

## Zoom In on Dementia & Alzheimer's

**Blood Tests for Alzheimer's Disease: An Overview**

**Thursday, November 21, 2024 | 1 p.m. EDT**

**Transcript of Zoom with Suzanne E. Schindler, MD, PhD**

**Associate Professor of Neurology, Washington University School of Medicine**

The information provided in this transcription is a public service of BrightFocus Foundation and is not intended to constitute medical advice. Please consult your physician for personalized medical, dietary, and/or exercise advice. Any medications or supplements should be taken only under medical supervision. BrightFocus Foundation does not endorse any medical products or therapies.

Please note: This transcript has been edited for clarity and brevity.

**NANCY LYNN KEACH:** Welcome to Zoom In on Dementia & Alzheimer's. I am really thrilled with today's program and excited to get going. So as people are coming in on the YouTube feed, welcome. And I want to introduce myself. I'm Nancy Lynn Keach with BrightFocus Foundation. BrightFocus Foundation funds research globally for dementia, macular degeneration, and glaucoma. And we have invested just over \$300 million in global research. And of course, we provide information programs to you, our supporters and our friends. This program is also made possible with educational support from Biogen, Genentech, and Lilly. So we thank them very much.

A lot of people pre-submitted questions on topics that are not specifically about blood testing. So we just wanted to flash up here and remind you that we've done, I think, about 20 of these episodes so far. So if there is a subject that you're interested in, please go to [BrightFocus.org/ZoomIn](https://BrightFocus.org/ZoomIn), and all of these episodes, full episodes are available for free. These are the world's greatest experts in this field on everything from diagnosis to genetics and Alzheimer's and the new drugs and what are lifestyle

interventions. So if there's something you're specifically interested in, you can go and see the whole program at this point still.

Those of you who attend these regularly can tell I'm rushing a little bit because this is a subject that is so exciting these days. And so many people have so many questions. So I'm jumping right in to introduce Dr. Schindler. Dr. Suzanne Schindler is a clinical neurologist and neuroscientist committed to improving the diagnosis and treatment of Alzheimer's disease. She completed the Medical Scientist Training Program in Neurosciences, a neurology residency, and a Dementia Fellowship at Washington University in Saint Louis. Currently, Dr. Schindler sees patients with memory concerns and coordinates clinical biomarker testing for the Washington University Memory Diagnostic Center. She leads the fluid biomarker core for the Knight Alzheimer's Disease Research Center and facilitates many collaborative research projects. Dr. Schindler also has a special interest in reducing healthcare disparities and improving access to diagnostic tests and treatments. And we know that because she's giving her time to be here today. Thank you so much for joining us.

**DR. SUZANNE SCHINDLER:** It's great to be here. Thanks for inviting me.

**NANCY LYNN KEACH:** Such a pleasure. So Dr. Schindler looked over everybody's questions. And we decided we would start a little upstream. And I'm going to ask Dr. Schindler, what are the first signs of Alzheimer's disease? Before we get to how you see them, but what are the first signs of Alzheimer's disease, in terms of what's happening in the brain?

**DR. SUZANNE SCHINDLER:** Sure, so when patients first come in and their eventual diagnosis is Alzheimer's disease, we hear often a pretty common story, and that is that patients have experienced a consistent decline and progressive decline in their memory and thinking, usually over six months to a couple years. And the sorts of things that we typically hear about are people repeating questions, not just once or twice, but on a pretty regular basis, misplacing items more often. We all misplace things from time to time, but when people start misplacing them a lot more often than in the past, that's concerning. When people forget appointments when they previously were very punctual, and when they start forgetting details of personal events, those are the sorts of things that are often

early symptoms of Alzheimer's disease. And it's just important to note that most of us occasionally have memory lapses, especially when we're stressed or sick or not sleeping well. But when people really are declining over months and we don't see a clear cause, we get concerned. And that's when we want to evaluate people.

I also just wanted to note that there are many, many causes of cognitive impairment. So it's not just Alzheimer's disease. It's everything from medication side effects to sleep disorders to stroke. And then Alzheimer's disease is, of course, very common as people get older. And it's really characterized by this neuropathology, these changes in the brain, these amyloid plaques and tau tangles that silently accumulate in the brain for many years before people develop any symptoms. When this pathology reaches high levels, many people develop this progressive cognitive decline. And as I mentioned, those initial symptoms from this pathology tend to be what people describe as short term memory issues like repeating, misplacing, forgetting appointments, and things like that.

**NANCY LYNN KEACH:** So when you use the word pathology, we're talking about seeing those proteins in the brain that appear with Alzheimer's disease. And how many years before symptoms may start appearing are those proteins building up in the brain?

