

Can you catch flu?

Another study says "NO!"

Seminars, webinars,

courses: your new CPD in Learning Zone

Mushrooms in the mitochondria:

DAWN WALDRON's surprising findings

Nutrition Business:

you are more than "just" a practitioner

Integrative Healthcare and Applied Nutrition

IHCAN

The practice and science of natural medicine

Alzheimer's is beaten:
\$6.6m Bredesen RCT
proves personalised
medicine is the answer

Alzheimer's is beaten: new \$6.6 million Bredesen RCT again proves personalised medicine is the answer

Stunning results published in pre-print show significant improvements in memory, executive function, brain processing speed and overall cognition in patients with early Alzheimer's and mild cognitive impairment using Dr Dale Bredesen's functional, medicine-based ReCODE Protocol™. The Protocol outperformed all the leading Alzheimer's drugs. Patients receiving the current standard of care treatment over the trial's nine months showed NO improvement. **Dr DALE BREDESEN** reviews the exciting findings with two physicians involved in the study: **Dr ANN HATHAWAY** and **Dr KAT TOUPS**.

The Evanthea randomised clinical trial has concluded, and the cognitive improvements exceed anything previously published. Dr Ann Hathaway and Dr Kat Toups joined Dr Bredesen online in January. This is an edited transcript of their discussion.

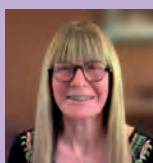
Dr Dale Bredesen: We've just completed the randomised controlled trial that we've been working on for three years now.

As many people may know, Dr Ann Hathaway and Dr Kat Toups were the ones involved with the proof of concept trial, the earlier trial. And when that trial came out, everybody said OK, well you have to take the next step and do a randomised controlled trial. You've got to have a group that's getting treated by standard of care and a group that's getting treated by the precision medicine protocol that we all use - and then let's see the difference. And it turns out the difference is absolutely striking. The difference has turned out to be greater than anything ever published.

I want to make sure to point out this is not yet a peer-reviewed paper. It will come out

as a peer-reviewed paper later this year. But the results are so striking that we want people to be aware of them because there really is something that can be done now for cognitive decline, as we've all been seeing now for over ten years. But this was the best proof yet in the trial.

Kat, you are the trialist among the group of the six sites, the one who has the most experience with trials, and I know you've conducted over the years, something like a hundred. Tell me how many of the trials that you've done in the past led to cognitive improvement?



Dr Kat Toups:

Well, some of them did. I did all of the first generation of Alzheimer medication trials before the new anti-amyloid

drugs. And some of them, like Aricept, did have some improvement, but it didn't last beyond a year. So you could have a mild improvement, but it wasn't sustained. And then I actually did a study with one of the first anti-amyloid drugs years ago, and we

showed that that drug could wipe out the amyloid plaques, but it did not translate to clinical improvement. So that drug never made it on the market.

So yes, this is quite exciting to be involved in these two trials where we don't just slow things down, but we actually reverse what's happening by addressing all of the underlying causes. And that's the difference. I mean, maybe medications can reduce amyloid plaques, but the process will keep going if you don't deal with the underlying drivers of the disease.

DB: You've made an important point, which is sustainability. As you know, Dr Lon Schneider from USC has published a paper about the follow-ups on people who went on Aricept. And unfortunately in the long run they did worse than people who weren't treated at all. So you're really essentially pushing things up to the front. You're front loading, but in the long run it's actually hurting you. On the other hand, we've published a paper showing people who even over ten years continue to have sustained improvement. And so actually let me ask



you, Ann, in your patients who've been treated for several years, are you seeing sustained improvements in the patients who continue to follow the protocol?



Dr Ann Hathaway:

Not everyone does, of course, but in the patients who continue to follow the protocol, we see sustained improvement. Improvement that not just stabilises, but they continue to improve. Not really my patient personally, but Judy Benjamin is an incredible example of that. You know, not part of the study, but just an amazing, an amazing result.

DB: We're seeing this again and again. I just got an email from one of the people who's now been on the protocol for eight years and her scores are still going up. Even though she was into the normal years ago, she's actually still getting better. So let's talk about the, the trial that's just been completed. We'll have a paper

coming out in the next several months, but meanwhile there is a free online preprint that describes all the details and summarises what we saw in this trial.

This was a randomised controlled trial. It was carried out at six different sites, and you can see it on clinicaltrials.gov. It was nine months. People were randomised either to group A, which was the precision medicine protocol, or to group B, which was standard of care. Essentially that meant going back to their primary care provider or their neurologist and having them do what they usually do.

I think we've all been impressed with the fact that there's not a lot of treatment going on out there. There is some Aricept being used, but in general people aren't doing much. And they're telling people, "Well, you're not that bad yet, come back later" - that sort of thing. And I've been horrified to see the sort of treatment that people are getting. In fact, our control group was very similar to the control group that was in some of the other trials that have been published. So I think it's good, it

helps us to match up with those trials.

Also, the degree of impairment was similar to other trials, in that these were people who had mild cognitive impairment (MCI). They were at the MCI stage or early dementia stage, that is to say, MoCA scores [Montreal Cognitive Assessment] of 18 or higher, but with symptoms and with partners who had noticed that they were having problems as well. So from multiple different analyses, it was clear that there was impairment going on - from symptoms, from partners, from their test scores, all those sorts of things.

