Identify Patients at Risk of Cognitive Decline Transcript

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Introduction and Guest Background

Welcome back to the reversed Alzheimer's Summit. I'm your host, doctor Heather Sanderson, and I'm delighted to introduce you to Doctor Richard Pitre. He's the CEO of Site Talks at Sites.

Richard has spent 25 years in the Alzheimer's disease field, and is focused on developing novel genetic tests for assessing the Alzheimer's disease risk.

The Gino Square test, developed in partnership with Thermo Fisher Scientific and Sampled, is aimed at clinicians assessing patients at risk of cognitive decline due to Alzheimer's disease.

In addition to pharma companies seeking high risk patients for recruitment into clinical trials. Over the past 25 years, Richard has developed diagnostic and therapeutic products for GE, UCB, Caltech, Laurentiis and Amersham.

Richard's academic training is from Bristol University in the UK and Harvard Medical School. Richard, thanks so much for taking the time to join us. Pleasure. Thank you.

So I learned about your test recently when I was at a conference, and I was so excited that we could put a number to this idea of risk. Like how likely I can't tell you how many children bring in their parent who's already suffering.

And they're sitting there wondering, well, what about me? We have the same genetics, or at least I've got half of her genetics in genetics or his genetics.

How worried do I need to be about this? And should I get started on the program? And so having a number to associate with that question as an answer is so valuable for people.

Can you tell us a little bit about how you arrived at creating this risk number?

How the Genetic Risk Score Was Developed

Sure. I mean, the motivation here had, I mean, is very much around exactly finding these patients at the earliest possible juncture when the chances to intervene are likely to be, you know, far more efficacious.

And so those patients really, as you describe their fall into two groups, you have the the symptomatic individual who made themselves realize they have a problem.

Or it may be that they've been referred to, you know, by a loved one or family member or indeed a younger individual who has been aware of a parent or grandparent that's been diagnosed previously and wants to know, as you said, whether they've inherited this risk.

So what we do is we look and what we've developed here is the most comprehensive description of genetic risk for late onset Alzheimer's disease, or the common form of Alzheimer's disease, typically manifests in, you know, people of 65 years and above.

But, you know, can actually a period little bit earlier sometimes. The way this works is that there's been a genetic mapping exercise that's gone on for, you know, the last ten years, really.

And through, a big consortium called the International Genomics of Alzheimer Program. And what we've been doing is collecting data from very large numbers of age, match people, some of whom have Alzheimer's and some of whom don't.

And then doing effectively a piece of detective work to pick out those genetic elements that seem to link to increased Alzheimer's risk. Now, working through that data with academic collaborator and partners in the UK, we've identified about 112,000 different DNA variants, all of which we carry to some extent, which confer a little bit of added risk or a little bit of reduced risk.

And what we've what we've basically built is an algorithm that detects those variants, then adds them up in a weighted formula to come up with a single number which describes genetic risk.

We then combine age and gender to come up with what we call apologetic risk score or genus score. That you mentioned. So one being the highest risk, zero being the lowest risk, and we can then essentially put people in different risk categories like that.

So most of our listeners are familiar with the about the genetic thing. And this is I know something that you're testing. How is your test different from just knowing your ApoE status.

Okay. So AP is a very important gene. We all carry the AP gene and it comes in various different forms. And and some of your listeners may know that if you inherit and you can, you can buy a test today from 23 in May and, and find out whether you carry one or more or two copies of the E4 version of the per week.

And if you do, there's no doubt you're a increased risk of Alzheimer's disease. It's a key genetic contributor, but the problem is that you can carry E4 and still never develop Alzheimer's disease.

Conversely, about 40% of people that develop outside this disease do not have E4 alone, so it's not a good descriptor of Alzheimer's genetic risk. What we do is incorporate.

E4 is one of the 112,000 different elements that we combine together to give a formal, accurate and descriptive genetic risk profile for the risk of developing late onset Alzheimer's disease.

And we can look at that. We published data in peer reviewed scientific journals, which shows how much better we are picking out high risk individuals with E4 or indeed high risk individuals without E4.