**DR. SUZANNE SCHINDLER:** So we've looked at this in a number of different ways. And we can see changes in the brain for about 10 to 20 years before the onset of symptoms in many people. And so these plaques just slowly start accumulating. And at first, it's a silent process. We do see the plaques are accompanied by other brain changes that don't look normal, so they're pathological. But our brains are just remarkably resilient. And so we compensate for a long time for this increasing level of pathology. But then at a certain point, we can't compensate anymore, and people develop symptoms.

**NANCY LYNN KEACH:** I think it's really interesting. So 10 to 20 years before you might start seeing the symptoms that you were describing, these proteins are very slowly building up in the brain. And that discovery has led to some confusion when it comes to blood tests that might be able to detect those proteins. So when should blood biomarkers or blood

tests be performed?

**DR. SUZANNE SCHINDLER:** Yes, so currently what we recommend is that these biomarkers, whether they're the PET scans or the cerebrospinal fluid biomarkers or blood biomarkers, that these should only be performed in patients who already have cognitive impairment and that these tests should only be performed by a clinician within the context of a comprehensive evaluation. And if the test is positive, then we know this pathology is present in the brain, and it could be causing or contributing to cognitive impairment.

However, it's important to note that many patients have other things going on as well that is contributing. So at this point, we can't just do a test and make a diagnosis without considering all these other issues. So we often say that we don't use these as standalone tests. We use them within the context of this comprehensive evaluation.

These tests are higher-stakes now because we use them to identify patients who might be candidates for some of these new amyloid-lowering treatments. So that's important. But I would also say that even if the test is negative, that's very helpful. Because a negative test tells us that this Alzheimer's disease pathology is not present and that we need to be looking for other causes of cognitive impairment.

**NANCY LYNN KEACH:** Right, because those symptoms that you described do not only appear with Alzheimer's and dementia, but for many other causes, some of which may be as simple as taking the wrong combination of medications or lots of other potential reasons.

**DR. SUZANNE SCHINDLER:** Absolutely. And a lot of other causes are reversible. So we don't want to miss those because we can often make people better if we do a comprehensive evaluation and find those other things going on.

**NANCY LYNN KEACH:** And I'll mention that when Dr. Schindler talks about a comprehensive evaluation, we're talking about brief cognitive tests. And last month, we did an episode with Dr. David Holtzman on "How Is Dementia Diagnosed?" And so if you are interested in looking at the series

of things you can do, what these tests are and how they're performed, you can take a look at that episode from last month. And we're also, within the next six months or so, working on a project to film some of these tests, to film cognitive tests, to film a blood test, and patients asking specific questions, to film a PET scan and so on.

And I guess I'll just ask before we go to the next question, which is really, are these blood tests predictive? Can they predict whether you're going to develop cognitive impairment? Let's just take one minute to talk about what are the standard tests that would be needed, along with a blood test, to get closer to your real diagnosis?

**DR. SUZANNE SCHINDLER:** So when a patient comes in to see me. So first I take a detailed history from someone who knows the patient well. Often that's a spouse or an adult child. And then I do a neurological examination. We do routine blood work. So that includes blood counts, blood chemistries, B12, TSH. We do cognitive testing, usually about a half an hour of cognitive testing, focusing more on memory, but also a number of other cognitive domains. And then we do imaging, so structural brain imaging where we're mostly looking for strokes, but any other structural causes that might explain cognitive impairment. And then sometimes we do additional tests. So we frequently find that our patients have sleep disorders that can be contributing to cognitive impairment. So we may order a sleep study. Sometimes we order tests to look for things like epilepsy. So it just depends on the exact context. But it is a pretty extensive evaluation. Of course, we're looking at other medical issues that are happening, other medications. So we're really looking for anything that could be causing or contributing to cognitive impairment.

**NANCY LYNN KEACH:** And so now I'll move to that question. Can a blood test tell you whether or not you're going to get cognitive impairment?

**DR. SUZANNE SCHINDLER:** So there's kind of two parts of that answer. So the first that I'll start with is that right now we don't recommend performing biomarker testing in cognitively unimpaired individuals. And there's a number of reasons for this. The first is we don't have specific treatments for individuals who aren't cognitively impaired. So there's not necessarily anything we would recommend differently if

you were positive. And then also we know that many people who are biomarker positive may never develop symptoms of dementia. And more concerning, there's certain risks of having, for example, a positive result. So some patients might lose eligibility for some types of insurance. So there's reasons that we're not recommending at this point that we do these tests on cognitively unimpaired individuals.

