Introductions and Study Background

I am so honored today to introduce you to two of my incredible colleagues, doctor Dale Bredesen and Doctor Kat Toups. These two are the leaders of the randomized controlled trial we recently completed, together with four of our colleagues, called a precision medicine approach for Early Dementia and mild cognitive impairment.

Doctor Bredesen is one of my most cherished mentors. He is a brilliant and kind person and one of the fathers of this work. Doctor Bredesen received his undergraduate degree from Caltech and his medical degree from Duke.

He was post-doctoral fellow in the laboratory of Nobel Laureate Professor Stanley Prisoner, then held faculty positions at UCSF, UCLA, and UC San Diego.

He was founding president and CEO of the Buck Institute for Research on Aging, and his laboratory studied mechanisms of neurodegeneration and published over 200 scientific papers leading to the first report of the reversal of cognitive decline in Alzheimer's disease.

He is the author of two New York Times bestselling books, and is currently Senior Director of the first Precision Medicine Program for Neurodegenerative Diseases at the Pacific Neuroscience Institute.

Next, we have my dear friend, Doctor Kat Tubes, who is a distinguished functional medicine psychiatrist, clinical researcher, and thought leader in the field of cognitive health.

She has collaborated with Doctor Bredesen as the lead principal investigator on now two successful multimodal precision medicine clinical trials to reverse cognitive decline in patients with mild cognitive impairment and early Alzheimer's disease.

The first trial had measurable improvements in 84% of participants. And we can't wait to share the even more impressive results in the recent randomized trial.

With decades of clinical and research experience. Doctor Toups is a sought after speaker, educator, and mentor in the Alzheimer's and dementia prevention community.

Doctor Bredesen, Doctor Toups a huge welcome to both of you. And thank you so much for joining me to talk about the exciting results of this study. Thanks so much, Christine. Great to be here.

Thanks for having us. We're so excited to share the results. It's really, really wonderful. So let's just start with that. Let's start by talking about what I'm sure everyone is excited to hear what the study was about. Exactly.

And what did we find? Doctor Peterson. Thank you. Christine. So this was the next logical step. So we had the first reversals of cognitive decline about 15 years ago.

Then we had over hundreds of documented, which we've all seen, improvements in cognition. And then we had the proof of concept trial, which I was the principal investigator on, which was published in 2022.

So this was the next logical step, which is a randomized controlled trial looking at a control group, which was standard of care versus a precision medicine protocol.

And then following them for nine months, it did not look at long term or sustained improvement, did not look at late stage dementia. It was actually meant to be like other published trials, MCI and early dementia.

It did not look at things like plasmapheresis and even stem cells and things. It looked at precision medicine

protocol, identify the problem, address it, and then do the follow up.

Can you tell us about the results or do you want to summarize the results. And then I can say a bit more about the study design. Yeah. Thanks, Kat. That's a great point.

The study results were phenomenal in that, it showed the greatest difference, the greatest effect, size difference between the control and the treatment group that has ever been published.

So we're very excited about that. The probability so p values for most cognitive parameters were 0.001. So 1 in 1000 chance that these were no different.

And so improvements in processing speed, improvements in memory, improvements in executive function, improvements in overall performance, improvements in cognitive symptom tracker from Doctor Burke, improvements in a 220.

So all of these cognitive parameters changed strikingly. Yeah, it really is remarkable not just the the magnitude of the results, but the statistical significance of those results was really remarkable, too.

Cat, do you want to talk a little bit about exactly what we did, what our multimodal approach was and what that means for how we manage the subjects in the study?

Dermott, I'd like to echo a little bit, even on the results, because that's the whole reason we did this, to show that this method works.

Trial Design and Multimodal Treatment Approach

So in our first precision medicine multimodal trial, 84% of our patients got better. In this trial, we've done even better. And this was a randomized controlled trial, which means we did have a control group.

We had a 2 to 1 randomization. So twice as many people received active treatment as people that just we call it standard of care. So they could do whatever the standard of care was for dementia that their doctor recommended.

But we tried to have them not make too many dramatic changes, especially in their diet, lifestyle supplements, the kind of things that we do work with in our study.

So we were just thrilled, for starters, with the magnitude of the results that we got. And, when people can look at our preprint publication to see some of them, I'd have to look at my notes.

But our active treatment group to translate these p values into maybe numbers, they they improved 14 points on their cognitive scores while our standard of care group declined.

And when you look at the preprint you could just look at the graphs. And there we have graph after graph after graph of the different markers and tests that we were doing with the patients.

And you can see everything in the active treatment group is improving. And everything in in the standard of care either stays the same or actually declines in a lot of the markers.