So we can differentiate to a far greater extent. So I want to just break down some of these numbers so that people can have a tangible kind of sense of what's going on here.

So if you have ApoE e4 for you have and please correct me because you are the expert in this and I'm just a clinician over here. So if you have E4 four four from mom, four from dad, then you have about a one inch two chance, a 50% chance of developing dementia over the course of your life if you have three four.

So just one copy. So one from mom or dad, and then you don't have a four from mom or Dad. You have a three or a two. I don't think I've ever seen A24, but a 3 or 4 is pretty common.

Then you have a 1 in 3 chance of developing dementia. The population at large has about a 13% chance of developing dementia, so these are significantly elevated risks.

ApoE vs Polygenic Alzheimeru2019s Risk

If you do not have a four, then my understanding is you have about a 9% risk. So a little less than the general population. So about a one inch ten risk.

Now what you're describing is, creating a number that is even more specific to that. So how do we know if you have A44? Are you in the camp? The with 50% that gets dementia or the camp.

That's the 50% that does. And we know of course, we've been talking a lot on this summit about all of the lifestyle factors that influence this. However, these genetic factors and understanding them.

If we know that we actually have an 80% risk or a 90% risk genetic of developing dementia, then we know we want to work that much harder, that much earlier in our life.

To prevent this is that we know this, right? Absolutely. I mean, you know, if whatever test you're using, if it puts you into high risk category, you need to remember that it's it's not a diagnostic test.

Okay? So it is not predetermined that someone with a high polygenic risk or even a low polygenic risk will or will not develop Alzheimer's disease. You correctly mentioned that it's a combination, really, of genetic input, but also lots of environmental and comorbidities that contribute to overall Alzheimer risk.

The point is, if you test early and you find your a high genetic risk, then the the rewards for taking on management, proactive management of those other lifestyle environmental risks are that much greater in terms of mitigating your overall risk, either the time in which you might develop, Alzheimer's disease or indeed the rate at which you're decline associated with Alzheimer's disease might occur.

So let's go back to the employee story. So you know, about 75, if you think about the Caucasian populace, this is genetics get quite complicated quite quickly because depending on ethnic background, you know, the influence can be a bit different.

But typically in a Caucasian population, 25% of the population carry one or more copies of the paper. We four form of paper. We, 75% of people carry none.

So let's take that 75% group. If you're in that 75% group, you think you might be feeling quite smug. You know, I'm very low risk genetically, but we know about 40% of Alzheimer's disease comes from that group.

So in the absence of an E4 risk, how do you assess genetic risk? Well, our test is able to identify people that don't carry E4 but have very much in the E4 like risk.

We can stratify in a sort of distribution. Those at the high end of that curve, so we can pick out with clinicians, those at highest risk who will benefit more from those sort of lifestyle.

You know, interventions and treatments of co-morbidities. And conversely, we can pick out people that do carry E4 who were still at relatively lower genetic risk overall because they E4 risk is mitigated by some of the other genetic elements that they may have inherited from one parent or the other.

So so what we're describing here is a far more comprehensive look at the genetic landscape in any individual, and how that will contribute to a lifetime genetic risk.

Got it. So if someone already is symptomatic, I see a lot of patients in their 70s and 80s who are suffering in their children. Adult children usually bring them in or a dear friend or caregiver.

And is there a reason for them to get this test? If they already have symptoms, might they want to inform anyone genetically related to them, or what's the utility for someone in that category?

So. So you may be aware of this publication that came out, in 2020, there was a a Lancet commission that was basically put together a meta analysis of all the data, associated with the impact of these lifestyle and co-morbidity treatments.

And they concluded that something like up to 50% of the risk for Alzheimer's disease was modifiable. Now, that's a huge amount.

Why Risk Matters for Prevention and Early Action

You know, even in a high genetic risk individual, that's definitely a prize worth, you know, going for. Right. But the most important thing I think they published, in addition to that, was that even in people with early symptoms, taking

those lifestyle, you know, modification steps, even at that point in the symptomatic phase of the disease, still had, you know, very managed, manageable and measurable benefit to the patient.