But now kind of getting back to your question, a number of studies have shown that some of these tests, particularly p-tau217, really are quite good at predicting who's at higher risk for developing cognitive impairment. They're not perfect. So there's a fair margin of error. But yes, we use them to identify individuals who are at risk for developing cognitive impairment for enrollment in clinical trials so we can find the people at highest risk for developing cognitive impairment, put them in clinical trials of treatments that might be preventative. And we are hoping that some of those trials will be positive, meaning that we'll find that there are treatments that we can give people who have these positive biomarker tests who are still cognitively unimpaired that will prevent them from developing dementia symptoms, or at least ameliorate their symptoms. But that's not where we're at right now. Those trials are still a few years out in terms of reading out. So hopefully those are positive and we will change our recommendations. But at least for right now, we don't recommend testing in individuals who are cognitively unimpaired.

**NANCY LYNN KEACH:** And you gave me a good segue to Jackie's question, the first question in the chat, which was how accurate is p-tau217? And let's backtrack a little bit. So different scientists are very quickly developing different types of blood tests or blood tests that can look at different things in the blood. So why don't I hand it over to you. The question is, how accurate is the p-tau217? And I believe it's the most accurate so far of what we know, but perhaps you can set the stage a little better.

**DR. SUZANNE SCHINDLER:** Yes, so as you mentioned, there are a number of different types of blood tests that are associated with amyloid pathology and tau pathology. And the p-tau217 test in head-to-head studies are definitely superior. And they're really quite accurate in determining whether amyloid plaques are present. And they're also pretty good for telling us whether these tau tangles are present. And when we



directly compare these to FDA-approved CSF tests that have been used for years to help us with diagnosis of Alzheimer's disease, we find that these p-tau217 tests are really performing very similarly. And then the p-tau217 tests, in some cases, are performing better than the FDA-approved CSF tests in telling us whether this tau pathology is present. So we think that these p-tau217 tests in particular really are performing very well in telling us whether someone has this Alzheimer's disease brain pathology or not.

There are some caveats. So we have not studied these tests as well in minoritized groups or individuals with certain medical conditions. Chronic kidney disease is a particular concern. So in those patients, there's more uncertainty about their performance. Although, in some studies, particularly when we use these biomarker ratios, so ratios of two different types of tests, they're still performing very well, even in populations with a lot of health issues. So we really do think that they are performing well. And there's multiple tests available now that really have quite good performance.

**NANCY LYNN KEACH:** As you're trying to get a diagnosis, you're taking a blood test. You may be getting a cerebrospinal fluid test also looking for those proteins. You may get a brain imaging scan, a PET scan. And we have a YouTube question from Terry: How important is it to determine APOE status? So this, I think, is a question that we want to do a few more programs on genetics. So is there or will there be and should one get it, some kind of a genetic test for APOE and other potential genetic signals now or in the future?

**DR. SUZANNE SCHINDLER:** Yeah, so genetic testing is kind of complicated. And it's important to know that there's really two different categories of genetic factors associated with Alzheimer's. So one are these what we call highly-penetrant mutations, that if you have them you will get Alzheimer's disease. But these mutations are extremely rare. So less than 1% or 1 in 1,000 people with Alzheimer's disease has one of these mutations. And people that have these mutations, typically half of the people in their biological family has Alzheimer's disease, often with an early age of onset. So those are really the genetic forms of Alzheimer's disease that most people think about.

On the other hand, there's what's common in 99-plus percent of people, which is genetic variants that are associated with Alzheimer's disease. But they put you at higher or lower risk. And the one that people are most familiar with is APOE. So APOE is a protein that carries lipids. And there's different forms of APOE So there's APOE 2, 3, and 4. And we know that people who have this 4 allele version are at higher risk. And you get one from your mom, one from your dad. And if you have two of them, your risk of developing Alzheimer's disease is about 10 to 12 times higher than people who don't have one. However, there are still people who have two APOE 4's who do not develop symptoms of Alzheimer's disease during their life. So again, this is still a risk category. And so for that reason, we typically do not do this testing. So as part of our diagnostic workup, we do not do APOE genotyping. Where we started doing it is we know that individuals who have two of these epsilon 4 alleles, APOE4 4, are at higher risk for complications from treatments, these anti-amyloid antibodies. So for patients who are candidates for those treatments, we do this APOE genotyping, this genetic testing. And that's really to inform our discussion about the risks and benefits of treatment. But that's not part of our diagnostic process.

Also through 23andMe and other kind of direct-to-consumer genetic testing, you can find out all sorts of genetic variants that you may or may not have. Again, these are just a risk. So you may have all of these different variants that are bad and still never get Alzheimer's disease. So again, for that reason, we don't typically use these genetic tests to help us in our diagnostic process. Instead, we use these biomarkers like p-tau217 that tell us whether you have the pathology or not. So these are not telling us about your risk for developing pathology. They're telling us about whether you have the amyloid plaques and tau tangles in your brain at that time. So that's really the big difference between genetic testing and biomarker testing. Genetic testing is, for most people, just giving them some idea about their risk versus the biomarker testing is, is this pathology present in my brain at this time?