So so we're we're just again thrilled with these results. So we call this a multimodal trial. And now what we've learned, and Doctor Bateson has written and taught so eloquently about for years is that there are multiple contributing factors for dementia.

It's not just one thing, and it certainly isn't just your genes, because we have people that don't have Alzheimer genes, just as many that get cognitive decline.

So what we do is we cast a wide net with our testing, and we test every thing, any of the major things that we know

contributes to neurodegeneration and cognitive decline.

And that's kind of the that's discussed some in our paper, the various things we're testing. But but the general premise is let's test all of these things.

Figure out what are the treatment targets for that specific patient. So it's not not the same protocol for everybody by any means. We do the same testing for everyone.

But the treatment is precision medicine. So it's individualized. And we determine those treatment targets. And then we decide a treatment plan to work with all of those things.

And that's what we think is really important. Of course we started with diet and lifestyle and sleep and stress. You need that for general health, for healthy aging.

And we worked with people on that. But beyond that, we looked at things that I believe people often miss the infections that affect the brain, viruses, Lyme disease, toxoplasmosis.

We looked at toxins, chemical toxins, mold or mycotoxins. We looked at, hormones, the lack of trophic hormones for people because the brain is full of receptors for all those hormones.

So we believe that that and the studies show that replacing these hormones can have benefits for cognition. So, we of course work with nutrients, B12, vitamin D, minerals.

And we worked with lipids and blood sugar. Those things have been well known for a long time to contribute to dementia. So we just we looked at all of these various things and we worked as fast as we could, to try to get things in balance because we only had nine months to move the needle.

But when you look at the results, you can see how dramatically we moved the needle in nine months. Yeah, yeah, you really can. You know, I think whenever a new study comes out, there's a tendency to ask it to or expect it to answer every possible question.

And I know that we've encountered that a bit as we've started talking about the study results. So, you know, as clinicians and researchers were asked to explain what a study was truly designed to show.

So, Dale, from your perspective, what was the core question this trial was meant to answer? And and what questions were did we sort of intentionally leave for future work?

Yeah. So as I mentioned earlier, we're looking at the next logical step. The question is in a in the most well-accepted approach, which is a randomized controlled trial with that generally accepted approach, could we reproduce the findings that we had seen earlier?

As I mentioned anecdotally, proof of concept. And the answer was, as Kat said, not only reproduce them, but actually did a little better than before. And so you can see the striking difference.

And in fact, it does raise the issue. Is it ethical anymore to continue to do these control groups when you're looking at treatment for cognitive decline?

Because we all know now and this study shows that we can do much better. So it may be that future control groups are going to have to be some sort of precision medicine.

And then you're going to add things on there, be it a drug or a procedure or what have you. So this was meant to answer the question in a in a what is accepted by everyone a randomized control does this show effect is I mentioned that it was not meant to look at things like what about sustained improvement?

What about for people who have a very late stage dementia? So we went from 18 and above on the Moca scores,

which is MCI and early dementia, and we did that purposefully because that's what other trials have done.

So that allowed us better to compare to other trials that have been published. And as I mentioned, we have the greatest effect size of any published trial.

So we're very enthusiastic about that. Again, it was not meant it was not meant to look at things like stem cells or plasmapheresis or new columns or all these other things.

It was a precision medicine approach. Now, the good news, you can always add things on top of that. And but this gives us a place to start. Yeah. And I think the other thing too, that it wasn't meant to show is it wasn't it wasn't designed to be able to show which of these things is the most important impact.

I know that we plan to evaluate the data more to see if any patterns emerge, because I know we all have our own thoughts about that, but it really was designed to show that this group of interventions, when we do like what you talked about, Kat, where we figure out all the things that are out of balance and then we address them.

Does that approach have a significant effect? And the answer was a resounding yes. Yeah. And because there are differences across patient outcomes and differences in what was done, for example, some of the patients at one side got hyperbaric oxygen, others did not.

So you can now take all these disparities and look to see what were the things that actually were associated with best outcomes. So I think that we're going to be learning a lot from this.

And there's going to be data mining from epigenetics and from imaging and from all these different modalities for a long time to come. This is really teaching us a lot.

Yeah, it really is. Kat, when, you know, when we look at the results overall, let's maybe dig into what types of changes we saw in the people who received the personalized intervention compared with those who didn't.

Because I know you have some fabulous stories, and it's always nice to hear, like the real people stories. What happened? Yeah, yeah, definitely some great stories.

And it will maybe be fun later to go to rights in case reports of of we all had of course some stunning success stories. Let me start by saying in my cohort at my site, every single patient in my active treatment got better and all, but one of them were testing completely normal by the end of the study.

