

Zoom in on **Dementia & Alzheimer's**

Can Non-Drug Interventions Really Reduce Your Risk of Alzheimer's?
What We Know and Don't Know About What Works

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Transcript of Zoom with Laura D. Baker, PhD, Professor, Gerontology
and Geriatric Medicine at Wake Forest University School of Medicine

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

NANCY LYNN: Well, good morning and afternoon and evening, everybody! And welcome back to those who've been on the program before, and welcome to those of you who are new. Thanks for joining us for our tenth episode of Zoom in on Dementia & Alzheimer's. It's very exciting today, we've received over 110 pre-submitted questions from all of you on this very important topic, and hundreds and hundreds more throughout the year were submitted. So, we have a lot to get to. I'll try to go a little bit quickly. We once again want to thank BrightFocus for hosting this. BrightFocus funds research globally for Alzheimer's disease, macular degeneration, and glaucoma. And also want to thank Eli Lilly and Company and Genentech for providing funding that in part supports this program.

A lot of the questions that you guys have submitted were not on this specific topic of non-drug interventions. And so I just wanted to show again, if your question for example, was about hereditary—"My mother has it, my sister has it, will, I get it?", here's an episode from John Hardy on, "Is Alzheimer's Hereditary". And we have all these topics where we

have hour long shows that you can access on our website or write to us, and we'll send you a link. So if your questions are related to any of these, I know there were many on stages of Alzheimer's, how it progresses, on the drugs, and on genetics, you can go refer back to those episodes. And we'll be revisiting them as we go forward this year with our whole new round of episodes.

So let's see. I am going to, while you're looking at this slide and noticing which episodes you might want to go revisit, I will introduce Dr. Laura Baker, who has a fiber optics outage in her area so is joining us on her cell phone. Dr. Laura Baker is professor of gerontology and geriatric medicine at Wake Forest University School of Medicine. She is an international leader in the areas of cognitive aging and lifestyle interventions to protect brain health and prevent cognitive decline, Alzheimer's disease, and related dementias. And she's been an investigator for over 55 clinical studies. We really have the best of the best person today to answer questions on non-drug interventions. Dr. Baker co-led the COSMOS-Mind study, a 3-year trial of daily cocoa extract and/or a multivitamin in over 2,000 older adults, showing multivitamin related benefit on cognitive decline. She and her team recently completed the EXERT study, a clinical trial testing whether regular physical exercise can protect against continued cognitive decline in adults with mild cognitive impairment. And currently Dr. Baker leads U.S. POINTER, the largest multi-site trial to date testing the effects of a 2-year, multi-domain lifestyle intervention on cognition in adults who are at increased risk for cognitive decline and dementia. Welcome, Dr. Baker. And thank you for being here. Thank you. Welcome.

Roger or Mason, can you bring us to the next slide. Now, I did this last night, Dr. Baker, as I reviewed everybody's questions, these hundreds of questions, and it was overwhelming. This is not in any particular order, and this is not even everything that everyone wrote and asked about: diet, herbs, Prevagen, Neuriva, melatonin, coconut oil, light therapy, sensors. It's overwhelming the amount of interest and obviously the amount of reading people are trying to do to understand how to how to deal with this. And then I stuck some of the risk factors over here on the other side. And I'm so I'm going to just kick us off with a question from Gail from Orlando, she asked, "What in your opinion is the single most important

factor in preventing mental decline and aging?" And I don't think that's fair cause I don't know if you can come up with a single answer.

DR. LAURA BAKER: Wow!

NANCY LYNN: Let's say your top 3.

DR. LAURA BAKER: But I you know I couldn't possibly come up with a single answer. But first of all, I just wanted to say, this is an impressive list. Love the interest. And really, this group, people who are asking these questions, I myself will not be in the field forever, I've been around a while, and it gives me so much confidence and joy to see young folks having these kinds of questions, because it gives me confidence that this area of work that's so important will continue on and get stronger. And so I'm just, I see this list, and it just makes me very happy that these questions are coming out. And the other disclaimer I just feel like I need to make is I don't know something about all of these things, and I wish I did. I mean, I have opinions, but I don't have the scientific evidence to speak on all of these topics. The topics that I can speak to that were listed on some of the trials that I've finished are exercise for sure; diet, yes; vitamin supplementation, yes; sleep, yes; multi domain, kind of lifestyle interventions, yes. But I see a lot of things here that I have opinions, but really that's all it would be. So just wanted to put that out there. I wish I had more information for you.