**NANCY LYNN KEACH:** I think it will be very interesting to see if there will be a day, one day, not now, but 10 years, 20, where you are taking a blood test that can look at your proteins, that can look at your genetics and have a much more precision diagnosis. Do you think that's in our future?



**DR. SUZANNE SCHINDLER:** We're getting more and more sophisticated. So yes, I think that we're getting to the point where we're having panels of biomarkers. Actually, some of these blood biomarker tests for Alzheimer's disease have incorporated APOE into predicting risk for being amyloid positive. However, we've learned that p-tau217 by itself is just so predictive that we're not incorporating that. But yes, I do think that over time, we'll have more personalized, individualized assessment of individuals for what's going on in their brain and what their risk is like for the future.

**NANCY LYNN KEACH:** And I'm just going to mention, I am going to get to the questions in the chat about Down syndrome. I'm going to do a few more setting-the-stage practical questions first. But since you were just talking about p-tau217, Heather is asking, does the p-tau217 test perform the same across different ethnicities? Do we know if it does?

**DR. SUZANNE SCHINDLER:** So that is a great question. And that's something that we're actually looking at WashU with a number of different centers that have a fair number of Black individuals as well as white individuals. And with these really high performance tests, we are really not seeing a difference in terms of how the blood test levels are affected or are related to amyloid pathology in the brain. So that's good. So it looks like these blood tests work. But there are caveats. A number of studies, including studies of the use of blood tests for screening have found a lower rate of Alzheimer's disease pathology in Black individuals and Hispanic individuals. So the blood test is still working. But the rate of pathology for some reason is lower. So there's still more work to be done on this. But at least in terms of using this as a diagnostic, it generally looks like it works. Again, we think that these ratios are helpful. And I won't go too much into the weeds there. But by using ratios of two biomarkers, it seems like it reduces the influence of some of these factors not related to Alzheimer's disease pathology like chronic kidney disease. So it seems like they're working pretty well.

**NANCY LYNN KEACH:** We're getting some questions from, I can tell, from some stealth scientists that want to ask more technical questions about the blood. So before we get to those more specific kinds of questions, let

me go to the questions that were asked really broadly by people for this episode. And that is, are these blood tests clinically available? How do I get a test? When should I get a test? And are they covered by insurance? These are probably the most common questions that we get.

**DR. SUZANNE SCHINDLER:** Yes, so there are at least five blood tests for Alzheimer's disease that can be ordered today by clinicians in the US. So those tests include C2N's PrecivityAD2 test. Fujirebio has a p-tau217 to Abeta42 test that you can obtain through LabCorp. There's a Janssen/LucentAD test. There's an ALZpath test. Lilly has a CertuitAD test. And then Quest has an AD-Detect test. So all of these companies have tests that you can order today. And I should say that these companies often offer more than one test. And I would not recommend using any tests that don't include p-tau217 just because p-tau217 is really quite superior to, for example, p-tau181 or p-tau231 or Abeta42 to 40. So some of these tests incorporate multiple biomarkers, including p-tau217. So I think that's great. But I wouldn't use a test that didn't have p-tau217.

And I should note, none of these tests are FDA-approved, although some companies have already submitted their application to the FDA, and it's being reviewed. We expect that over the next year that there will be a number of tests that have been at least submitted for FDA approval. And we expect some will be FDA-approved within the year. So this is exciting.

So you asked about the cost of these tests. So there's quite a range of costs. They range from about \$200 to about \$1,500 for a test. Notably, the CSF tests that we use are around \$1,000. So some of these blood tests are cheaper. Some of the companies offering these tests have sliding scales for lower income patients. Right now, I've heard from colleagues that sometimes it seems like insurance is reimbursing those tests, but sometimes it takes a while for the bill to show up. So we're not sure whether those tests are actually being reimbursed. There's no tests that we think are routinely being reimbursed by insurance. But Medicare is working on codes for reimbursing these tests right now. And we expect that next year that some of these tests will be covered by insurance. So over the next year, we expect that some of these tests will be FDA-approved and some of them will be reimbursed by insurance. So that will

really change things.

**NANCY LYNN KEACH:** It will change things. And I think there's so much confusion about this right now. And so I want to say, like I often do on these programs, that if you're confused, you are not alone. So there are five tests you mentioned that are available. And people are asking for the names. We will send those names to you. Well, first of all, can someone just go to Quest or LabCorp and say, I want one of these tests? And is that advisable? That's the number one question. And the second part of that question, can they just walk into their doctor's office and say, hey, could you order me a blood test? Or how is it working in real life? What's the way it should work and how is it working?