And I had people with markers that, you know, 18, 19, 21 so these were people that were starting out pretty impaired. And the natural progression when you're at that level is that you're going to continue to decline.

And instead we were able to reverse things for the patients. I think the the stories of what happened in people's lives that that really tells is why we do what we do.

I had one patient who was still working part time. She was on the younger end and she was still working part time. By the end of the study, she took on two volunteer jobs.

She said, wow, my brain is working so much better that I can do more.

Patient Outcomes and Personal Success Stories

And she took a job at hospice in the SPCA, where she had to undergo training, and she was able to learn these new things and she felt like despite the fact that we had people spending, you know, 1 or 2 hours a day doing some of the supported protocols, parts of our protocols.

She found more time in her day instead of less time. Right. Because that's one of the things, oh, you have to exercise and you have to do brain training for you, mindfulness work.

But it does end up opening. So much more ease as people's brains are working better. So that was a great story. And I had one of the things we haven't gotten into, but we had so many unexpected medical and health benefits from what we did.

Which of course not surprise to us, but it might be surprise to some people instead of side effects of medication, we had, you know, lowered blood pressure, lowered weight, you know, lower inflammatory markers, even improvements in people's immune functioning.

So I had one, one gentleman, he, was in his, he was over 75, so, you know, not, spring chicken. And when he came in, he said, I need three joint replacements.

I cannot walk up the stairs. I have to hold on and pull myself up. It's so painful. Well, partway through the study, his joints were fine. He doesn't need any more joint replacements. Like what?

An unexpected benefit of everything that we were doing for him in the study. And additionally, that gentleman had a fairly serious autoimmune disease, myasthenia gravis, and that myasthenia gravis result the symptoms resolved.

I was looking at his antibodies partway through the study, and they antibodies that you see with that immune disorder were coming down, down, down. But he had no more symptoms.

So besides his this guy tested with a perfect score partway through the study on his cognitive issues and said I can do anything I want in my life now.

You know, I'm rebuilding a car with my grandson that's very highly technical, this type of car. And, and I can do that, and I can crawl under the car and I can, you know, both physically and mentally do things.

So these were some of the kinds of stories we saw clinically of the improvement, I'm sure. Christine, you have some as well. Yeah. I mean, it was just you know, it's so it's it's emotional when you have people tell you that they feel like themselves again.

Like you, your work has that. Well your work, Dale, that we're all implementing has helped someone to to reconnect with themselves, to be who they who they always have felt like they are.

And I, I always think those stories are so powerful. And one of the one of the ones that pops in my mind when you say that is one of my subjects who, was an instructor, a fitness instructor, and was having difficulty just remembering the sequence of the classes that she was teaching, she couldn't even do that.

She had to have notes. And by, you know, about halfway through the study, she decided to pick up a class and travel Italian because she could learn again and she could think, and she could remember.

And it's just, you know, you can't you can't test that. You know, we don't have a cognitive test that tests for the ability to feel like yourself and to do things like you used to do before.

So it is the stories really are amazing, and I do hope we have the opportunity will. And I think some of that will come out in the planned documentary as well.

Yeah. So, as the documentary, I don't know if you've talked about that in these interviews, but we do have some very wonderful filmmakers that have been filming since the end of the first study, and then filming a lot of people as they've gone through this study.

So we're hoping that's going to maybe get out by the end of this year. I think it's a lot of footage for them to edit and put together. But we're we're excited that that will show some of the real features, assets and faces in this study.

Yeah, and not just all the positive outcomes, which we're super excited about, but some of the struggle along the way, too, because this is it's a lot of work for people to to do this.

But then you get to see the triumphs of how worthwhile it is in the end. Let's talk a little bit about how we evaluated people's cognitive function, because we talked, you know, about the real life, the lived experiences.

But how did we set about to do the measurement so that we could actually show that this intervention made a difference? Yeah, it's a great point because, you know, there's just been this whole article about what is Alzheimer's disease.

When do you define it? Because there's this push to do treatment. Earlier with antibodies that sort of approach it. But they've got side effects. So how you know, how do you decide when to go.

So we were very clear about we wanted to have specific criteria. People had to have complaints of cognitive decline. They had to have it so that their partners noticed, in other words, their AQ 21 score, which is the partner's measurement of how are they doing, had to be in the MCI or early dementia range.

Then they had to have abnormalities either on Moca or on CNS vital signs, where CNS vital signs is a more sensitive online measurement of cognitive decline.

So they really had to have multiple parameters that all said, yes, this is a person who has cognitive decline. Now, we didn't require that they specifically had cognitive decline due to Alzheimer's.