These people were treated for nine months. And then during that time we looked at what

happened to their cognition, what happened to their epigenetics, their biochemistry, their physiology, all these sorts of things. And so when we look at the end here, the striking thing was the difference between those in the control group who continued to go downhill with their memory, downhill with their overall cognitive scores, versus the ones treated by Dr Hathaway, Dr Toups and the other four physicians that I'll mention here, Dr Craig Tanio, Dr Kristine Burke, Dr David Haase and Dr Nate Bergman.

At those six sites, as an average, the treated patients went up, up, up through the nine months. Very striking. They had improvements in their overall cognition, improvements in their composite memory scores, improvements in executive function, improvements in their processing speed. Really striking. They had improvements in their symptoms. Their partners noticed: this wasn't one of these things where it was so small that the partners didn't even notice, which has happened in other trials. These were clearly noticeable by the partners. So by all criteria, these people were clearly better. Now, some much better, some a little better, but by all criteria they were better.

I think it's helpful sometimes to have an illustrative case or two. Kat I should mention that in your group, every single treated patient got better. That's unheard of in the Alzheimer's field. So congratulations for that! Can you mention just one case as an example?

KT: And let me say, with every patient getting better, all but one of my patients tested in the completely normal range by the end of the study. I had people that started with mild Alzheimer's and then some with MCI, but even those down to MoCAs of 20/21. [26 or above is generally considered normal.] So we had people coming from a place of very clear impairment into complete normalisation. Now, do they have farther to go? Sure. As Ann mentioned, people can still keep getting better and better. And one thing I wanted to say was by doing the full court press, we worked fast and furious because we only had nine months to move the needle. But what I saw in my cohort is a lot of people by three months had already made phenomenal gains.

And so if you're working with everything at once, which is what we did, and give people the proper support, they can shift so quickly. My one patient that didn't test completely normal, I would mention, was still working on resolving mould issues in her home, which we know is a neurotoxin problem causing degeneration in the brain. But she doubled her scores on her CNS vital signs neuropsychiatric battery. So she was still clearly improving.

I have one patient that is such an interesting story, because not only did everything normalise for him cognitively - he scored a perfect score on his MoCA at one point - but it also resolved all of his medical and physical issues as well. This gentleman was scheduled to have three different joint replacements. He told me he could barely

get up the stairs. He had to walk sideways and hold on because he had so much pain. Guess what? All those joints are normal. Now he has no more pain. He doesn't need joint replacement surgeries. What a wonderful side-effect of our study!

He also had myasthenia gravis, which is a pretty serious autoimmune disease. And basically we resolved all the symptoms of that. And I was watching his antibody levels come down because of the treatment. I believe we got him off of blood pressure medicines. So you know, the exciting thing is not only that what we're doing is turning around the cognition and helping people reclaim their brain and their cognitive function, but it helps everything else, because, of course, that's the whole premise of what we do, right? Everything's connected! The brain is connected to the body. So as we address all of these drivers, they all help the brain and vice versa.

DB: You brought up a really good point, which is that people get better, not just cognitively. In the trial we saw statistically significant improvements in systolic blood pressure, in diastolic blood pressure, in BMI, in homocysteine, in haemoglobin A1C, in lipid profiles. So again and again, we're seeing this improvement not just in the

brain, but also in physiology. It's really striking to see. Dr Hathaway, could you mention one of the patients who came through, just an illustrative case and what you saw.

AH: Enthusiasm counts for a lot. And all my patients were enthusiastic because we looked for that in our selection. My patients who were the most enthusiastic did the best. One of the things that we ask people to do to get into ketosis, meaning a ketone level between 1 and 4. This woman's ketones were 3.5 to 4 within a month of starting the protocol. I think she was probably "gifted in ketosis" in some way. Some people struggle with getting their glucose down. For some people, it's easy. So each individual is their own interesting challenge.

But this particular woman, who's an APOE4, by the way, homozygous [two copies = high risk] lost 35lb. She got rid of all of her joint pain, muscle aches etc that were keeping her from being able to exercise. She was enthusiastic about all aspects of exercise, including the high-intensity interval kind of exercise, which is quite demanding. She quickly lost 20lb, and then the other 15 came off slowly. Her scores were dramatically improved within three months, and of course, by nine months they were really excellent. During the study she decided she was going to become a health coach and took a health coaching course. She was just amazing.

DB: One of the earliest patients I had wrote back and said, "I have a new life now". She started her new nonprofit. She went back to school. She said she was going to do all the things that she wasn't able to do before. It's great to see. You mentioned the scores, and I think there's a huge amount of data which is going to be one of the best outcomes from this, that we'll be able to look at the



"This really has told us we have to change our thinking now to recognise that something can be done. This is now really the first effective approach to cognitive decline. Please don't wait". - Dr Dale Bredesen, MD, professor emeritus/former CEO Buck Institute for Research on Ageing, Chief Scientific Officer of Apollo Health, author of *The End of Alzheimer's*.

epigenetics, the imaging, all the biochemistry, and the biomarkers - of course, these are all critical. But one of the points I wanted to mention is that, as you can imagine, when these people started, their average scores for their cognition were of course below average. So if you're looking at average for their age, most of the people that are making up the average don't have cognitive decline. So of course they were below that. But interestingly, at the conclusion, the ones who were treated were actually above the average, above the 50th percentile for people their age. That's above the 50th percentile for people who are not cognitively affected.