**DR. SUZANNE SCHINDLER:** Yeah, so as I mentioned at the beginning, we only recommend using these tests within the context of a clinical evaluation, so part of an evaluation for cognitive impairment. And so there is a risk that someone with cognitive impairment just goes and somehow gets a test and it's positive. And then they just attribute all of their cognitive issues to Alzheimer's disease, when in fact, maybe they have a low level of pathology that the test is picking up, but their real problems are because they're taking a medication that causes cognitive impairment and they just need to be weaned off that medication. So that's one reason we do not want people just going and getting these tests outside of a clinical evaluation. And various groups are working on appropriate use criteria that really stipulate this. And we obviously can't control the ordering habits of all physicians. But we really want the test result to be integrated into a clinical assessment.

**NANCY LYNN KEACH:** Yeah, so I'm going to say, it's a little bit like the Wild West. And it's very heartbreaking. After one of these episodes, I had an email from somebody who said, I went to LabCorp, I got the test. I thought it was going to get reimbursed. It wasn't. It was \$763, and I can't afford that. And I asked Medicare if they would approve it, but they said that my doctor had to say that it was medically necessary. And so this person was absolutely at their wits end.

**DR. SUZANNE SCHINDLER:** That's a terrible story.

**NANCY LYNN KEACH:** Terrible.

**DR. SUZANNE SCHINDLER:** Yes, we don't want things like that to happen.

**NANCY LYNN KEACH:** And so I think what I'm hearing you say is that-- well, this isn't what you said, but this is what I'll say. In an effort to try to bring these things to the public as quickly as possible, sometimes things are made available before everybody is fully informed about how best to use them. And I think that's the case here, and that the field is trying to create and implement standards for how these blood tests are used. And so I think I would say this. Before anybody goes out like this woman did who had watched an episode about blood tests-- and, of course, people are very excited about them-- before you just go out to get the blood test, if you have questions and concerns, please email us and we will try to help direct you to somebody who will be current on the best ways to use these tests.

And another issue with just trying to go get the test yourself is that it is not easy to understand or read the results as a non-doctor or non-neurologist or scientist. There's enough disagreement just among the scientists and the doctors about what the results might mean. So that is another issue. This woman, and I bring her up because it hit every problem that you could possibly find along the way, she couldn't find the results. She wouldn't have known what they meant if she got them. So it's not like it says, yes, you have Alzheimer's, no. It's giving a very technical blood analysis answer that's not really usable. So I don't know if you want to say anything to this. I just want to make the point.

**DR. SUZANNE SCHINDLER:** Yeah. So there actually are appropriate use criteria that were published by the Alzheimer's Association two years ago. And they recommended you having expert dementia specialists using these blood tests. And that was pretty much it. And the Alzheimer's Association is working on more appropriate use criteria, again tailored to more a dementia specialist setting. We do expect the primary care doctors are going to use these tests. And that's actually good because it takes a year to get in to see a dementia specialist in some cases. But we really do need primary care doctors to be educated about these tests before they order them. And these tests should require the order of a physician in almost all cases. So it sounds like somehow the person you

were mentioning got it outside of that system. But generally, these require a doctor's order. And the doctor ordering them should know why they're ordering them, that they're using the appropriate criteria. And they should be able to interpret the test, explain the test, all those sorts of things. So a variety of groups are working on educating people on how to use these. But at least for now, people should not be ordering or getting these tests outside of the recommended uses.

**NANCY LYNN KEACH:** And at this stage or at a future time, how many times would you need to get tested? Would you want to get tested when you're 50 and before you have any symptoms? Obviously you've recommended right now, no, because you wouldn't do that. But do you think there'll be a time when you would get a series of tests? Could blood testing at some point be used to monitor progression, like seeing if the proteins are getting worse and worse or better and better, if you're under a treatment? How do you see this, let's say, now versus in the future?

**DR. SUZANNE SCHINDLER:** So when we look at these levels, for example p-tau217, we find that they don't change that much over a couple year period. So if you get a test today and you get a test a year from now, two years from now, even three years from now, the results will be very similar. So it's definitely not the sort of thing where you would do an annual test. Probably what you would do if you had cognitive symptoms is to get one test, and in general, the best test you can get. And then that's the answer. And then you wouldn't need a test for another few years. The exception might be people who had kind of a borderline value. But for most people, you're either clearly positive or clearly negative.

It's hard to know exactly what will happen in the next few years in terms of these prevention studies. But if they work, if we find treatments that make it so that people don't develop symptoms who are biomarker positive, I do think that we would start screening people for biomarker positivity. Again, it's probably something we would not have to do that often. But again, that's a few years out, depending on the results of these trials. So we're still a little ways away from that.