We know that about 60% of people who will have complaints of progressive cognitive decline at that age, we were in the 45 to 77 range are going to have Alzheimer's disease.

So most of these did. But as we saw when we used the biomarkers, some of them did not. And in fact Cat had a remarkable patient who turned out to have progressive super nuclear palsy.

So again, we're going to learn something more by the fact that she actually had improvements in that person. So my guess is that most likely we're going to end up about two thirds of these people actually had Alzheimer's disease.

We have the biomarkers. So we can say about half of them had abnormal. Pete out, but virtually all of them had abnormal a-beta 42 to 40 ratios. And so that's why not everybody knows what A-beta is.

So that's the amyloid levels that I think we heard about. So all but one of the patients at all six sites, everyone had elevated amyloid levels. And we know that that that starts years and even maybe decades before some of the other brain biomarkers start to elevate.

So obviously we had chosen clinically very well because everybody had elevated amyloid. But that was not a criteria to come into the study. As Dale mentioned, it was all of the other cognitive complaints and measurements.

Exactly. And I think it's a, you know, a really great thing that we we did this from so many angles is, as you mentioned, the the study partner, usually a spouse and sometimes an adult child.

We ideally right that study partner to live with the subjects so that they could give us reports and also help them with the protocol if needed. And, I had one patient that did not qualify for this study that was so clearly impaired, but she was hiding it from her husband.

She didn't want to say that she had this problem. So when he did the rating scale, he said she had no problem. And sadly, we could not take her into the study because he was unaware and couldn't adequately rate how she was doing.

And I think that's a such an interesting point that so many people, when they start to have cognitive decline, they feel shame. They they're afraid to talk about it and that it's going to diminish how people think about them and they don't want to burden their children.

And sometimes, in this case, their spouse. And I think we need to change that conversation. We need to put it into the light of day, because as we're learning from our studies are so much you can do about it.

This is not a hopeless, fatal disease at this point. For a majority of people. So I hope then that more people can take hope and acknowledge when they're having symptoms and not feel ashamed of that.

Yeah. And I think you make such an important point that just that, you know, people avoiding recognizing their own symptoms or, or, you know, acknowledging that they have something that's changing is now going to keep them from having access to this potentially life changing intervention.

Yeah. And I would add, Christine and Kat that, you know, as you develop Alzheimer related dementia, you go through four phases. And in fact, unfortunately, 45 million of the currently living Americans will die of Alzheimer's disease if we don't do better.

So the first phase, you're pre-symptomatic, you don't have problems, but you can already pick up abnormal markers like the 40 to 40 ratio that Kat mentioned.

Second one is CI subjective cognitive impairment, which may last ten years, where you know something's wrong but you're still able to score normally on testing.

The third phase is MCI mild cognitive impairment, where now you're not scoring normally, and then the fourth phase is dementia, where you're actually having trouble with activities of daily living.

Now, all of these trials are in the last two phases. All of the people we should be getting to are in the first two phases. If we could just make that change from the last two phases to the first two phases, there will be very little dementia.

Well, that comes back to what you say so often, right? Let's make dementia optional because if we go after those first two groups, we have the potential to do that.

Exactly. We have the ability to do it now if people will simply come in earlier. That's interesting. One of my study patients, who did beautifully in the study, lovely, lovely woman.

And and I said I was still recruiting at that time. I said, do you have any friends that might be interested in this kind of study? And she said, I have a lot of friends that have cognitive problems, but they all think it's normal, and they think that I am crazy to worry about this and do all that I'm doing in the study.

But, I mean, this woman got her memory completely back, reverse aged in so many ways, and I think we also have to change that conversation that it's normal to have cognitive decline with aging because there are, you know, still brilliant people in their 90s that can, you know, think abstract way.

And at high levels. And that's what we need to aspire to and not just think it's just normal. And everybody has this cognitive decline. Yeah. But I, I can't tell you how many times people have said to me, I went to my doctor complaining of cognitive problems, and my doctor said, it's just normal aging.

And we've seen people even into the dementia phase where the doctor will say, it's just normal aging. We've got to get rid of that idea. We can all do better.

And even people who are relatively normal can do much better when they get on the right approach. Yeah. It's such it's such an important thing to change this conversation.

How Cognitive Decline Was Measured

And hopefully what we're doing here together will be a piece of that as well as obviously the study. Well, I think it's important because our results show that there's something that can be done.

And so before, you know, recent years with the work that we're doing, it might be kind of reasonable to say, oh, well, everybody has this. Oh well, it's no big deal when you didn't have anything that you can do about it.

Right. But I think that's no longer valid. We have to shift that thinking because now we know so many things can be done. It changes everything. Yeah.