So a suggestion that you can actually reverse some of these early symptoms, which is really exciting, and perhaps that's, you know, your experience in your own clinic, which I know, you know, you've spoken very eloquently about the past.

So I think that that's a really important thing to bear in mind for a lot of this work from The Lancet Commission, which was taking the top clinical, experts and scientists from across the world, US, Europe and other places as well, and was a consensus document with a huge number of authors, I think, really went under the radar a little bit because of the Covid pandemic and the unfortunate timing when it came out.

So a lot of clinicians, even specialist clinicians, have missed this. And we need to go back and educate them and patients about the benefits of this work, much of which stems back from the so-called finger studies that, Professor Mia could tell.

So, Finland, now based in Sweden, actually, you know, set up and managed over a number of years long term activation studies, which identified some of these factors that can be modified, to change risk.

So that's, that's really, really important. That's something that's available to everyone today. Also, of course, on the radar now is the possibility of, you know, disease modifying therapeutics becoming available.

We know about the Biogen story, the FDA approval, but as yet the lack of reimbursement for the fighting drug. But there are other Biogen like drugs coming through.

Just last week, Eisai, actually submitted their, their file, their dossier with the FDA for review. We know that Eli Lilly. We know that Roche and other companies also have similar drugs coming through their pipeline.

So, you know, as well as these lifestyle modifications, genuine disease modifying drug therapies, you know, maybe, you know, not too far away. We all hope so.

And yet yet another reason to to want to understand risk, I think. Yeah, there's there's refrain right from the conventional community, at least as I see it, that there's nothing you can do.

And so why would you want to know your risk? It will just stress you out. Create a new problem. If I'm a neurologist and I've got namenda and aricept and those are my options, and really my message is to get your affairs in order because this is just a down hill slope.

Then to understand risk really makes my job a lot harder, right. So I'm not going to offer this test to people. And yet what we're seeing in well-respected journals like The Lancet is that there is so much that we can do.

And certainly I would I would sort of push back that we don't have to wait for drugs like aducanumab to be available. And that there really, I think will get even better outcomes by addressing these modifiable risk factors, getting rid of whatever's causing the inflammation, the plaques and tangle formation, and that ideally, what we'll do in the future is as those drugs become available that reduce plaques and tangles, the kind of scar tissue of inflammation in the brain is it will do all of our work first to get rid of the inflammation.

And then we'll add those medications just temporarily to kind of clean up that scar tissue and create space for neurogenesis and, and neuroplasticity that can help patients, achieve, you know, dare I say, a cure, or something, at least going in that direction.

So I'm wondering, do you see it kind of similar playing out similarly? I absolutely do. And I think, you know, we are not alone in believing this. The the advent of the brain health clinic.

Which is really targeting people who, you know, today have no disease. They have no symptoms. But but they

need to raise awareness about what they what they may be in for in the future and then start managing that, that outcome, the early present pre-symptomatic stages.

It's much easier to preserve or reduce the rate of decline of neuronal loss. And it is to replace, and, and so anything we can do to help that, I mean, you know, as well as the sort of various, you know, dietary and lifestyle interventions, you know, just sort of social and physical activity can have a huge impact.

You know, the lack of isolation, treatment for hearing loss has been shown to have benefits as well. Otherwise people tend to, you know, they're they're lacking a lot of, you know, natural stimuli.

And it and it sort of forces them to, to interact less, which is not a good thing. So all these things, you know, have very material benefit. And, you know, that there are, I think, a greater number of clinics and clinicians now recognizing this, but there's still a lot of work to be done on educating people.

I was at World Dementia Council meeting in London about a month ago. And when, you know, some of the authors of that Lancet Neurology report stood up and talked about modifiable risk in that sort of 40, 50, 60%, ballpark.

You know, even the experts in the room were quite surprised and were wandering around in the coffee break talking about this number. And and it's the price. It's there now.

It's it's as you said, it's not dependent on FDA approval or reimbursement for kind of math. It's it's something that we can all be doing today. Right.

So how would does someone know if this is a test that they should do? I mean, obviously from where I sit and like, everybody should do this, everyone should know their Alzheimer's risk.