Just as Kat said, her patients ended up being in the normal range for their cognition, which again, is unheard of with these sorts of treatments. So that was very, very exciting to see. And of course, the ones who were in the control group started out below average and went further downhill during that time. That brings up another key point here, which is the "bounce". So the people who were in the control group after nine months, they were offered six months of free treatment so that they could get the benefit. And we have just one site - Dr Craig Tanio - who's reported what happened, and you could see [the scores] went down, then they went up strikingly. But Kat, you made a really good point the other day, which is that even waiting that nine months is not a good idea for these people, because it makes it tougher. They're continuing that process. And maybe if you could say something about your patients who were in the control, but then switched over at the end of the nine months and began the treatment, what happened to them?

KT: So my personal feeling is, for starters, we have shown tremendous benefit in all measures of cognition with this study. And so we know this works. And I feel like the need to have a control group in the future should be done away with, because I watched my patients decline, those that were not getting active treatment. Once they rolled over into the active treatment, they did not improve as quickly as my patients that I had gotten earlier in the process. So I feel like the longer you wait while your brain is degenerating,

the harder it's going to be to turn that ship around. So they did improve, absolutely, but it wasn't as rapidly as the patients in the treatment group.

DB: It's a really good point and it really brings up the issue of ethics in standard control groups, in standard of care treatment control groups. And so I wonder whether there will end up being more use of historical controls, because the historical controls, you could see that they clearly went downhill. There's less of that as people are catching on and people are trying to do some of the things themselves. And so the control groups tend to do a little bit better, even though we saw that there was some decline overall, they tend to do a little bit better than control groups from, say, 20, 30 years ago. So people are kind of catching on to this. Ann, I know you're an expert in BHRT, in bioidentical hormone replacement. How many of your patients ended up being treated with bioidentical hormones?

AH: Well, every woman who was in my study was treated with BHRT. As you know, I have spoken at great length in many different venues about the incredible power of estradiol for brain health, for cardiovascular health, and for bone health. Fortunately, at this particular point in time, menopausal hormone replacement is having a moment. There's a lot more positive being written about it, being talked about it. There's multiple books. The number of women physicians has expanded tremendously, and that group of women is reaching the mid-40s now. And they are all not going to be putting up with no hormone replacement: we are going to be getting our hormones. I could talk

about that for two hours. But the importance of using the right hormone, topical estradiol, that's bioidentical, and real progesterone, is extremely important. And also replacing testosterone at a low dose for women is also important. All of those things make a huge difference in terms of overall health and in terms of cognitive health.

DB: The issue often comes up about age. In this trial, people were from 45 to 76. And the average age in this trial was 65. Now, we've all seen younger people. When I was training way back in the 1980s at UCSF, we never saw people in their 40s and 50s with Alzheimer's disease. It's a relatively common thing to see now. So things have changed along the way. But in this particular case, the average age was 65. There were 50 patients who were in the treated group and there were 23 who were in the control group. It was originally meant to be 2 to 1. We got a couple of extras in the treatment. We had a dropout in the other group.

So some people would say, well, why wasn't it 1,000 people? So here's why. When you have something that has a tiny, tiny effect, you have to have 1,000 or more patients because you won't have a statistically significant difference. So we started by calculating what it was going to take to see a statistically significant difference? And the answer was between 50 and 60 people. So we ended up with 73. We wanted to go a little bit beyond that to make sure that we had that.

The other factor here is this trial cost \$6.6 million, and we are truly grateful to Diana Merriam and the Four Winds foundation for the support of the trial. If you do 1,000 people, that will be an \$80 million trial. →



Judy Benjamin was diagnosed with Alzheimer's at the age of 67, following her mother's passing after a 20-year struggle with the same disease. After receiving her diagnosis, Judy made major adjustments to her diet and lifestyle. This journey led her to a fortuitous meeting with Dr Dale Bredeesen, ultimately becoming his "patient zero" as she adopted his groundbreaking, clinically validated protocol for treating and preventing cognitive decline: <https://www.judywalks.com>.

→ There is actually one treatment where now the trial costs have exceeded a billion dollars. Hard to believe, but there. It does cost a lot of money to do these trials, as you can imagine. And you're generating a large amount of data. You've got a lot of people involved. As we were going through this preprint, looking at all the acknowledgments and all the co-authors, I realised what a huge effort this was. This really does take a village. It is a huge, huge effort for years and thousands of hours on a lot of people's parts. So, yes, great to do one for 1,000. You know, if we come up with \$80 million to do that, that would be a consideration. But the key here, and this is why the statistics are so important, is to do enough people to see if there's a statistically significant difference. And the answer is, we saw a huge difference. And in fact, the statistics were not at the 0.05 level, which is the standard accepted. Most of these differences were less than 0.001. So a very high degree of significance.

KT: I think it's important to note that this is replicating our previous proof of concept chart. So this isn't a flash in the pan. This is replicating the results that we had in the first trial. And we've done even better in the responses in this trial than we did in the first trial, which already was exciting news, that 84% of our patients got better. So now we're seeing, even in some of the sites 100% of people had improvements. So I think that's an important thing to know.