**NANCY LYNN KEACH:** I'm going to go to some of the questions in the chat now. And I'm going to encourage everybody, now is the time. If you

have questions, you can raise your hand or put them in the chat. There are a couple of questions. I'm looking to try to read it verbatim. But basically, I believe the question was, do you recommend these tests for people with Down syndrome-- this is Evelyn-- since there is such a very high rate of Alzheimer's in Down syndrome individuals?

**DR. SUZANNE SCHINDLER:** Yeah, so there's actually major efforts to study Alzheimer's disease in Down syndrome. So Down syndrome is caused by having not just two 21st chromosomes, but three 21st chromosomes. And it turns out that the protein that makes amyloid is on the 21st chromosome. So people with Down syndrome make more amyloid. And they do develop Alzheimer's disease, often in their 40s, 50s.

This is a really complex topic. And just generally, I think that it would be best to talk to a neurologist that's an expert on this area about that specific scenario. Just generally, my philosophy is I try not to order tests unless it's going to benefit the patient in some way. So if I had a patient with Down syndrome who was developing symptoms or who wasn't developing symptoms, I'm not sure if a positive p-tau217 would necessarily affect anything I did. So I probably wouldn't order it. Now, if that same individual was maybe interested in a clinical trial or something like that, then a test may be appropriate. But in general, we don't recommend just ordering tests to order tests. We try to only do things that we think are going to help our patients.

**NANCY LYNN KEACH:** And I think we always talk about and encourage people on these Zooms to participate in clinical trials that are appropriate for them. And I think Amanda or somebody may have, but could you put again, if you're looking or interested in participating in a clinical trial, you can go to our website, look, read a little bit more about clinical trials. And sometimes it's a wonderful way to get very good care and very good information by participating in these trials. And we are doing a subseries to this where each episode, we take one trial and we talk in depth for an hour about that one trial. And I know some of you are going and volunteering for these studies, which is fantastic. So we do have separate episodes specifically on trials. But definitely there will be a trial for Down syndrome. I see, Ms. Gelbard wrote, are there findings with ethnicities in



Ashkenazi Jewish population? So I think rather than going through each subgroup, are the blood tests really at this stage being used to define differences between populations? Or is that not their use at this time or not what we're finding at this time?

**DR. SUZANNE SCHINDLER:** So there's actually quite a few people using these blood tests around the world and looking at the results in different populations. A lot of that work is ongoing. And I would say that just generally, it looks like the blood tests work, but there may be a different prevalence of being amyloid positive in different populations. And it seems like it's highest in non-Hispanic whites for some reason. And also there may be a different prevalence of non-Alzheimer's disease dementias in other populations. So for example, in other populations, cerebrovascular disease or a disorder called LATE may be more prevalent. So there's a lot of work going on right now on those topics. And I don't think we have the answers yet, but there's really many studies looking at many populations. And so a few years from now, we'll hopefully be able to answer those questions better.

**NANCY LYNN KEACH:** Yes, I mentioned I was at a conference yesterday. And we've been hearing that Black Americans or African Americans are two times as likely to get Alzheimer's disease. And I finally asked, because Black Americans are actually testing lower in amyloid than non-Hispanic whites. Is it possible that we're wrong when we say Black Americans are twice as likely to get Alzheimer's disease? Maybe it's not Alzheimer's. It may be vascular dementia or some other type of cause of dementia. And the experts said, yes, it looks like that is going to be the case. So one of the things that we're learning just now through blood tests and other types of testing are differences. And I guess I want to just say broadly, we don't know everything yet. The scientists are really still just learning, to be more specific, about the various causes of dementia. But the science is moving very fast. And that's kind of why we're doing this, is to try to bring the public along with us.

**DR. SUZANNE SCHINDLER:** And just to add to that, for a long time in these large cohorts, we just went by clinical symptoms, whether someone had dementia. And it was really all-cause dementia. It wasn't Alzheimer's

disease. It was just dementia or not. And we didn't do biomarker testing on thousands and thousands of people because it was too expensive or just not an option. But now with these blood tests, we can go back and there's banked blood for a lot of these large studies. And we can go back and find out, yeah, no, a lot of these people who had dementia did not have Alzheimer's disease pathology. So they did not have Alzheimer's disease. The next question, though, is what did they have? And so we need to find biomarkers for all these other disorders. We don't know.

**NANCY LYNN KEACH:** And will there be different treatments? You obviously don't want to take one of the new drugs that's an anti-amyloid drug that targets amyloid if you don't have amyloid in your brain.

**DR. SUZANNE SCHINDLER:** Absolutely.

**NANCY LYNN KEACH:** And this is something only within the past few years that we've been able to detect, which is very exciting. Ramesh wrote, does p-tau217, is it also positive in other degenerative brain diseases?