No matter what your age or genetic risk, so that you can be proactive. But that may not be your answer.

Lifestyle, Modifiable Risk, and New Therapies

How do we know if this is a good test for someone? Okay, well, so, we don't make that decision ourselves. What we do is if people come to us, I mean, we are telling clinicians and experts about what the test can do, and then we leave it to that clinician in discussion, in consultation with their patient to decide whether it's right for them.

It's a big deal to know you're outside of a risk. You cannot, know that risk, you know, and we don't want to we don't want to leave people with that knowledge without professional clinical support around them, which is why our business will only ever, you know, sell this through, registered clinical practices.

You know, you might recall that when 23 me started offering their apiary test some years ago, they got into trouble just for sort of putting it out there, and then worried people were turning up on their doctors doorsteps and creating a bit of a problem.

And of course, a lot of, you know, concern, you know, for, for, for a lot of people as well. So, so I think it's much better handled in that way. And that's very much our, our plan.

That said, we are committed to, to telling people about the test and, and if they have questions, then directing them to clinics in their own locality who are registered and able to offer that test.

And in the US today we have about 70 clinics, registered to do that. And that's that number is growing significantly every week. So there is clearly a lot of appetite amongst the clinicians.

And I think ultimately amongst the general public to to understand that risk. And so for someone listening, and we have some of the attendees from Australia, all over Europe, the UK, the US, Canada.

So for someone listening around the world, how would they go about finding a provider who offers this test? Can

they go to your website? Yeah, there's information on our website and there will be an inquiry button on the website.

So if they came to us, we could then direct them accordingly. At the moment the registered we have, we have in North America, it's mostly in the United States.

We have a couple of clinics in Canada, that have come online recently as well. We've got, you know, fewer clinics in, Europe, in the UK at the moment.

But that's that's something that we are focusing on. You mentioned Australia. We don't have specific, clinics registered there yet, but there are clinicians that we're in discussion with, you know, thinking about adding this to their to their services that they can provide. So, yeah, there's there is global interest here.

One thing I should say, Heather, is that, at the moment, the validation work we've completed and published has all been just through sample access and access to appropriate data in the Caucasian ethnic background.

Now, this does not mean that the test will not work in other ethnic groups, but we haven't yet proven that. In fact, I met in London with my technical team just yesterday to review where we are with generating data that will be able to to publish and talk through, performance in non Caucasian ethnic backgrounds.

But that's coming very soon. There's nothing to stop a clinician using this test on someone from another, ethnic group. But that actually at the moment we can't make, you know, a lot of statements yet that are backed up by published data on exactly how accurate test would be in that group and got it.

Got it. That's really helpful to understand that. And I appreciate you acknowledging that. Right. Because so much research is done on white men and then extrapolated to say that this is the truth for everyone on the planet.

Well, and that's the problem. But we do know, even if you just take the AP example, that we covered earlier in this discussion, you know, we know that EPO has a differential effect on different ethnic backgrounds, probably because, you know, the rest of the genetics are having a, a modifying effect from the AP for allele if people are carrying that.

So, so, so we need to and we in fact, we are at the moment just analyzing data from those different groups so we can make adjustments to the algorithm if needed, which, generates that score.

And it's not likely to be a kind of does work, doesn't work situation is likely to be it works to, a greater or lesser extent. And we need to be able to quantify that before it can be used reliably in everybody.

And of course, we are absolutely committed to making this available on the widest possible basis. And then how much does this cost? That's a great question that we get asked very regularly, and it's one that we struggle to answer.

And I'll tell you why. We provide this test to a clinic. And that clinic then decides how much they want to sell the test to the patient for. So in some cases, that could be, you know, a simple sort of past through time cost.

So, so, so, you know, but in other cases, the clinic wants to add this into part of a much wider, set of services, you know, diagnostic services and then possibly ultimately clinical management services.

So we know that some people offer, you know, lifestyle and sort of, you know, dietary supplement type approaches as part of an overall treatment package.

And our test is therefore incorporated as one element of that. So so we don't really have a lot of visibility about what clinics are actually charging.