So one of the things that is common in the discussion of studies that are done with patients with cognitive decline, with Alzheimer's disease is, you know, kind of this expected course of decline and as opposed to improvement.

So let's just I know we've talked about it, but let's just very specifically call out the difference between what we expect people to experience without treatment, for example, and what we were able to show in this study.

Dale, do you want to take that one? That is such an important point because we hear all the time about things like, oh, well, this seemed like it was prevented.

The problem. That's not what we're doing. We are reversing the cognitive decline. So you're right, there's there's a big difference, a fundamental difference between you're watching the natural decline.

And now you're slowing a little bit versus you're taking that decline and you're actually making people better. You are reversing the decline and people are actually improving.

And that's what hadn't been available in the past. And we're of course, now all seeing it for the last decade or so, which is wonderful to see. So yes, in this study, unlike in most others, we didn't just slow decline, we actually reversed the decline and made people better.

And often, as Kat was saying, often all the way back to very, very good scores in, as she said, everyone except one of her, her patients or subjects ended up in the normal range.

So it's important for people to understand that that is available. And that particular patient of mine that had not improved fully. She improved 50% on her neuropsychiatric testing on CNS vital signs, and her PTO was going down.

So she was on the road. But there was an interesting issue that she was spending. She had to spend a lot of time remediating mold in her home during that time.

And so my hope is that, you know, now that that's been done, that she will continue to get better. And I wonder, even if you want to mention anything about the mold testing that we did in the study, Christine, because I think it was pretty novel for studies.

Yeah, I think that's a good thing for us to talk about. You know, we did the Army testing environmental, you know, relative maltiness index of the dust test in your home, which evaluates for basically like the amount of mold that's present that isn't typical in a normal house.

So molds that usually are grow in the presence of water, like water damage, drywall and, and under flooring and behind walls, things like that. And so we did that test as a baseline.

Well, in part cap, because of what you guys realized in, in the pilot study, that people that had a heavy burden of mold but didn't address it didn't get better.

And so we wanted a way of being able to quantify that and then also require people to take action on that to be a part of the study, which I think was also quite novel.

Right. And so what what we did was we had all of our health coaches and study coordinators trained by one of the environmental testing experts, and then we asked our patients not to dust their home for two weeks so we could collect fresh dust.

And then they had to consent, of course, for this testing ahead of time. And then our study coordinators and health coaches went and went through their home and tested all the dust.

And so that was a fascinating thing. And we have yet to collate how many people in the study were above the threshold. But I know more than half of my patients came above the threshold for what we determined was a problem.

And and what we asked them to do was agree in the informed consent discussions and in our consent. We asked them to agree if they were above a certain level of muddiness in their home, that they would hire a mold inspector to come and evaluate their home for possible sources, and if they needed remediation or cleanup of the mold, they had to agree to do that or move out of their home for the duration of the study if they weren't able to remediate.

And that was a big ask for people. We knew that we agonized about this, but we felt so strongly all of us did that. When people have mold in their home, that's causing toxicity for them, you're inhaling it and it's going right through to your brain.

And it's not certain strains are known to cause neurodegeneration. So this was a novel thing that we did. And I think, you know, will, there's more to come as we analyze the data on that.

We'll probably have to write a separate paper on the mold issues. Yeah, we probably will. But let me say let me segue way back to the patient that ended up having progressive super nuclear policy in my site.

He did have a big problem with mold. And they started the remediation and it was bigger than expected. And so he and his wife did move out while the remediation was completed.

And he I mean, he was testing cognitively normal by the end of the study. He came in with a lot of motor symptoms, and we knew that something was wrong in his cerebellum with the degeneration that he had there.

But he was diagnosed after the study with progressive super nuclear palsy, which is supposed to be a progressive neurodegenerative disease. But I told him, we need to change the name for you.

You have super nuclear palsy, but it's not progressing. It's going the other way. He was, you know, improving in all kinds of ways, including his gait and his vision.

And so you know, it's just such a fascinating story. And he happened to be one of the high moral people as well. Yeah. Yeah. The disease formerly known as PSP, that's a good one.

So when, you know, we, we kind of started with the single intervention concept. And then we've talked a lot about multimodal intervention and how and how and why we think that that makes a difference.

So there's always going to be some criticism about the fact that this wasn't a single intervention study. And, Dale, from your years of studying this disease and from a biological and clinical perspective, why do you think it was so important to evaluate this as a comprehensive, multimodal approach, rather than continuing to do one single testing, one single factor at a time?

Reversing Decline vs. Slowing It

Because we could have done that, we could have done, you know, let's do mold the first and then let's do this next. And so maybe explain to our listeners why we thought it was important to do it differently.