So answer to the first question, what for me is the you know the number one? And you know I'm a little biased, very biased, actually because of my work. And I'm biased not just because this is what I study, these lifestyle modifications, and how that could protect against memory loss, could enhance brain function with age. I'm biased not only because of the you know I get to see me the results of our studies, and I'm encouraged by them. But it's also related to what I see with the participants. The participants, they give us feedback all the time about how these things are changing their life, and I think that's what keeps me driving forward. So if I were to answer the question, I would have to say, and it's going to be very vague okay, but maybe it's a good starting point for the conversation, is whatever you can do, a person can do, to build up the resilience of the body and therefore build up the resilience of the brain. I

think that is the starting point, and that might mean something different for each person. And so, you know, each person comes to the table, the aging table, with different toolboxes, toolboxes with different kinds of tools in the toolbox, depending on your life experiences. And what gives one person resilience against cognitive decline might be very different than what gives another person resilience against cognitive decline. And that's our job as scientists and clinicians, is to figure out how can I put you, a patient, a participant, in your best place to resist pathology as we get older? I know that's probably not the answer you wanted. But how about we start there.

NANCY LYNN: We can start there. But I think that's frustrating.

DR. LAURA BAKER: I know.

NANCY LYNN: But accurate and I understand. So I'm going to ask some of the specific questions. So you mentioned exercise, diet, and vitamins. So I'll start with some of the specific questions we got for those.

DR. LAURA BAKER: Okay.

NANCY LYNN: I think people wonder what kind of exercise, and again I'm sure, different for different people, but in particular some have asked about weight training. You know, is weight training better than other exercise? And in my experience having done this for 15 years, I have stuck in my mind that it's like 45 minutes of brisk walking 3 times a week, or something like that. Is it all of the above? Does it depend, obviously depends on what you can do. But what's your response for exercise to maximize the benefits of exercise?

DR. LAURA BAKER: Okay. So, my initial work that I did for maybe 15 years, that I'm continuing to do was really focused on what you mentioned as the cardiorespiratory part, the aerobic exercise. And because there was a while ago, let's see beginning in 1990, where Art Kramer from University of Illinois Urbana-Champaign just really showed that in cognitively healthy older adults...wow! you put them on a 6-month program, structured exercise, higher intensity exercise. They have, you know, supervision. And wow, you see major brain changes, and no one had ever shown that

before. So that really set off a whole bunch of studies really focused on exercise, aerobic could be medicine for the brain. And I think since his first paper was put out there have been a whole number of different studies that have been shown that yes, there's hope. I'd have to say there's also a number of studies that said we don't see anything, there's no impact here. And as a scientist, I'm always looking at why did some people get negative? Why did some people get positive? And so, even having this conversation, I have to talk about that. So, because you're trying to understand the literature right? And what value is aerobic? So this is an important point for non-pharmacologic interventions. Whether we're talking about vitamins or exercise or diet. The consistency of results has everything to do with the consistency of the methods. And if we have widely variable methods, do not expect consistent results. And so, a lot of the inconsistency in the exercise field has been related to inconsistency in methods. And now since 2015 on, we're all starting to use a more standard protocol, and we're getting more and more consistent results.

So exercise aerobic, yes, I was always a big advocate of that. In the EXERT study that we just finished not too long ago, I'm extra excited about that EXERT, extra excited about that, because what we found was that it wasn't necessarily the aerobic part that kept people with mild cognitive impairment from declining, it was the volume.

NANCY LYNN: What do you mean by volume?

DR. LAURA BAKER: Our study was, let's just say in 12 months, it was supervised, and that's why we were really watching it for 12 months. We had a low intensity group, so stretching, balance, range of movement, and then a more, a higher intensity aerobic. And they got all the same social support. They had to get out, go to the Y.M.C.A. They had to get out of their home. They had that. So they had a lot of social stimulation. And what we found is neither group declined. Those 2 groups with mild cognitive impairment, we compared them to what you might expect, like using other comparison trials like studies like ADNI. ADNI declined on our primary measure. No one in our EXERT group declined. So our new thinking is that at least for people with mild cognitive impairment, any consistent exercise over time could be beneficial for brain protection

against decline.