So we always direct the patient that comes to us to clinic. And they can discuss, you know, what it is exactly that

clinic offers and whether that's appropriate for them.

And then what does it require in order to get the sample. So is it as simple as saliva okay. Or what. What do I have to do to get you the test so that you can run it?

This is a really simple thing actually. And this is one of the beauties of the test. It's, you know, it's readily available to everyone. So, typically we send out a saliva collection kit to the clinic or a bunch of kits so that the clinician is sitting on these, on these kits.

These are very simple. You all to Covid testing. Everyone is used to giving saliva samples. Right. So these are really straightforward. The clinic and the clinician may choose to administer the saliva collection.

Step in their own clinic with the patient in front of them.

Who Should Get Tested and How It Works

Or in many cases, the clinic just simply forwards these test kits to the individual in their own home. They're really simple to use, and then you pop the sample into a UPS collection box.

It's pre labeled and goes to the reference lab, which does the extraction of the DNA from the saliva sample. So you know over 90% of the samples are collected that way.

If the clinic happens to have a blood sample already, you know, in in store or something like that, because they've seen the patient, you know, recently and they have that blood for some other reason.

We can also use blood as the starting point. What happens is the lab extracts DNA either from the saliva or from the blood, and the results are exactly the same.

Regardless of that starting point. But of course, most people would rather give a bit of saliva than have a needle to extract some blood into that, or have, stuck up their nose into their brain.

We're all used to that, unfortunately. And it's not the most pleasant thing. I mean, and the other thing to bear in mind have been you mentioned, you know, other tests as well that might be out there.

You know, most of them are far more invasive. I mean, cerebrospinal fluid, you know, from a spinal tap or even injection of a radioactive dye to look for these.

They'll build up with these amyloid and talc proteins in the brain directly or indirectly. These are very expensive and very invasive techniques, which, you know, really not suitable for this sort of earlier stage, you know, risk assessment, they may be used latterly, you know, if people want to, to look more closely at, to dynamic changes.

So to see whether or not that risk has become manifest at the level of an ongoing pathogenic pathogenic process or not, but these are not suitable for, you know, the early phase of risk assessment, we would argue.

Well, in my understanding, is that genetics actually are more predictive of symptomatic dementias, whereas the the presence of beta amyloid plaques or tau proteins, whether you're looking on imaging or looking in cerebrospinal fluid, there are 30% of people over 65 have an plaques and tangles present to have a diagnosis of dementia, regardless of their cognitive function.

So the utility of that, from from where I sit and my understand ING of the literature at this point is that your tests would actually be more helpful, not only less invasive, but more helpful in predicting a cognitive decline.

Right. What we actually care about. I think that's right. I mean, I spent 15 years of my career with GE healthcare developing the amyloid Pet imaging agents that allow you to to understand whether someone's building up, you know, plaque in their brain or not.

And we've known for some years now that there's a there's actually quite a good association between ApoE4 and amyloid deposition, but not between a powerful amyloid and, you know, deposition and cognitive decline, which is what, you know, most people are really worried about when they come and see their physician.

So so we very much being careful to, to look at the ability to predict cognitive decline associate 80 because that is the most, you know, see, for most people the most serious, clinical consequence of the disease.

So, so for that reason, yes, we would agree with you that that, that, not only is this important to the patient and their clinician, but it's also important to pharma companies because if you're recruiting into a clinical trial and that trial is powered on whether a group of patients decline cognitively over the next 2 or 3 years, you want to enrich that population for people most at risk of decline, to show that your drug is actually having a beneficial effect there.

So for that reason, you know, we do to work with pharma companies as well to help them understand, you know, finding right patients for their trials and also potentially to find, ultimately, genetic signals in a patient that links to a specific response to that drug, which I think is the ultimate kind of goal, really, in terms of personalized medicine, finding precision, very precise medicine, very precision medicine. Yes.

This is so exciting. To think about this idea, I think we're socialized at this day, in this day and age, that there's going to be a pill that's going to fix things.

And, I obviously, don't feel like we're there yet. Certainly. But this collaboration between lifestyle medicine prevention and then if you end up with cognitive decline to do all that work and then add that extra layer of the pill or the I. V., whatever it is that can be developed to make it a little easier.

