Health, Duke University*

Well, we still have a long way to go there as well, but at least what has come together is this vision. As we heard about today, you can envision what a patient-focused care pathway or care journey would look like, how patients are experiencing it, and I think starting with that is the best place. I would emphasise that it is very hard to make big, system-wide changes, given the complexity of healthcare and all of the specific evidence questions along the way that we've talked about. But laying out a pathway for how you could start getting this pathway moving for some patients, as Jeff has talked about, is I think the best place to start. That's what all of these cardio-renal-metabolic programmes are doing now.

Very important for this is the availability of biomarkers you can track. That doesn't necessarily need to be blood tests. In the case of Alzheimer's I think it's relevant too: BMI, exercise, nutrition markers, things like that as well. And using the markers to help develop validated guidelines for practice faster. We have a lot of those. It doesn't mean they're always followed in cardiovascular disease, but at least it helps inform care, and gives specific guidance that can be used to scale up the most effective ways of implementing that guidance for particular kinds of patients, given their own backgrounds and preferences and where they're getting care.

And I would really encourage trying to identify risk stratification approaches, starting with the patient risk groups where there is the biggest opportunity to move risk progression and affect downstream costs and outcomes, and then building out from there. You see that all the time as new treatments and new diagnostics come along. In the case of cardiometabolic disease and GLP-1s and GIPs, it's been in the higher-BMI groups first, and in the people who have progressed to more significant diabetes or renal disease. But those models can then be expanded out to a broader range of the population, if you've got an infrastructure in place and the data to support them.

I would just encourage you: it's not going to be perfect from the start, but get going, especially in higher-risk groups or settings that can then be scaled. I think that's the way we've seen progress in other areas, moving from downstream, fragmented care to a more upstream, person-centred model, with the data infrastructure and the care teams all built around that. That takes real resources and new kinds of investment to make it sustainable, but it's really important, and you have to start somewhere.

Fiona Carragher, *Chief Research and Policy Officer, Alzheimer's Society*

Really helpful. Larry?

Dr Larry Chambers, *Senior Fellow, Brainwell Institute*

I just wanted to bring you up to date with what we're doing in Ontario, Canada. For a number of years now we've been establishing memory clinics run by family physicians and nurse practitioners. They all go through a training programme, and the idea is that in any community there'd be one primary care memory clinic. As we know, at least half of family doctors don't like to deal with dementia at all, so they refer their patients to these clinics. The clinics have a standardised assessment process that they're trained to do, and where biomarkers come in, they can add the biomarker to their assessment process. They have a lot of expertise. And as you know, our government pays for all these services.

These memory clinics tend to be in group practices, and we have about 100 of them across the province. So in Canada it's just a matter of making the one or two biomarkers that are available affordable. At the moment they're not paid for by the government, but that's how, in Ontario, we're more likely to use them.

Fiona Carragher, *Chief Research and Policy Officer, Alzheimer's Society*

That's a real, embedded primary care model. Any comments from the panel? Vanessa, do you want to come in on that one?

Dr Vanessa Raymont, *Associate Professor, University of Oxford, and Director, Dementias Platform UK*

Yes. I was curious, Larry: is that an initiative that's been organised centrally within Ontario, or is it more from the bottom up, with individual practices organising themselves as a group? Who leads on this?

Dr Larry Chambers, *Senior Fellow, Brainwell Institute*

It's interesting. It was a family physician in Waterloo, Ontario, Linda Lee, who had this idea about 10 or 12 years ago, and she developed the programme across the province. The programme is not fully funded by the province in many ways, but it's based in these primary care health teams, which are funded by the province. They receive a global budget each year, and they have auxiliary staff to help with the process. The family physician benefits from a nurse practitioner and a social worker doing the assessments, and then they present their assessment to the physician, who makes the final decision about the next stage. And they also do follow-up care as well, of course.

Dr Vanessa Raymont, *Associate Professor, University of Oxford, and Director, Dementias Platform UK*

Really interesting, Fiona, and thank you, Larry, because I think it is about trialling a combination of models in different settings, isn't it? Ultimately there will be clinicians in different settings, whether secondary care or primary care, who have the expertise, the interest, the time and so on to do this type of work. You could almost see a hub-and-spoke model, where you've got primary care physicians in certain sites doing this type of work, feeding into secondary care sites again. Some of them are going to be more focused on prevention and case identification, some more on following up people who already have dementia.