Now, what about cognitively healthy adults? We don't know that yet. I mean, it may be that you need to turn up the volume a little bit more on the intensity for cognitively healthy people. So maybe aerobic is going to be the most impactful for protecting against decline. Or it may be that you need, if it's volume and you're cognitively normal and healthy, that means you can do aerobic for 6 months, or you can do a lighter yoga, you know, stretching, balance, range of motion, but we may have to double or triple that amount of time to get the same volume, if that makes sense. So I think for so long we were so focused on exactly what is the critical ingredient. Now, our attention is starting to turn with it's how much medicine, exercise medicine, you give to your body, and if you're on a low dose medicine, it may take longer to see the effects. So low dose with being stretching, balance, range of motion.

Does resistance training have benefits for cognition? This is what we know so far. There are some studies that are going on right now, looking at specifically at resistance training in the U.S. POINTER trial that we're running now, resistance is one of our components of our physical activity. So we will know, we are tracking that. We'll have very precise metrics for that. But what we do know so far even in absence of these results yet, is that resistance training prevents, it reduces risk of falls. A person with a high risk of fall is a high risk for cognitive decline. That connection has been made, and very recently. Fall risk is associated with cognitive decline. So whatever we can do to reduce our fall risk, you're reducing your risk for cognitive decline.

NANCY LYNN: That was awesome. So let me see if I can recap what you said.

DR. LAURA BAKER: It was long-winded I know.

NANCY LYNN: No, no, no, it was great, because you're giving us that precision. What I heard, and we lost a little bit of audio, was that it is consistency and intensity that matter, or volume, as you said the amount, and that you do it consistently and regularly like a medicine for aerobic, and that that has shown biological changes for people who have mild cognitive impairment. We don't know for sure in healthy people yet. And

that resistance helps to reduce the risk of falls. And that U.S. POINTER study is going to give us additional information about the exercise components. Is that a good simple recap?

DR. LAURA BAKER: Yes, that's good.

NANCY LYNN: Okay, because that's helpful for me, because I do remember reading studies of the volume of the brain, you know the volume, less shrinkage from consistent aerobic exercise and that type of thing. And actually, somebody asked a very interesting question, Jeff from Massachusetts, where he said, I'm wondering if the non-drug interventions like we'll talk in this case, he was reading that they affect the cognitive function, you can see a change in cognitive function, but are they actually changing us biologically, these non-drug interventions? And I think you've already answered it. But I wanted to give you a chance to address that. Is it just that we're seeing improvement or less decline in cognitive loss? Or are we actually seeing biology change?

DR. LAURA BAKER: Yeah. So that's a good question. Can you hear me okay? You can hear me. Okay, so that's a good question. And I think it may first of all depend on who we're talking about. So someone who's cognitively intact is not in the pre-clinical stages of Alzheimer's disease, it may be a very different story about how to answer that question. For someone who's in the early stages of mild cognitive impairment related to Alzheimer's disease, it may be a different answer. Someone who's in the early stage relative to another type of dementia, it may be another answer to that question. But I think what we are collecting biomarkers. We do have imaging. We have, in EXERT we have some cerebral spinal fluid, although it wasn't a procedure that many people volunteered to do. We didn't quite perfect messaging it towards it. But we have blood biomarkers as well, and we are just starting to look at those blood biomarkers. But really that's going to be key, and we have all of that blood in POINTER as well. And imaging, we have microbiome, we have imaging microbiome, and we have a cardiovascular factor. So we will have a better sense of whether it's actually improving or preventing decline. I think just from my collective work so far, I really focus on people who are at risk, higher risk, so these people have memory problems, family history of memory

problems. They might be cognitively okay, but in that cohort in my focus, I really don't do a lot of normal aging work. I think what we're seeing more is protection against decline. Not so much reversion. We're not seeing that. But I never expected that. I'm so happy with resilience, resistance to decline. To me that is the biggest success that we can have, especially with people who are at risk for decline.