Yeah. So you know, we we've spent 30 years in the lab looking at the molecular pathways that drive this process. And the surprise was you start even with the simplest, the amyloid precursor protein one protein sitting in your neurons, sitting, crossing the membrane in your neurons.

And this thing actually turns out to respond to a whole bunch of different income, you know, inputs. So it's it things

are coming in that are hormonal, that are impact trophic factors.

For example, Metron one, a trophic factor, actually binds directly to the ATP. It interacts with a p75, which is one of the trophic. This is an NGF receptor.

One of them it is no. It's good to say that to Cat. Yeah nerve nerve growth factor. And guess what. Recently it's been shown that it has to do with detoxification as well.

It has to do with hormones. Estradiol actually turns on a set of genes. And one of the set of genes is the one that cuts the ATP to make it so that you make and keep synapses.

So everywhere we looked, it came in as trophic factors hormones, detoxification, energetics, metals. By the way, this thing binds metals. So when you look at this you realize it's not a simple situation.

It really is a network illness. It really is a whole systems biology illness. And then ultimately, as you know, we realized that there is this beautiful switch which is whole body wide between connection and protection, just like you go parasympathetic, sympathetic, all these same sorts of things are part of this, you know, anti-inflammatory, pro-inflammatory, all these things.

You are literally switching when you get exposed to these insults, you are going into this protection mode. And part of that is you are downsizing this amazing 500 trillion synapses.

So you just you see it again and again and again and again. And it made us realize, okay, if we're going to change the function of that network, we're going to have to intervene at multiple sites.

And it's beautiful how well it has worked to intervene at all those different sites. And I can speak to the single variables. I was just going to ask you, because of all your experience with multiple trials, right?

So, you know, I read was Research center for 13 and 14 years. I did over 100 trials and at least 20 of those were were long term trials in Alzheimer's.

And I want to say that even when I was doing that some years ago, I know one of the trials I did was with a drug that could wipe out the amyloid plaques, but nobody got better.

They did get well and and, you know, we're still these, you know, 15 years later still having anti amyloid drugs in the picture. And, you know, maybe some people get better for a couple months, but it doesn't get them.

Well and then they continue to decline. So in all of my Alzheimer studies they all failed. So medications a single medication a single pill, I just realized this is not the answer.

This is not how we get people. Well, and as I, you know, came to the functional medicine table, the precision medicine table and learned all of these other contributing factors, as Dale said, a systems biology network approach.

It works. And, you know, we can keep holding our breath and pouring billions and billions of dollars into drug development, but we're not seeing anything remotely close to the results we're getting from the multimodal approach.

And I would add, I think that the place where the drugs is going to be on top of the precision medicine approach. So now we can address all the various infections, toxins, metabolic changes, etc., and then begin to bring in targeted drugs that could be very helpful when used in the right way.

And I would add you mentioned the anti amyloid work approach has failed. So now there are the first results with anti-TNF approach. They are also failing.

So even though people said well it's about the tau it's not about the amyloid. Well it's that's not also not showing what had been hoped. So again I think that there's a such an opportunity here to combine specific drugs with the precision medicine approach to get the best outcomes.

Yeah, it really makes sense. Right. And in sequence, like first addressing the underlying contributory causes of why your brain is declining. Because otherwise just giving a medication it's going to still keep declining.

Oh yeah. Yeah. And then analogy that I often use for patients is basically if, if we use the medications as the first intervention where we're basically ripping the scab off without healing the wound.

And so the multimodal approach helps to bring in that healing process so that then we could come in and kind of clean up the mess that that created. You know, the fundamental change that's happening here is to go from treating the pathology to treating the physiology.

So what happened before is, oh, pathology. There's amyloid. There's tau. Let's get rid of it. That has not worked. But looking at physiologically, why is it there.

Well these are anti-microbial peptide and anti-microbial protein respectively. They are coming in because of these insults. So let's recognize that address those insults.

And then at the appropriate time remove these in a gingerly fashion, not ripping them off blood vessels and things like that. Yeah. And that was actually going to be our next question was, you know, every study is a stepping stone rather than a final answer.

Mold Testing and Environmental Factors

And so in this study, I think we've just talked about how this trial kind of clearly contributes to this field and what some of the possible future questions are like, will it will it be good for us to do this first and then combine it later with some of the medical, the medication interventions that have been developed?

Those are all questions that are going to need to be answered. Dale, what do you think is the next step? I know we're fresh off just spending three years to get this study done, so asking you what the next trial should be is probably a little raw, but let's just pretend that we were planning that.

What would you say would be the next step? I think there are so many, Christine. I think there are so many exciting avenues opened up by this study and the proof of concept that preceded it.