DB: Yes, that's a great point. So now you know the evidence. If you take all the evidence together, there's a lot of anecdotal evidence, multiple published papers, hundreds and hundreds of patients, people are seeing this time and time again. Then we have the trial that you mentioned, the proof of concept trial, where the majority of people improved. Then there was a replication of that independently by Dr Heather Sandison and her group that saw virtually identical results [<https://pubmed.ncbi.nlm.nih.gov/37355891>]. And now we have a randomised controlled trial. So anyone can say "I don't believe it". But in fact, it IS sometimes hard to believe because it's so much better outcomes than have been seen in the past. But it fits very much with what people are seeing every day. And we're now seeing also what it takes to get that.

So let's talk about that for a moment, because we see that the low compliance, just as Dean Ornish had noted years ago with his cardiovascular work, less compliance, less outcome. No big surprise. Better compliance, better outcome. But, Ann, you mentioned a few years ago, you know, the compliance is not easy. You're doing something, but yet you've been able to put together a really fantastic team. So, Ann, what do you say to people to get the good compliance that you and your team get?

AH: Well, you have to work with each individual.

“People get better, not just cognitively. In the trial we saw statistically significant improvements in systolic blood pressure, in diastolic blood pressure, in BMI, in homocysteine, in haemoglobin A1C, in lipid profiles. So again and again, we're seeing this improvement not just in the brain, but also in physiology. It's really striking to see”.



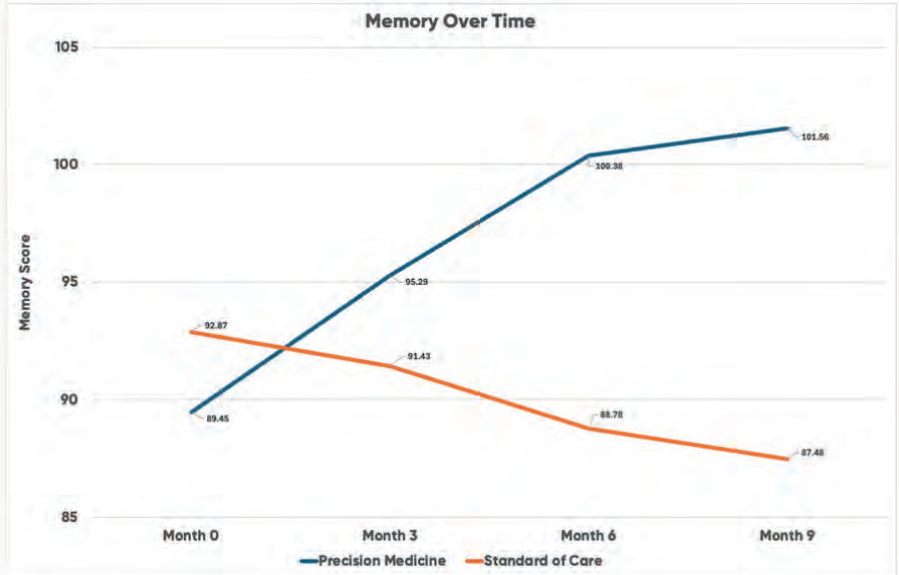
I had a phenomenal nutritionist, Kia Sanford, a phenomenal health coach, Lynn Killips, and Stacy Hawkins, my psych coordinator, just phenomenal at their jobs. And so we worked with these people in the study who were already, you know, chosen because they were on board. They really wanted to do it. But we had very close communication between all of us as a team. When someone picked up that someone had fallen off here or there, we were on them immediately to help them correct course and get back into whatever was the problem. People fell and had to see a physical therapist and a massage therapist. And so we would facilitate things like that to make sure that we kept them as active as possible, as on track as possible. We tracked so many things as a group. We tracked how much sleep they got, how much deep sleep, how much REM sleep, heart rate overnight, oxygen level overnight, etc. Kia tracked their diet extremely closely, knowing why they were missing ketosis that day. They had their entire diet written down. We use a chronometer that our nutritionists were able to literally get the information online. We used a lot of different wearables and trackers in the study.

The Oura ring was very helpful and HeartMath was very helpful for stress reduction. That was helpful in our first study, and helpful in this study. We're very grateful to them. Ketosis was measured by a blood ketone metre on a regular basis. So there was a lot of work and a lot of coordination between all the people on each of our teams to get this to work. And some might say, well, wasn't that extremely expensive? And, you know, our answer is, well, yes, it's expensive, but what's the cost of assisted living for a year once someone has dementia? It's a lot more than the cost of treating a patient in the early stages of mild cognitive impairment, early dementia, compared to five years in.

KT: You need the coaching to help get started and, and get this program assimilated into your life, but you don't need it forever. That's not a forever cost. But we definitely learned from the first study that having the coaching and the support with nutrition and exercise, just to help with integrating all the aspects of the protocol – that helps people to shift very quickly. So like in the first study, in this study every patient was assigned a nutritionist, a health coach, and an exercise coach. The exercise coaches were amazing. And I had people that never exercised a day in their life turn into regular exercisers - because we did require that they exercise six days a week. Patients had to be motivated to be in the study because they had to have a certain level of compliance with every aspect of the protocol. And if they were non-compliant, we had to discharge them from the study. So that did help the motivation for people. But I hope that everybody else will be motivated by the results that we got to institute their own programs if they're having problems, because it just made a huge difference.