**DR. SUZANNE SCHINDLER:** So just generally, it looks fairly specific to Alzheimer's disease. That's not absolute with other disorders. So there's one specific mutation that is associated with higher p-tau217 levels. And there's other kind of noise and data that makes us worried that it's not 100% specific. But in general, yes, we think it's pretty specific to Alzheimer's disease and seems to be elevated quite significantly in Alzheimer's disease relative to other brain disorders. But I would just note that people with Alzheimer's disease often have other brain disorders as well.

**NANCY LYNN KEACH:** I think that's a great point. Diseases don't come just in ones. And you can have a whole company, you can have more than one type of dementia as well as other diseases going on, cardiovascular or diabetes or otherwise. So it's not that simple as just finding this for one disease.

We have a YouTube question from Joseph. Is there any effective therapies to counteract the negative effects of pTau tangles? Is there an eye

medication in the works, possibly? I'm not sure if that's a typo or if that's accurate. Because we do fund vision and brain research. So I think there is an eye test for detection. But let me let you answer that.

**DR. SUZANNE SCHINDLER:** Yeah, so there's actually almost 150 different treatments that are being studied right now in clinical trials. And there's been a perception that we're only working on amyloid. And that's not true at all. There's actually many, many different types of treatments that are being studied. And some of them do specifically target tau. For example, there's a drug, it's a little bit of a complicated mechanism, but it lowers tau levels. And there's anti-tau antibodies. So there's a number of anti-tau drugs that are being studied. And researchers are very interested in combination therapies. So not just anti-amyloid treatments, but maybe anti-amyloid treatments plus anti-tau treatments or anti-amyloid treatments combined with treatments that reduce inflammation. So people think that that's very promising to attack Alzheimer's disease via multiple angles.

**NANCY LYNN KEACH:** There are some questions. I love that you're talking about combination therapy. Because I think our field truly believes that that is the future, although we don't know exactly what that combination will be. But we've had a couple of questions, one from Craig, about combination detection options. From Craig, is the most sensitive and/or specific to test battery plasma AB 42/40 combined with p-tau217?

**DR. SUZANNE SCHINDLER:** Yeah, so there's been a number of different head-to-head studies of different blood tests that have been performed. They've analyzed the data in different ways. In general, what we see is that the mass spectrometry-based tests, including one here at WashU and then one done by C2N diagnostics, typically come out at the top in terms of performance and are a little bit more accurate than some of the other tests that we call immunoassays. And the C2N tests that they offer is a combination of Abeta42 to 40, plus pTau, it's called the percent p-tau217 ratio. Where we think that may be particularly helpful is more in a research setting. So it seems to be very sensitive to low levels of pathology. When we look at people that are cognitively impaired, it seems like the difference between that kind of more rigorous measure in the amino

assays is smaller. So the amino assays seem to be working. Just p-tau217 by itself, seems to be working pretty well in people that are cognitively impaired. So I think many of the tests are performing well in the context that we would use them clinically. When you start to look at clinical trial and research applications in people that are cognitively unimpaired, that's where we're really pushing the boundaries with the tests and where the exact test really matters.

**NANCY LYNN KEACH:** So in the last couple of minutes, if someone on this Zoom wants to get a blood test, wants to know if a blood test will help them, is having some symptoms and is concerned, what's their path, just simply, and the cost? And I will just mention, because I can't remember if you mentioned it or not, that the PET scans that are often used, at least for confirmation of amyloid in the brain, are \$6,000 or \$7,000, between \$5,000 and \$7,000. And so this is a much faster, more accessible, inexpensive way to do this type of work. So does someone just go to their doctor? What's the pathway?

**DR. SUZANNE SCHINDLER:** Yeah, so my recommendation would be to start with your primary care doctor. And if they think it's reasonable to go to a neurologist or dementia specialty clinic, some primary care doctors are using these blood tests right now. But if they're ordering them, they should know what they're doing, first of all.

**NANCY LYNN KEACH:** Right.

**DR. SUZANNE SCHINDLER:** And if they don't know what they're doing, then they should refer you to someone who doesn't know what they're doing with them. In terms of the amyloid PET scans, so Medicare actually started paying for them. There is some spotty coverage though. So I hear that they're covered in some areas, but not other areas. We still have to fight with some private insurers to pay for them. And the amyloid PET scans, sometimes it takes a while to get one because we only have them at specialty centers. So there's still drawbacks to the amyloid PET scans, even if that's an option.

So in terms of the patient journey, so first you should see your primary care doctor, then get referred to a memory specialist. And really dementia

specialists are very aware of these tests. And we find that there's actually a lot of different factors. We look at which biomarker tests to perform, whether that's an amyloid PET scan, a CSF test, or a blood test. And so one patient, I may order a blood test, another patient, depending on different factors, I may order an amyloid PET scan. So it's really a complicated decision right now. And it's something that I usually spend, I don't know, 5 or 10 minutes talking to my patients about, going through the reasons to do one test versus another.