NANCY LYNN: Two things quickly. One is Robbie pointed out, she said, "I thought that she said that volume and not intensity is what's most important in exercise?" I was kind of conflating them so can you clarify?

DR. LAURA BAKER: Yeah, so in exercise physiology, the volume we always talk about is how much is completed in per unit time. So I apologize for not clarifying that earlier. So you could, one way to think about that is, you could exercise lighter. The walks are less intense, but to get the same benefit for the body, you're going to have to walk longer. If you're going to do that, you know, a 20-minute light walk is not going to be the same as a 20-minute brisk walk. But if you want to do the light walk, just do it 2 or 3 times longer, and maybe you'll get the same benefit. That's the volume part.

NANCY LYNN: So let's jump to diet. Mediterranean diet? Depends on the person? What would be your overarching advice regarding diet?

DR. LAURA BAKER: So for diet, I think what we've learned so far, and you know there's some evidence that's pointing us in one direction. So you know, Nik Scarmeas' data shows, you know, really pushes, shows a lot of beautiful epidemiologic work showing the benefits of a Mediterranean style diet. And basically, that's the lower saturated fats; the lower processed sugar; higher levels of unsaturated fats like, salmon and the olive oils; higher levels of greens, leafy greens, berries. And then now we're also starting to talk about the MIND diet when I start adding some of those components in there. That's Martha Clare Morris' MIND diet. So there's a lot of historically, a lot of epidemiologic data showing that this Mediterranean diet could, does reduce, is associated with lower risk of developing cognitive impairment. And the problem with epidemiology, it's not a problem with epidemiologic work, epidemiologic work is so important. But a lot of times what we're finding is when you put those to clinical trials you don't see the same effects. And you know that's for all

the reasons that all the scientists in the room know already. But so we've had some difficulty making progress in the diet realm of, you know is it a treatment? Is it prevention strategy?

Now, I talked a moment ago about the variability in the methods for exercise. Just use your imagination for a moment to think about the variability in trials of diet. And it's not just the prescription of what exactly you're asking people to take. But what do people actually do? That's a whole different, you know, we can ask people to do X, Y, and Z, but whether they do it is another story. So, we've got the human element that does, it makes the diet studies, the clinical trials of diet studies very difficult. So we know that Martha Clare Morris and the MIND diet and all of her observational work shows that it was associated with lower decline, lower risk of decline. But her latest study that Lisa Barnes published in New England Journal of Medicine, showed that hmm, maybe it doesn't in a clinical trial setup. However, I think there's always a comma or but and an and on some of these studies. It was such a large study. It was a diet weight loss study. Everybody going into that study was either overweight or obese and there were some methodological issues that may have contributed to, you know, no effect. Maybe not. But there was just, there's some questions still that I think there's a lot of ongoing post hoc analyses now trying to figure out are the responders, the people who followed the diet more closely, are those the ones that showed benefits? So we don't know that yet, so I hate to talk too much about the MIND diet until we have more information. We're using the MIND diet in POINTER. We're hoping those other analyses show some benefit. I also believe that the results of one study never settles a question. There are different people, different diets for different people and the people that were included in the MIND trial may be very different than the folks that are at risk for impairment, which are the ones that are included in POINTER.

So in terms of diet, what we know, you know the POINTER is based on some of the mostly observational evidence from Nik Scarmeas and from Martha Clare Morris. There's some new data coming out looking at specific components of diet. I really, I'm not a reductionist in my science. I'm very much of a composite. It's got to be applicable to real life. So I really don't have a lot of interest in a single element. It's more how is it

relative? How does this new diet component integrate into a person's whole diet? Can we improve or protect cognition there? As an example, cocoa flavanols, we just finished that study. It's the COSMOS-Mind study and I'm very excited about the multivitamin results. But our primary intent was to see if cocoa extract, cocoa flavanols you know the key, the critical ingredient, active ingredient in dark chocolate or cocoa. It's from cocoa beans and the equatorial region, that's where it's from. And we were just sure we were going to get a benefit of cognition from regular use of, regular intake of cocoa flavanols. We were sure, based on the epidemiologic work showing that regular intake of cocoa flavanols in the equatorial region has had huge effects on cardiovascular disease. These people who live in that area who consume this on a daily basis do not have cardiovascular systems that look like other people their age. And the link between cardiovascular disease and cognition. Surely, surely we're going to see a cognitive effect. Nope.