DB: This really has told us we have to change our thinking now to recognise that something can be done. This is now really the first effective approach to cognitive decline. Please don't wait. People should get evaluated, get on active prevention or early treatment, because there's so much that can be done.

It's been pointed out that support groups tend to help with getting



Participants' gains in their memory scores were particularly impressive. In addition, after declining for nine months on standard-of-care treatment, patients in that control group were offered six months on the precision medicine protocol and demonstrated markedly improved cognitive scores.

even better outcomes Kat, I know in the first trial you had a support group – what are the things that you add on to get better and better outcomes?

KT: In the current trial my health coach and nutritionist facilitated the support group for the patients in the active treatment group. They met monthly. And then once the patients that were in the delayed treatment crossed over into active treatment, they were able to join the group as well.

People found that immensely supportive. People that were further along in the program were able to help people that were just coming to it to let them know that maybe they had struggled with ketosis, or exercise, or brain training...definitely that support probably was a factor of why my patients did well. We just secured funding so that we're going to be able to continue that support group for our patients to stay the course.

Patients had to have a study partner – usually the spouse - to come into this trial for two reasons. One, we validated that they had impairments in all these different areas. The study partner had to also, with the rating scale, show us that this patient was truly struggling in certain areas of their life and their memory. So the study partners were needed for the rating scales, but they were also needed to support their loved one to help implement this program day to day as well. So both the patients and their study partners came to the support group.

DB: Ann, if you have 100 people who come to you on just a day-to-day basis, what percentage, just your guess, are appropriate for getting into your protocol versus those that just say, "I'm just not going to be able to do this"?

AH: Well, the ones who end up talking to me in general are those who are interested. So for people who come in, who take the time to think about it, make an appointment, come in to get help with their diminishing cognition, I would say 95% decide to at least go ahead and try the protocol. And I would say 90% continue.

DB: Fantastic. Because of course, we want to make this available to everyone possible. And as you indicated, it's far less in terms of cost

→ than going to a memory care facility. And it's far less in cost actually than other therapeutic options that are out there. So in fact there are some real advantages. And of course it's also more effective, has fewer side effects and improves your overall health. So it's kind of a no-brainer that it's actually the best thing going here for, for many reasons. We've got some excellent questions here.. First one: what's the best way to get started?

One way is just to go on <https://www.apollohealthco.com/know-your-cq>. It's a free cognitive test and you can go from there, because it does sneak up on you. There are a lot of people that think they are really not having problems. They'll find out.

Next one is about the Buck Institute having a trial about achieving ketosis. Yes, this is about the conceptual nature [of this approach], the looking at the inflammatory piece, looking at toxicity, and looking at energetics - mitochondrial support, what molecules interact with APP itself.

APP is amyloid precursor protein, which is a receptor that sits in your neurons, especially near synapses. And it literally is a switch that's looking at whether you are going toward connection, or are you going toward protection.

When things are bad, you go toward protection and makes the amyloid, which is an antimicrobial, which kills herpes and kills various fungi and kills various bacteria.

When things are good, you're making something called SAPP -alpha - soluble APP alpha - that's building new synapses. That's connection. So you got connection protection. All these people that we're seeing are on the protection side. We've got to get them back over. We've got to get rid of the things that are causing that.

So the Buck Institute is where a lot of the conceptual nature of this came from. And of course, Dr Hathaway and Dr Toups are experts in functional medicine, which

is the translational piece of this. How do you actually tell what's going on and what to address? I think that's where we're headed. Now, as far as this particular trial, which is for ketones only: in general, we haven't found that single items are that beneficial as much as an overall precision medicine protocol. However, I'm interested in the results of the trial. We'll see. It's important to point out, though, that whether or not any specific thing helps, it still may be part of an overall optimal protocol. That's the change in thinking that we all have to undergo.

KT: The requirement in our trial was that people achieve ketone levels of one to four, so kind of mild to moderate ketosis. And Dr Hathaway mentioned her patient that went almost up to four very quickly. Most people don't do that. But what we observed in the first trial was sometimes when people did go deeper into ketosis, they had additional benefits. Some people's brains light up with ketosis, and other people don't notice as much. So it's not a one size fits all necessarily for everyone. But for the purposes of a study, we had to standardise what people were doing with the diet. I did exit interviews with a lot of my patients, and I have to say, uniformly, they would all say they had so much more energy. Their energy was steady throughout the day. They didn't crave sugar. It's a shift for some people to really shift into ketosis if they're eating a lot of carbs in their diet. But uniformly, people appreciated the benefits of the ketosis.

DB: It's a great point. And as a neurologist, to say that someone had Alzheimer's, we would look for a PET scan that showed reduced glucose utilisation in the temporal and parietal lobes. And so, yes, you are improving that by getting those ketones, because now not only do they have the glucose, which they're not utilising well enough, but they're getting better insulin sensitivity. So now the glucose is working better. Now they're getting the ketones as well. So they're becoming metabolically flexible. It's like a Prius that's run out of both fuels, and now you've got both fuels working again, which is why you see these tremendous improvements.