Number one is just the data mining, the epigenetics, all the things that we put together. That's going to take some time. Number two is adapting this to Lewy body to Parkinson's to follow temple dementia.

As we already talked about, there's already a PSP person. We have single examples now of people improving PSP, Lewy body disease, macular degeneration, ALS, cortical basal degeneration, posterior cortical atrophy.

It's amazing. So now we can use these same principles to start to it's not going to be an identical protocol because it's personalized, but they're going to the same principles to use this for those.

And then of course we want to know how long can this be sustained. We've already reported anecdotally people who have sustained improvements for over a decade.

Can we keep people improved until, you know, for the rest of their lives, can we make their brain spans equal to their lifespans? That's the key. And Kat, in fact, maybe you could talk about you've had people who then went off the protocol after the trials in the past who did not do so well.

So it really does mean keeping up with doing the right things to get the right outcomes. So I think that the there's so much that can be done really to to take that next step to making dementia a much less common problem.

Yeah. Kat, I would love for you to share your experience from the pilot study and the follow on from that, because I think that's an important thing for people to hear.

Yeah. You know, it's interesting, I was just about to send a questionnaire and an email to all of my patients from the first study, because we just got funding from Paul Health to have a continued support group for our patients from this current study.

And they told me I could invite the patients from the first study as well. So I need to make contact with them, and I want to give them a questionnaire and find out how they're doing.

Some of them I know, some of them I don't know, but I've definitely seen with patients both in the study and my own patients in my private practice before that, that the changes that we're teaching people to make, it's it's you can't just say, okay, my brain's back and I'll go back to the lifestyle that led to that degeneration in the first place, because we have seen them crash again, and you can only pull them back so many times.

I did inherit a patient from Doctor Craig. Tanya? Who was what? Tanya. That was one of our investigators in the study a few years ago, who moved to my area in California.

And in the move, he had stopped all of his protocol that had helped him. So we got him back on what he needed, and he got better. And then Covid hit, and then he fell off the wagon again.

And then he got worse again. And so we had to get him back on everything again that he needed to do. So we do have to teach people how to change things for life.

It's just like the GOP drugs. People lose weight with the drug, and then they can never stop the drug because they don't. They just think the pills going to keep their weight off and they don't change what happened and what caused the weight gain in the first place.

So we definitely have many, many patients long term have been able to maintain their brain health and and their physical health by sticking with all the facets of their individual programs.

And could we make it simpler? I mean, that's the harder thing to determine. We know this works. Which parts can we throw out? Can we throw out the stress reduction and the mindfulness practices?

We used hard math in the study for that, which is, you know, a lovely way to get people that don't want to meditate or not able to. Meditation is not for everyone, but having some kind of mindfulness practice we know that, that it increases your synapses in your brain.

It's it's, you know, one of the things that enhances brain derived neurotrophic factor. So can we throw that out? I mean, we had people spend ten minutes a day doing that.

We know we can't throw out the exercise because that's essential for healthy aging. So it's tough. But there's things involved with the program.

Why a Multimodal Strategy Matters

We know we can't throw out the diet. People can't go back to a horrible diet that's inflammatory when raises in blood sugar. So I think some of the questions are, you know, what are the essentials.

But we feel like the essentials that we have. And in this study we know they worked for people. And I think that goes back to what you said earlier Dale.

Right. Like if we can catch people in these first two phases, then the intensity of the intervention is likely to be less. Whereas when we wait until people are way over here in MCI and into dementia, then it's a much heavier lift and the amount of change in the amount of intervention that we have to ask of them is much greater.

It's just so much easier to do this earlier. Right. And ounce prevention. And Dale wrote a good book about that in this last year about things that you can do to help prevent this in the first place.

I think that obviously, I think more studies looking at prevention, but that takes huge numbers of people over longer periods of time, which means a lot of money that would be needed for those kind of studies.

But I think more of that is essential. And I would just say also to the the genetic aspect of this, we have people that respond beautifully that have two copies of ApoE e4, which predicts a very high risk of Alzheimer's disease.

So that's not a barrier. But for people that have two copies in ApoE4, you need to try harder and earlier because of those risk factors. So I think, you know, learning about the kind of things that we do to turn it around.

If people can use that for prevention, that, of course, to me is where this an ounce of prevention, that's where we want people to be. Yeah. But you should no longer worry.

People used to say oh my gosh I thought I was ApoE4 for I don't know what to do. You know, am I going to take my own life. No you don't have to worry about it anymore.

Find out early. There's so much that can be done. Of course, apoe4.info is a great place where people go, and there are over 8000 people on there. Were able for positive and most of them doing very, very well.