NANCY LYNN: Wow!

DR. LAURA BAKER: So I you know, but we did see really positive, really nice effect of the multivitamin. So I can't really speak to specific individual components. We generally look at whole diets. And I think when POINTER finishes, we'll report out next summer 2025, I think when we report out, we have so many metrics, quantifiable metrics, on adherence that I think we'll be able to answer some of those questions. But until then I kind of have to waffle.

NANCY LYNN: Okay. So we're going to invite you back in the summer of 2025.

DR. LAURA BAKER: Okay.

NANCY LYNN: Will you come back? And that's really interesting, though we won't keep eating dark chocolate, but we will take a multivitamin. I'm going to call on...

DR. LAURA BAKER: You can eat dark chocolate if it gives you quality of life, you know so that important.

NANCY LYNN: I agree. I agree, that definitely gives me quality of life. So does drinking hot cocoa. Monica has her hand up. Can we unmute Monica.

MONICA: Hi, thanks so much for doing this for us today, I actually have so many questions. But I'm going to ask just one, which is. I've been reading about saunas. There's a Finnish study, or several, I guess, where people who took five saunas a week had a 65% lower rate of developing Alzheimer's as those who had one sauna. And this is in Finland, I guess, where everybody's saunaing all the time. In the article it said something like, well, we can't... Anyway, I want to because I have a Y.M.C.A. with a sauna, I'd like to know if that's something that I should be doing?

DR. LAURA BAKER: Oh, definitely, get in there. Definitely get in there. Because so I think so much from a clinical trial perspective, I think some of these results are interesting, but I always have to as a clinical trialist, as I'm always thinking what's different about people who prefer, who like to take those? Those who self-select to take saunas. And but I say that, so I'm always cautious about making recommendations based on epidemiologic work. I think epidemiologic work is absolutely critical to set the stage for clinical trials. But I also know though, there's another whole line of research, looking at heat and heat shock proteins and its effect on cognition. And I think we don't know yet, but there is something out there in terms of what we're discovering and what we're learning is there's something about heat and the importance of heat for resilience. And I don't know what form that takes yet, but if that sauna looks appealing to you in that YMCA, I'd definitely go jump in there.

MONICA: Thank you.

NANCY LYNN: The people taking the saunas are clearly less stressed than us.

DR. LAURA BAKER: Absolutely. That's possible. There's a lot of ways to reduce stress and exercise is one. I think some people would say just a little bit of alcohol might do it. I'm not here to advocate, but I'm just saying. And that maybe is an important point here, when I started saying,

how can you build, how can each person build their own resilience? What we have learned is stress reduction, stress management is key. And what is going to reduce stress for one person is going to be different than what reduces stress for another person. So as a homework assignment, I guess from this, I think it would be important, it's important that we all take stock of what stresses you and what does relieve your stress. At least just for a short period of time so your brain and body can have a moment to recover and do some of its maintenance rather than being at the ready at all time. So that's really important. It's important in our clinical trials. But we always take into consideration stress and stress management and the impact of that effective management on brain health and resilience over time.

MONICA: Thank you so much.

NANCY LYNN: Thanks, Monica. It sounds like with diet, with exercise, with stress, it's hard to say exactly, you know, is green tea good; is red wine good; is what did we have, pig brain peptides or turmeric? But is it easier, perhaps, to say what we know that's not good, like don't smoke? Or a lot of sugar? Or is that just not helpful?

DR. LAURA BAKER: Yeah, no, yeah there are some things. Yeah, there are some we do know in terms of diet. We do know some. And I think it's probably what most people already know in this room. But so, we do know about high levels of saturated fats and their consequences for the body. And you know it's just it's cardiovascular effects that will always affect cognition. I think, when I'm in the community talking, and we talk about the heart health, and vessel health they're oftentimes surprised that what happens below the neck affects what happens above the neck.