KT: This also caused weight loss in some of our patients that needed to lose weight. And of course we found ways to support the people that were already thin and didn't need to lose weight, with additional protein and collagen and things like that. But, there was tremendous weight loss for some of our patients. Ann mentioned 35lb lost. The gentleman that I spoke of that needed the three joint replacements lost 35lb as well, which helped. Interestingly, we had diagnosed his sleep apnea and then the sleep apnea got much better, of course, once he lost the 35lb. So yes, the ketosis part has, has been an interesting thing for both of our protocols.

DB: You brought up a really good point, which is there is a difference between the person who comes in and wants to lose some weight and does have some extra adipose to lose, versus the ones who are frail. There is a difference there in the way you treat them to get the best outcomes.

I would also mention that about half of the people that we had in this trial were APOE4 positive. There were six that were APOE4 homozygous, and then the rest of the half was heterozygous. And the question was, did they do better

or worse than the other? In our earlier trial we did look at that and it turns out that they both had statistically significant improvements. And we do see on a daily basis, people who are APOE4 do very well on this protocol. But we'll see. Those are data we have not crunched yet. So there are tons of stuff still to look at. I'm interested particularly in the correlations. The people who got metabolic improvements, are they the ones that got the best cognitive improvements or not? We have looked at the biomarkers and so we looked at amyloid levels, GFAP, NFL and P Tau217.

What was interesting was the GFAP, which is the one that reflects the ongoing inflammation in the brain.

KT: That's glial fibrillary acidic protein..

DB: Yes. So, this is actually a protein that is in your astrocytes, not the neurons. And what happens is as your astrocytes are responding with inflammation and they're responding with attempted repair. They will actually get bigger. So they make this protein, which is an intermediate filament protein in the astrocyte. As the astrocyte balloons up it's telling you you've got active astrocytes in your brain because of inflammation and attempted repair. So the good news is it was statistically significantly improved in the treatment group and not in the other group.

But with P tau [the proteins that form neurofibrillary tangles], what



“We are beginning to understand that there are certain pathogens that are targeted by amyloid and certain pathogens that are targeted by alpha synuclein. So, for example, alpha synuclein tends to be good at killing *E. coli*. It tends to be good at killing *Staph. aureus*. Amyloid beta tends to be good at killing herpes simplex. So this is beginning to tell us what’s going on in the brain”.

we found was something interesting - and now others are seeing the same thing. But initially we were not aware of this. When you lose weight, your P tau goes up without any change in your brain. You just see P Tau. When your weight goes up, your P tau is low. So you can imagine there were people where they would lose a lot of weight, they would do much better cognitively, but their P Tau would actually shoot up as if they were having more problems. Now over the nine months, it would start to come down again. And so it did turn out that there was just a barely significant improvement in P Tau, but it wasn’t impressive. And I think that’s partly because a lot of people in group A lost weight, whereas we know that people in group B did not. In fact, they gained a little bit of weight on the group B side. So I think that there’s a bit of a compromise there in the P tau.

KT: Well, we might need to analyse that separately. It just occurred to me that we should look at the people who didn’t lose weight versus the people that lost weight, and then see if we see a different signal there. I think another interesting thing is about the amyloid; we found that all but two of the patients were positive with the levels of amyloid, which was pretty interesting.

DB: The vast majority of these people had the amyloid-related Alzheimer process occurring in their brain. Now, that doesn’t say that they didn’t have some Lewy bodies there. About 60% of people who end up with Alzheimer’s at autopsy will have some Lewy bodies as well. So there can be multiple processes as we’re understanding these much more from the physiological side instead of the pathological side.

“Oh, there’s some bad stuff. Get rid of it!” No! Why is it there?

We are beginning to understand that there are certain pathogens that are targeted by amyloid and certain pathogens that are targeted by alpha synuclein. So, for example, alpha synuclein tends to be good at killing *E. coli*. It tends to be good at

killing *Staph. aureus*. Amyloid beta tends to be good at killing herpes simplex. So this is beginning to tell us what’s going on in the brain.

And it’s not so surprising in fact that you’ll often have these multiple things. You have the P tau, you have the amyloid, you have the alpha synuclein, and you also have the TDP 43, which is another response like amyloid. And TDP 43 tends to be something that responds to viruses that get into your cells. So we’re now beginning to understand this whole process more from the physiological response side than from this old idea of there’s something bad, get rid of it.

KT: This is important because what you’re hearing is that we have these markers of things accumulating in the brain with Alzheimer’s and neurodegenerative brain processes. But the thinking now is that they are antimicrobial. So they can happen in response to toxins, but also infection. So one of the things that we did in this study is we tested a whole battery of

infections and these become our treatment targets when they were positive, to reduce the burden of all these infections in people.

AH: And for those people who know that HSV1 - herpes simplex virus type 1 - is associated with an increased risk of Alzheimer’s disease, it makes sense that if you have untreated high HSV1 in your body and in your brain, your body’s then going to make more amyloid, which then is going to go ahead and start more destruction in your brain. We treated many viruses, but especially we look for HSV1 and treat that.

KT: And of course, now we’ve just found out in the last year, right, that there’s a huge correlation with multiple sclerosis with other immune disorders because of the viruses. But it’s always been part of our paradigm with the treatments that we do tests for. When you have viruses they activate the immune system and then immune problems release all kinds of inflammatory chemicals that can further the neurodegeneration. So I think one question, that I can imagine people are saying, is “Well, →



what do we do about the herpes?” Since that is such a big, big thing. And I would say most of us treated our patients with, with valacyclovir, which is a well-known antiviral approved for long-term use with herpes. We still don’t really know how long do you need to treat, but I think pretty much all the investigators used valacyclovir for herpes.