Certainly is is a really, really exciting thing to look forward to in the future. And I appreciate that you were collaborating with pharma to go in that direction. Right?

Because we need to get out of this dead end kind of trap around just reducing beta amyloid and really shift the focus onto cognitive function. How is this individual experiencing the world?

What are they able to do? Is their executive function, their is their memory, their do they recognize their children? Those that's where the rubber meets the road, right?

This is what's really important to people. I don't care if I die with a bunch of beta amyloid plaque in my brain, if I my cognition is totally perfect.

And so to to see you collaborating with pharma, where as we're kind of shifting out of this emphasis so much on plaques and tangles and towards good cognition, it's just exciting.

I think it's, it's it's even more exciting than that in the sense that, you know, we're beginning to recognize that Alzheimer's disease is a it's a phenotype.

It's we could describe it clinically, but it's probably different ways to arrive at that phenotype. Okay. So and that means that, you know, perhaps not all individuals with Alzheimer's disease are going to respond equally to one particular drug intervention, particularly if we go early in the disease process.

You was testing it previously, you know, looking at inflammatory mechanisms. You know, some inflammatory mechanisms may be driving the disease in one individual or group of individuals, but not in others.

And so, you know, peeking out through genetics, the right group for the right treatment, I think will be really important. And, and of course, oncology and cancer drug development has looked like this for 25 years, but we've been very slow in our own field in Alzheimer's and dementia, because we're only just really understanding and appreciating, you know, the strong genetic drivers behind the disease.

Global Availability, Cost, and Sample Collection

It was not that long ago in conferences where, you know, you you would struggle to find experts in the room who would accept that late onset Alzheimer's disease had a strong genetic component, whereas I think now that has completely changed.

So, you know, we are at a new dawn. I think of drug development approaches for Alzheimer's treatment. And, you know, we can only hope that there'll be a successful, you know, new phase in that, in that effort.

And then you're, careful to say late onset diagnosis of Alzheimer's. So let's just speak a little bit to the early onset, because I don't think you guys are checking for AP or the person's.

That's right. So, so, you know, it basically is a rare form that runs in families, early onset Alzheimer's disease, which is specifically associated with mutations in one of three genes, as you said, the amyloid precursor protein or ATP, for short increase in the limb one increases in two genes as well, which are involved in the metabolism and the chopping up opium, alloyed into these sort of toxic fragments that ultimately form the plaques.

So, yeah, I mean, families that that inherit those sorts of mutations tend to know that they, you know, they tend to be causative rather than just risk associated, although it's more complicated than that, because actually, while there are causative mutations or other mutations which seem to be more, you know, sort of less penetrative, in other words, you can have some of these variants that don't necessarily cause early onset disease.

So at the moment, our test is not designed to pick those up. So, it's not that we, you know, we're not interested from a research spectacle. We have not validated the ability of our particular platform, to identify those reliably.

And in fact, you know, the way that technology works, it may not be the most appropriate for those things. So I think, it's more likely that, patients will be referred to other forms of, genetic testing available in of teaching hospital type environments for that.

Fantastic, fantastic. So what do you, I know we've talked a lot about looking forward and, seeing kind of the future of the research in the future of drug development.

What are you most excited about? You've spent decades in this field. And like you said, it's a it's a new dawn. So what do you hope it looks like when we're chatting ten years from now?

What I hope is that centers like yours and, you know, and brain health clinics in general are a phenomenon in everyone's life. You know, it's just something we do.

It's been normalized. Everybody knows at a certain point, you know, they're going to go and check out their brain health, look for risk and then take appropriate mitigating action.

You know, put the pharma companies out of business. You know, we don't we don't want to be taking amyloid busting drugs that you have to, you know, infuse because they're, you know, antibody based drugs at the cost of, you know, tens of thousands of dollars per patient per year.

It's not sustainable for health care systems to be able to provide that, whether it's a national health system like we have in the UK, or whether it's a more of an insurance backed CMS system in the US.