NANCY LYNN: It looks like we lost her. Well, while she's coming back on, since we have Dr. Rossi. Sorry, Sharyn, to put you on the spot. I'll just keep going in general and also if you want to enter more questions into the chat room while Dr. Baker is re-calling in from her phone. I wondered if you could talk a little bit, I want to go back with her to the multivitamin. Oh, that's a great question Robbie, about vegan diet, red meat or not red meat or meat, so we'll ask her that when she comes back. But meditation, yoga, acupuncture—she was just talking about stress reduction in general. Do we know if there's any kind of specific stress reduction? Is there

evidence on whether meditation is helpful, or yoga specifically? And I'm putting our Dr. Rossi on the spot. But what can you tell us about that?

DR. SHARYN ROSSI: Yeah, definitely, I think it's still just in line with what Dr. Baker was saying. You know anything that's going to reduce stress, things like cortisol and all the other hormones that kind of get released when you're stressed out have negative impacts on cardiovascular health, as well as your brain. So meditation, mindfulness has really come into light recently, as you know. Even if you just take 10 minutes and breathe deeply, there is some evidence showing that, you know, that can restore kind of brain rhythms that are helpful and healthier for memory formation and things like that. So I think just the overall consensus of trying to reduce stress as much as possible. I know that that's not always possible for some. And then engaging in stress reducing behaviors, and whatever it is for you personally that makes you kind of feel more healthy and vibrant in your life, whether it's taking a walk or meditating, or being social with friends. Any of those things are really helpful.

NANCY LYNN: Yeah, I was actually just going to talk about social engagement, because I know that that is a big factor. And I know that in the original slide I put up about risks that hearing loss, vision loss, those are risk factors for cognitive impairment or dementias. And I think, in the sense that they stop you from being more engaged. Can you talk a little bit about the social engagement?

DR. SHARYN ROSSI: Sure, it's interesting that you just brought that up because I was just at the National Institute on Aging Cognitive Summit and they showed all these great results in a cohort in the study of people basically showing that restoring hearing loss with hearing aids promoted cognitive improvement. And then somebody raised their hand and basically said, what Nancy just said, is it really, truly a function of you hearing better physiologically like in your brain? Or is it because you're better able them to engage with people and interact with them and those kinds of interactions are restored? So social isolation, especially with the Covid pandemic really came to light, I think, for brain health, because people we're just very isolated and then their trajectories of cognitive decline really got a lot worse. So that's really come to the forefront as

well. So anything that you can do, even if it's an online support network or something like that. It doesn't matter whether you're in physical contact with somebody, or just actually having conversations and having those connections. So those interpersonal connections are really important.

NANCY LYNN: Yeah, and I'm going to give a shout out for a program called Dementia Friendly America, which I heard a presentation on recently, and they try to do memory cafes and information and support groups all across the United States. Because I think what definitely happens is that people, if they're starting to feel cognitive impairment and are embarrassed about it, or just are staying home and becoming more isolated, this can increase your decline and also obviously affects quality of life. So if folks are interested perhaps we'll bring a speaker on at some point from the Dementia Friendly America program, because I know they're really trying to beef up and also create what's called sort of aging friendly communities, really age friendly. And so that people don't end up getting isolated or not knowing who to ask these kinds of questions to, which is part of the reason we're doing this. You want to at least be able to say, I don't know, does lion's mane really work? And maybe if Dr. Baker comes on, we can ask her about that, although what I'm gathering from her answer is that until something is really tested in clinical trial, a scientist like Dr. Baker can't really answer those questions. And so jumping to the idea that if it doesn't cause you harm and it feels positive for you, do it within reason. And that these types of clinical trials for non-drug interventions are really just starting at the forefront in terms of what's proven or not proven. And these are great questions. Thank you all for putting these questions in the chat about adaptogens and about pure oxygen. These were again all part of the questions that came in earlier, and if we don't get Dr. Baker back shortly, we'll when we send you the recording, we'll send you answers to some of these questions in written form and have her back.