Dr Larry Chambers, *Senior Fellow, Brainwell Institute*

I put in the chat the article I wrote, which is an evaluation of the clinics. What we were able to show is a 50% decrease in referrals to specialists by putting patients through this method. And we'll never in Canada have enough geriatricians to do the work that we're talking about here. We also have a residency programme in family medicine called Care of the Elderly, and we have more Care of the Elderly specialists in family medicine across the country than we do geriatricians.

Fiona Carragher, *Chief Research and Policy Officer, Alzheimer's Society*

That's just fascinating, so helpful. Jeff, were you going to come in?

Professor Jeff Burns, *Professor of Medicine and Co-Director, Alzheimer's Disease Research Center, University of Kansas*

A really quick comment: we're seeing this naturally develop as we roll our tools out and train folks. Within a practice, somebody shows more interest, and we're seeing referrals within the practice to that person for the memory assessment. They're the mini memory clinic. We're actually taking that model and now trying to encourage that kind of mini memory clinic built within a large clinical practice, and then that person hooks up with us as needed. Same idea, and it's developing organically.

Fiona Carragher, *Chief Research and Policy Officer, Alzheimer's Society*

And I think what's fascinating about that model, and actually about what we've heard throughout the session, is that in my experience of leading large-scale system change, with diagnostics and biomarkers as the catalyst, strong local clinical leadership is one of the absolute success criteria. You really need someone like you described, Larry: somebody who just wanted to do something differently, who knew that there could be a better way to support their patients, and that's led to something quite significant within Ontario. So it's one of the things that we need to consider in our field: who is there, and how do we have this cadre of new clinical leaders coming through, for that kind of real change and pull on the ground?

And Louise, to come to you, I think probably for our last contribution, and great to have it from a primary care physician. Louise?

Professor Louise Robinson, *Regius Professor of Ageing, Newcastle University*

I don't know how many other primary care physicians are on, but it's always good to have at least one when primary care is featuring so prominently. Thank you to the speakers; it was really interesting. Mine is really just a comment, an observation, as a primary care physician for many decades now.

Jeff, I thought your system was just incredible, firstly for the integration that you've shown. But it's a typical chronic disease model. It's the typical model that's been used for the management of non-communicable diseases in the UK for 20 years, and globally. You put primary and community care at the centre, but you embed them, with support, training and mentoring from their secondary care colleagues, and also the appropriate multidisciplinary environment to enable the work to be done efficiently, and to allow the specialists to see the complex cases, which is what they're there for.

I first saw that in diabetic care 35 years ago as a GP trainee. So this is not rocket science, and Fiona knows that's my favourite phrase. It's not rocket science, and it subsequently happened with asthma and with hypertensive care, with all these common diseases. But it seems to be an approach that has not been followed from a mental health perspective, which is where dementia sits in the UK, because services have become increasingly fragmented. So it's just my point about learning lessons from other chronic illnesses, as Mark said, and about that systems approach and how you manage the efficient use of time and skill mix.

Fiona Carragher, *Chief Research and Policy Officer, Alzheimer's Society*

Such great points, Louise. It isn't rocket science, but it's absolutely hard graft to do, and I think that's what we're finding on this call. Jeff, do you want to respond to that? Because a lot of what you've said, I think, resonated with Louise.

Professor Jeff Burns, *Professor of Medicine and Co-Director, Alzheimer's Disease Research Center, University of Kansas*

I think that's right on. I don't have the best perspective on the other chronic diseases, but I think hypertension and diabetes followed the same kind of path, where it started with specialists and is now a primary care problem with specialist support. We've got to push that along. It isn't rocket science; it's actually not that hard. What I do is not that hard, and I can train people to do it. So we have to change the mindset a little bit there. And necessity is going to drive this. There's just no other way. Like hypertension and diabetes, there's no other way to do this than doing it well in primary care with specialist support. So I agree completely with everything you said, Louise.

Fiona Carragher, *Chief Research and Policy Officer, Alzheimer's Society*

So just finally, thank you to all our speakers and to all of you for being here. I think that was a really fantastic conversation and discussion. It does feel that we're all on the same page, but there is something about how we work together much more on learning across the world, and, equally, as came out really strongly, how we learn from other clinical conditions that have gone before. So back to you, Lenny, in a wet Wales, from a sunny Kent.

Lenny Shallcross, *Executive Director, World Dementia Council*

Actually, halfway through it got quite sunny, but there we go. I would just say thank you all, and thank you, Fiona, for chairing it so well. We will circle back to the people who spoke, just to check what you said, with the transcript, and we'll include the chat and all the links that are in the chat there. And yes, from a very wet Wales, thank you all for participating, and I hope you have a good rest of your day, or start of your day, or end of your day, depending on where you are. Thank you very much. Bye.