So I think prevention is going to be a huge part of the solution to this kind of, you know, Sassoon army. I mean, you know, if we think about the the financial and societal impact of Covid up over the last couple of years, we're all fed to the fact that.

But that will pale into insignificance compared with this of late onset Alzheimer's disease wave, which is going to hit us because we're an aging population and the biggest, you know, lifestyle risk for late onset Alzheimer's disease is old age, as you pointed out earlier.

So if we can understand at a younger age and when it's time to actually take steps to reduce overall risk, that is

going to have a huge impact and be hugely beneficial to both the individual and society as a whole.

And the associated costs of looking after this. People. Yeah. So because we have this aging population, that's the fear of God. And everyone of but there's not enough young people to take care of them.

All right. So prevention and I just want to echo what you've said over and over that my clinical experience is that the earlier we intervene, the earlier in the disease process and the younger someone is when they start to notice decline and start to take action, the more confidence they have that they can fully recover.

And this becomes a lifestyle, right? You can't fully recover and then slide back into a standard American diet and and not getting in the exercise or stressing yourself out all the time.

Ethnic Validation, Early-Onset Disease, and the Future

But if we can maintain a brain healthy lifestyle, then we can at the very least delay the onset of dementia and at best stay cognitively cognitively fit for the rest of our lives.

And then you don't need that support that caregiving support that that may not exist just because of the demographic shifts that are happening. These radical demographic shifts across certainly the Western world.

But, my understanding is that every continent on the planet is aging, except for Africa. So there there are massive shifts in my lifetime, and I hope that for my generation, I'm in my 30s, late 30s, and, I would think that Alzheimer's is optional for us, with very rare exception.

And so working together to do the testing, to do as much risk mitigation and prevention as possible for my generation, we should get to a place where, like Doctor Bateson says, this is a rare disease.

And that that is worth looking forward to. And certainly, because of these demographic shifts that you and I both are privy to, I think a lot of people don't realize it.

Right, because it's not happening quite yet. But you can see it on the horizon. Certainly Germany and Japan are experiencing this, that yeah, we have to do something if we have to do something that needs to be a solution and fast.

Yes. And I think that's exactly what clinics like yours have come in, you know, you know, we shouldn't pretend that some of these, you know, lifestyle changes unnecessarily easy for everyone to actually having clinical oversight.

Well, first of all, I think having a a test result that says, look, you know, you need to take this seriously. You're in a high risk group, you know, don't panic that, you know, it's good.

We found this out at a relatively young age and you know, but but now that you know this, take it seriously, okay. And and but but even then, you know, having some oversight, some clinical oversight, some regular interaction with clinical professionals, I think is going to help.

We've seen this from, the American College of Genetics in other disease areas that having that result, that's, understandable by the patient. On the one hand, but actionable, on the other is critical to, to, to sustaining that sort of healthy lifestyle.

So, you know, even in that early, you know, that patient that you've described with early symptoms, it's not too late to do something. But the prize perhaps, is, is that that, you know, that stage earlier we know that amyloid and tau building up 20 or 25 years before symptoms occur, you know, and genetics give you an even earlier insight into those most at risk, most likely to end up with amyloid and time in their brains.

So, yeah, it's it's a huge opportunity that, is in front of this at the moment. And our job, my job is to try and get the message out about this test, about the value of it.

And, and talking to clinicians like you is absolutely a part of that. Thank you so much for your time, Richard. This has been very educational for me.

I've learned a ton. It's a pleasure to speak with you and thank you for sharing my passion and enthusiasm about this work. There's a lot of work to be done, and it's nice to know that there are smart, dedicated people like you around the world who are working to create a solution to this problem.

So I want to make sure everyone knows the website to go to if they want to make that inquiry about getting this test. If you go to the, site talks website dot six group.com, we will direct you accordingly, to to the appropriate information that you may require, talk to you about how the test works and, and then if you're still interested, direct you to, to a clinic that's registered in your own locality and it's called the Alzheimer's risk test, right?

That's right. Great. So, again, thank you so much for your time and for the work that you're doing in this field. I couldn't be more grateful. It's been a pleasure.

My pleasure. Thank you very much. And.