DR. SHARYN ROSSI: So I actually have an answer for the oxygen because there is study showing that hyperbaric chambers actually are really helpful for brain health. And there's somebody in Jerusalem that's doing that work. We fund him for a different project, but happy to share that work after. And then the vegan diet question, I mean, it's interesting. Again, I

think that what seems to work for you, I know lots of people are vegan, but there is evidence out there that your body doesn't really process plant protein in the same way as it processes animal protein. So it's thought that you can use that animal protein, maybe more efficiently than the plant protein. At the same time, if you eat too much animal protein, it actually activates a signaling pathway in your cells that prevents waste clearance. So again, like there's some science out there on how to eat best to promote these kinds of like waste clearance mechanisms in your body. There was just a talk at ADPD on centenarians, so people who live well into their hundreds, and the main readout there is that they have more efficient waste clearance of, you know, toxic proteins.

NANCY LYNN: Can you say that again? Oh, more efficient clearance.

DR. SHARYN ROSSI: Yes, waste clearance, and almost like a hyper immune system that is able to basically protect you over time from whatever insults you are kind of seeing throughout your lifetime. So those were some key factors taken out of that work from the oldest of the old study.

NANCY LYNN: Yeah, she brought up earlier also the idea of heat, which I find very compelling. And we also have a lot of people now promoting ice baths. So do you have any knowledge of those types of extreme heat and cold as treatments?

DR. SHARYN ROSSI: I mean, I can tell you, my take having not really researched these things. I mean cold water swimming, cold water baths, I think the whole idea there is to kind of reduce inflammation, because the more your body is kind of developing heat, the more inflammatory factors you're going to have. And I see Dr. Baker back here, but I mean, I kind of think that any way to push your body away from what it does all the time is going to keep it kind of plastic and young. And that's kind of my take on that. But Dr. Baker is back, so I will be quiet now.

DR. LAURA BAKER: No, I listened. I heard your response. I don't disagree with anything that you said, so I don't really have anything more to add to that.

NANCY LYNN: Okay, I'm going to, I want to just since you said there was positive evidence on the multivitamins, I just want to see if you have a particular recommendation for folks in terms of, is there a particular kind of multivitamin? You know since there's something that shows us positive evidence.

DR. LAURA BAKER: I have a strong opinion about that. No, no, I feel very comfortable about our results. And our finding was that in 2,200 people across the United States we had a pragmatic trial, so it was all by phone and mail. We administered daily multivitamins and then tested cognition over the phone using really the best we could do over phone in about an hour-long assessment. So it wasn't quick. And we had annual assessments at baseline and 3 years later. And our adults are just, for context, our adults were all 65 and older. So if you're less than 65 who knows, may not apply to you. But what we found is that we used Centrum Silver and we used Centrum Silver that is very similar to the current compilation of the essential vitamins and minerals that they're using right now. So I think it's essentially the same, so if you chose the latest version of Centrum Silver, it'd be fine, or the Centrum Silver for women or men. I mean, there's some slight differences in amounts, but we feel comfortable that what we found would generalize. What we found was that those who took, were randomized to the multivitamin versus a matched placebo over 3 years, that we saw not only protection against decline, but also improvement in cognition. Now, and then those who were on placebo did decline.

The other important finding, I think that I just I'm excited about it, we're just trying to figure out what's our next step, is that for people who reported significant cardiovascular disease at baseline, so I'm talking about stents, they've had CABG, they have more significant cardiovascular events that have occurred that have required medical intervention. And what we found is those people who reported more significant cardiovascular disease at baseline, they even showed more potent effects to the multivitamin. Which to me is just, I'm excited about it because we have so many people in the US who have even mild to moderate stage cardiovascular disease. It's really for the Americans, that's part of aging. That is just to be expected in aging. I don't know if it's our culture. It is part of aging. But what we found is that the potency, the benefit for