DB: And this comes right back to the idea of a comprehensive protocol. And as you know, a paper just recently appeared showing what happens if you take people with Alzheimer’s and just treat them with valacyclovir. The hope was, it’s gonna go away. No, they actually did worse than controls if you just use that alone. And I suspect that’s because now you’re getting in and you’re creating more inflammation as they’re trying to mop this stuff up. So you’ve got to do the whole thing; you’ve got to use it all together as a precision medicine or functional medicine or systems medicine approach.

Another question we’ve had is that when testing for Lyme, the pre-publication said we used IGeneX. What specific panel or tests did we test for?

KT: We tested the Lyme immunoblot for both *Borrelia*, which is a classic Lyme, as well as *Borrelia miyamotoi*, which is relapsing tick fever that is common in some of our areas like here in California. So we tested immunoblot for those, we tested the FISH test, Fluorescence In Situ Hybridization, for *Babesia* and *Bartonella*. And those were the main panels that we did with IGeneX [<https://igenex.com>]. The rest of the co-infections, like animals, plasma, Ehrlichia, we used our LabCorp testing, that’s at Quest and LabCorp. And then all the viruses that we tested were also through LabCorp. We tested herpes, we tested cytomegalovirus, mycoplasma, toxoplasmosis, HSV, HHV6, anaplasma. A lot of these tests we were able to get through commercially available lab companies.

DB: A question here about NeuroQ and full disclosure, I was involved in creating it. So all I can say is it’s got six different components in it. It addresses some of the things we’ve talked about.

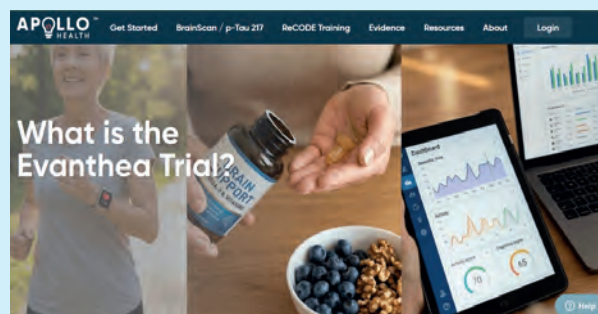
But supplements are supplementary. I think that’s the most important point to realise. You’ve got to get at the fundamentals. The great news is we now have a foundation, so we can now begin to ask what happens if you add stem cells? What happens if you add intranasal peptides? We’ve got a foundation that we know and we’ve proved works.

A question here about Lewy Body Disease. Lewy Body Disease [Lewy Body Dementia] is a close cousin of both Alzheimer’s and Parkinson’s. You have the alpha synuclein that you make in Parkinson’s, but you have the cognitive change that is very similar to Alzheimer’s with some differences, often with some visual hallucinations and things like that. So we do see people on this protocol do well with Lewy Body Disease, but you really have to focus in on the toxic part. Kat was just talking about toxins and how important it is to look for these. They are three different types. The inorganics - things like air pollution and mercury. The organics - things like toluene and benzene and microplastics and anesthetic agents. And then it’s the biotoxins, the things like trichothecenes and ochratoxin A and things like that.

KT: And by the way, he’s talking about mould.

DB: Yes, mould-related toxins. And this ochratoxin A is actually one that specifically damages the hippocampal neurons. So that’s a particularly important one. So please, if you’re dealing with Lewy Body Disease, make sure to see someone who is really good with dealing with toxins.

KT: Let’s say what we did as far as the testing for toxins. So we did panels with RealTime labs for chemical toxins, and we also did a panel with them for mycotoxins. In our first study, we used what’s now Mosaic labs. It was Great. Plain labs. So they also do testing for both of these. And they did not have both panels available at the time we started the study. But both of those companies will do panels for both mycotoxins and chemical toxins. And then we tested heavy metals through LabCorp. So Quest and LabCorp, and you can get blood levels of mercury and cadmium and lead and arsenic, which is what we did. And I would just say a caveat again to the clinicians. If you’re testing



The Evanthea Trial is a multicentre randomised controlled clinical trial testing a Bredesen-style precision medicine protocol for early Alzheimer’s and mild cognitive impairment against usual standard-of-care treatment. It has reported primary results in preprint and summaries (https://www.preprints.org/frontend/manuscript/8118568f183e2ba91ec2a1d3b3d08fb9/download_pub), and is on its way to publication in a peer-reviewed journal.

Apollo Health, home of Dr Dale Bredesen’s ReCODE Protocol™, say: “It is the first such trial in which contributors such as biotoxins, oral microbiome, and tick-borne illnesses have been sought and, when identified, treated”.

Apollo summarise the results as follows:

- Our protocol produced statistically significant improvements in memory, executive function, brain processing speed, and overall cognition, whereas the standard of care treatment did not.
- Cognitive symptoms were markedly improved by our protocol, as noted both by the patients and their partners.
- Statistically significant improvements in multiple health parameters occurred with our protocol: better blood pressure, body mass index, insulin sensitivity, HbA1c, lipid profiles (“cholesterol”), and methylation.
- The overall effect of our protocol was greater than any other treatment for cognitive decline - and 600% better (ie 7 times the effect of Leqembi, the Alzheimer’s drug (Figure 10 in the preprint).