I do think one of the, you know, one of the developments is going to be to be able to say, here are the top 3 or 4 things, instead of doing 15 things, we can now tell that these are the top 3 or 4 that are going to make you better.

And as you said, Christine, getting in early is so helpful. I think the sweet spot is that Scott, because before that, people don't worry enough. They're just like, well, I'll, you know, I'll think about that when I get it.

When you have CI, you know, something's not quite right. And now we've got good biomarkers. And yet virtually 100% of people who have CI can be reversed and really come back to normal.

So that's where we want to catch people and make sure that we don't have people who go all the way to dementia. And let me just translate for people who might not know it as CI, is that subjective cognitive impairment.

So that's the phase before you go into mild cognitive impairment where we can measure it. But when you have that little nagging sense like, you know, maybe I'm having too many senior moments or something's going wrong, you need to pay attention to that little inner voice.

And that is the best. If you've already, beyond the prevention stuff, that you need to listen to that voice and find somebody that can help you evaluate things and not just get a pat on your back from your physician saying, come back in a year.

We'll see if you've gotten worse because you lose that window of opportunity, because things will get worse for a majority of people. And I think that's what back to the study.

You know, seeing what happened in our delayed treat, we call them delayed treatment group as well as standard of care group. We allowed them to do whatever was standard care without making changes of what they were doing in their diet, lifestyle and supplements.

But and we also call them the delayed treatment group because at the end of the nine month trial, we had funding to give them six months of active treatment with coaching, supplements, medical, everything that the other patients did.

But what I observed was those patients were declining, and when they got into the open active treatment, it was harder because of that nine month delay to get them back as quickly as I was able to do with some of the other patients in the study.

So I, I do feel like I never want to be in a study that has a control arm with a delayed treatment group, because I do feel like the longer you wait, the more your brain can be degenerating.

And we saw that was, you know, some of the brain markers with some definitely with the cognitive testing for that group. That's a good point. But even with that we saw a number of people as you know, who steadily went down for that nine months.

And then boom really bounced when they saw I felt like yeah yeah. And even even when people are significantly you know when they're into mild, moderate, even more severe stages of dementia, even though we may not be able to pull them all the way back to normal, like all of the subjects, you know, Kat, that you were talking about.

Future Research and Prevention

But we can still accomplish quality of life improvements for those people and that that can make a big difference. So even though getting them in those first two stages is the most important, even when things have progressed further, we can still help.

Like being able to recognize family members is a really big deal and if we can do something that can help, brings enough memory back that they can recognize family members.

That's a huge difference in the quality of life for all of the people in that family. Yeah, that's a really good point that, you know, when is it too late to institute this kind of approach?

And the farther along when people are into moderate and marked dementia? Sometimes, I mean, I've had some where at least we could stop the progression, right?

They were getting worse, worse, worse, but they stopped getting worse. And then, you know, over time some things can get better. And of course, we've learned so many more things in the last few years that we we have a bigger toolkit to be able to help people with.

And I guess speaking of that, I would say to that, you know, the diet, lifestyle, stress, sleep is where everybody needs to start. But I would urge people to that are having even if they're having subjective a little worry, thinking something is wrong, that it's really worthwhile to find a precision medicine or a functional medicine trained physician that could test all the various things, because some of these things, like hidden infections, some which we did, dental microbiome testing and sometimes combing Cat scans, looking for what's happening in the, in the microbiome at the mouth, which there's certain strains in there that are linked to dementia.

And then also looking for hidden infections like in root canals and cavitation and things like that. So there's so many things that need to be tested that are not readily apparent by the basic testing that most physicians would be doing.

Yeah, that's really true. Well, I cannot thank you both enough for spending so much time with us and really taking so much care with going through all of the details.

It's a complicated study, and it was a lot for all of the subjects and for all of us. And so I just really appreciate the time that you both have spent with us to talk this through so that people can understand that there is still hope.

And I know that's been really the message that both of you have wanted to get out, that this study really does offer reasons for hope, for people, and that is a paradigm shift.

And that to me is really proof that there is hope. Thanks so much, Christine. Yes, thank you so much for helping us to spread the word. And we're it's just our pleasure and our joy to have been a part of all of this.

And, and so thank you. Thank you for having us. Absolutely. I invite you to discover more stories of Alzheimer's survivors and Alzheimer's Alzheimerssurvivors.org.

And I will include that in the show notes, along with the link to the study results at dementiareversaltrial.com If you, our dear viewers, have enjoyed this discussion today on the summit and I am sure you have, please join us for some of our other sessions where we continue to dive into my passion solving the root causes of cognitive decline.

Thank you for joining us.