But right now, the major drawback to the blood test is just the cost. And so I think that once these tests are FDA-approved and reimbursed by insurance, it'll be an easy choice just to go with the blood test. And then there are other reasons that I won't go into for which amyloid PET scan may be helpful or CSF may be useful. So I think we'll still be using all three modalities, but for many patients we'll just be able to do a blood test.

**NANCY LYNN KEACH:** And I'm going to probably go a minute or two over, but there's a question that came in that I think is very pertinent. Linda: if I tested through my doctor, the results will be placed in my medical record. I think it might be detrimental to me if I seek future insurance. And she clarifies life insurance, she's talking about life insurance, and maybe that's why many people sought outside testing. Could this happen with Alzheimer's testing? This certainly is a concern. Can you speak to that?

**DR. SUZANNE SCHINDLER:** Yes, this is a concern. And that's one major reason why we don't recommend doing this testing in cognitively unimpaired individuals. Because basically, these insurance organizations ask you if you have any reason to think you're at higher risk for Alzheimer's disease. If you're already seeing a doctor because of cognitive impairment, then the answer is already yes, basically. And so they already may exclude you based on that, which is unfortunate. But that's what happens. But if you're cognitively unimpaired, say that you have a positive result, but you're not going to develop symptoms for 15 years, having that positive result could have a detrimental effect. And hopefully, that won't happen, but we can't guarantee that won't happen. And so that's one reason why we just at this point don't recommend doing testing in cognitively unimpaired individuals.

**NANCY LYNN KEACH:** And a really quick closer, do you use the MoCA or the MMSE? Which test do you like?

**DR. SUZANNE SCHINDLER:** So we use the MMSE because that's what we've always used. So we have a lot of historical data with it. But there's good evidence that the MoCA is more sensitive and has kind of better characteristics. And we don't just use the MMSE, we actually use a half an hour battery of tests. So we look at all of those tests together.

**NANCY LYNN KEACH:** Thank you so much. Dr. Schindler, thank you so much for being with us. And I know it's hard to get through all of this because it's still not a perfect science, let's say. Everything is not perfectly understood. But I really appreciate your taking the time to speak about it so clearly so that the public is not just left in total darkness while the scientists are figuring this all out. So we're going to do the best that we can to bring everybody along with the scientists as they discover these fantastic breakthroughs that are happening in Alzheimer's right now. After 30 to 50 years of efforts that seemed to not be productive, now we realize, of course, you have to do that to get to where we're starting to get today, which is to start to have disease-modifying treatments and to start to have more precise ways and cheaper and faster and more accessible ways of diagnosing these conditions. So I want to say thank you, Dr. Schindler. And I hope you'll come back. Maybe we should only test once, but we'd like to have you come back more often to keep us updated. As these things become more sophisticated and accurate, the landscape is changing very quickly.

This episode will be emailed to everybody in about a week or so, along with resources. And these resources are also available on our website [brightfocus.org/ZoomIn](http://brightfocus.org/ZoomIn). If you'd like copies of any of the publications that are listed on this slide, you can email [info@brightfocus.org](mailto:info@brightfocus.org). And can we go to the next slide, please?

If you have suggestions for future topics, you can email us at [reply@brightfocus.org](mailto:reply@brightfocus.org). If there was something that wasn't answered today, that is a burning question that you have, you can send to this email as well: [reply@brightfocus.org](mailto:reply@brightfocus.org). And the next slide, please.



We should be having an episode on a clinical trial on December 5th, and then our next regular Zoom In episode will be on January 9th. We're going to give everybody off for the holidays.

And Jackie's writing, can the slide with available publications be emailed to us? Yes, yes, it can. Yes, it will, along with the site where you can find a clinical trial. And again, the emails are all out there. So if you don't receive this within a week or two, the list of resources and the link to the episode, please email us. Feel free to email us and also to go on our website [brightfocus.org/ZoomIn](http://brightfocus.org/ZoomIn) and you can see all of this stuff for free.

So I'm going to say thank you and thanks for coming. Thanks to those of you who have come to a bunch of episodes. We will keep bringing this to you, if you keep wanting it. So appreciate it. Thank you, Dr. Schindler. And I hope everybody has a great day and a great holiday coming up. Take good care.

### **Resources:**

Expert Article: [Alzheimer's Blood Tests: How Do They Work and Should You Request One?](#)

Blood tests mentioned:

- C2N Diagnostics - [PrecivityAD2<sup>®</sup>](#)
- Fujirebio - [Lumipulse<sup>®</sup>](#)
- Lucent Diagnostics - [LucentADTM](#)
- ALZpath
- Lilly - CertuitADTM
- Quest Diagnostics - AD-Detect<sup>®</sup>