CORE DESIGN AND PURPOSE

- The trial compares a comprehensive, personalised protocol (based on ReCODE/Bredesen Protocol) to standard-of-care management for patients with mild cognitive impairment (MCI) or early dementia due to Alzheimer’s disease.
- It aims to test whether addressing multiple potential root causes (metabolic, inflammatory, infectious, toxic, hormonal, oral microbiome, etc.) can improve cognition more than conventional treatment.
- The study was conducted at six US centres: Marin CA, Walnut Creek CA, Sacramento CA, Nashville TN, Cleveland OH, and Hollywood FL.
- The 73 participants were aged roughly 45–76 and were enrolled

for mercury you have to get an actual number. Otherwise, if you order a whole panel, you may just get a report that says less than four. Well I get worried if the mercury is getting at one and above. You know, I don't want to wait until it's already at 4 before I'm going to initiate some strategies like seafood avoidance and sulfuraphane to detox the mercury.

DB: So a person who has POTS - Postural

orthostatic tachycardia syndrome - and has brain fog and mild memory loss. And the pharmacist told him Aricept was contraindicated. He's already being treated for tachycardia in POTS. What about medications?

KT: POTS is, again, another multifactorial thing, but we've seen a huge epidemic with COVID - I know I developed POTS after

the first COVID. So I'm very empathetic with that. Like all things, you've got to kind of address everything. What's the inflammation? What's the toxin burden? What's the burden of infections? So there's not a single thing that's going to help mitigate the POTS. But one thing that I will say from already doing all those things in myself was oxytocin was personally helpful for me. They call it the love hormone, or the bonding hormone. But there is some data with POTS.

DB: There's one question here about what percentage of the people needed treatment beyond lifestyle. Lifestyles such as detox, gut infection, treatment, etc. I'm assuming it's 100%, everybody. And I think it's important to say this is not just lifestyle. We're actually getting at what's causing the problem and addressing those things. That's what gives you the best outcomes.

AH: I want to say something about that. Everybody got very similar lifestyle protocols, right? But beyond that, because of the very extensive amount of testing we did, every individual in this study got a different treatment protocol based on their specific results. What toxins did they have? What level of insulin problem did they have? Were they exposed to mycotoxins? Did they have mould in their living environment? How inflamed were they? How many antioxidants did they take? What intensity of antioxidants did they need? What vascular treatment did they need? Did they have clotting disorders? And so they needed supplementation for that. On and on and on. So each person's protocol was extensively individualised.

I just want to say that there are two types of things where I have seen what seems like a miracle. One is when someone who's living in mould moves out of that mould. Not always, but sometimes. Second thing is sleep apnea. I've gotten like three or four calls from spouses who say, "Oh, my gosh, he's back!" Or she's back, when just their sleep apnea was treated. So we do see miracles sometimes. You know, in general, we treat everything. We're very aggressive about that. But there are some miracles.

DB: We really are in a new era with this randomised controlled trial. And congratulations once again to Dr Hathaway and Dr Toups for the outstanding outcomes. [IHGAN](#)

at the MCI or early dementia stage, similar to major anti amyloid drug trials (eg for lecanemab, donanemab0.

- The protocol phase lasted nine months with about ten monthly in person visits, followed by safety follow up and an open label extension option for those initially in the usual care arm.

INTERVENTIONS AND ASSESSMENTS

- Precision medicine arm:
 - Extensive lab testing (nutrients, omega 3s, lipids, cardiometabolic markers, hormones, inflammation, metals, immune markers, etc.)
 - Evaluation for infections (Lyme and other tick borne diseases, HSV 1, syphilis, HIV, COVID), biotoxins, oral/dental pathogens, and other contributors.
 - Individualised treatment using diet, exercise, sleep and stress management, cognitive training, hormones, medications and devices (eg stress management or brain exercise tools) as indicated.
- Control arm: standard-of-care for early Alzheimer's/MCI, including routine medical management and general lifestyle advice; some participants could cross over to the precision protocol after nine months.

■ Outcomes: neuropsychological batteries assessing memory, executive function, processing speed, global cognition, plus cardiometabolic and other biomarkers (eg blood pressure, BMI, insulin sensitivity, lipids, HbA1c, methylation and Alzheimer's biomarkers like p tau 217).

REPORTED RESULTS SO FAR

- Participants in the precision medicine arm showed statistically significant improvements in overall cognitive index, memory, executive function and processing speed, whereas the standard care arm did not show such gains.
- The protocol improved several health markers, including blood pressure, BMI, insulin sensitivity, HbA1c, lipid profile and methylation-related measures.
- Effect sizes for cognition have been described as substantially larger than those seen in anti amyloid monoclonal antibody trials and lifestyle-only trials (eg reported as multiple-fold higher than lecanemab, donanemab, the POINTER trial, and the Ornish lifestyle study), though these are still pre publication comparisons.
- Some biomarker responses were complex, such as p tau 217 increases in certain patients who nevertheless showed marked clinical improvement, possibly related to weight loss or other metabolic shifts.