cognition for those who reported baseline cardiovascular disease, it improved those people it. They showed improvement in cognition and to the level of people who did not report any cardiovascular disease. So we know in cognition, what we study is that people who have cardiovascular disease are always going to perform worse, in general and statistically, than people who do not have cardiovascular disease. It's been published a lot. But what we saw is multivitamin increased the cognition function scores to the same level as someone who's reporting no cardiovascular disease. And that those people on the placebo they showed some practice effects, and you know, in the first year which we always see in cognition. But then they started, they continued on their decline that we expected. So it was a huge separation for people with cardiovascular disease. It was just a one a day Centrum Silver. And the reason I'm so excited about it, it's so simple, and that's why just you know, not everybody is as excited as I am, because it's, you know, too simple. And it's too inexpensive and but it's \$25 a year. And what's different, what I'm excited about this is that it's access to a potential you know supplement or potential agent that could slow cognitive decline that could be accessible to everybody, even people who don't trust medical care, people who don't use medical care. It's just, I just think there's a value. I'm not saying it's going to correct anything. It's not going to cure anything. But if it offers a layer of protection, that's all we're asking for. In my field in cognition and of looking for prevention strategies, we're not looking for the silver bullet. I'm not looking for the silver bullet. I'm looking for different layers of protection. So whether that's Mediterranean diets, some exercise, some resistance training, some stress management, better sleep, and a multivitamin. Then maybe if we layer all those, then maybe we get some more potent impact down the road.

NANCY LYNN: I think you just sold a couple of 100 orders of Centrum Silver. That's fantastic. I'm getting it. Speaking about, you know, it's inexpensive; it seems to work. Can you talk just for a minute about, and then I'm going to get to some more of the questions that are in the chat about music and dance and art, because I've seen amazing results from people with music. Having been on the tour with Glenn Campbell when he had Alzheimer's, and seeing the difference when he would sing and perform. When he wasn't, it was like a different person. And so something

scientifically is happening. It really hasn't been studied yet. But there, can you talk about that a little bit?

DR. LAURA BAKER: Yeah, so you're right. There's a lot of interest now, and a lot of new, you know there's a lot of observational work that's been described. But I think there's new studies now that are starting to scientifically explore in clinical trials the benefit of music. And it may not be music per se. It may be what it does it, how it activates the emotional biology of the brain to connect to brain signaling that has not been stimulated in the same way. So I think we're trying to figure out how much of it is music per se, and how much of it is what music does for the brain, and could you get access to it in other ways? So I'm very excited about that.

In POINTER we have a whole curriculum on the importance of music. I know there has been, you know, I imagine maybe some folks have seen the movie, there's a couple of movies out one is a documentary about the importance of music for people with Alzheimer's disease. And there's some work that was done. It's really nice documentary on that and how it really changes people. It makes them wake up, I think, to a different side of themselves. And I think we're all taking note of this as scientists like this can happen for people with dementia. How can we use this to build resilience against decline? So I'm real hopeful in the next 5 to 10 years we're going to have a lot more hard science about the importance of music. Just related to that, you know my question is, how much is it music, or is it what it's doing to us?

The other angle that I think is being looked at is social contact. So like Covid, during Covid, I think we all aged whether we wanted to or not. We aged exponentially due to lack of social contact. And we've got some new results coming out to show that yeah, that is probably what happened. And we're learning now, in part because of the Covid, the importance of social contact. And we've known that for years for our older adults with memory impairments, Alzheimer's disease, and people without social contact, they decline much faster. But there's a new study that's not so new but that Hiroko Dodge published a few, couple, maybe 2 years ago, showing that in an intervention a randomized clinical trial where people,

it happened during Covid, so that was a nice leveraging Covid for the benefit, but she found that people who received regular phone calls and video conferences and structured conversations, it wasn't just "Hi, how are you doing?" but it was more, it was deeper, to really get more, to learn more about that person, and let that person share. People who were randomized to that group showed these crazy whopping effects on cognition. And these were not, these were kind of like borderline people, so probably a lot of them were mild cognitive impairment. They were just kind of an at a high risk group. But I just, I'm very impressed with that study. And I think we should as clinical trialists, we should all take note of the importance of social contact. Not just "Hi! How are you?" but a deeper connection between people, and as a critical ingredient for improving resilience. I think in EXERT when we have equal contact of socialization in those 2 groups of low intensity and high intensity, I don't know for sure, but I suspect that social contact was a critical ingredient in that trial for preventing cognitive decline.

NANCY LYNN: I'm thrilled to hear your answer. I actually was speaking yesterday with the executive director of an organization called Music Mends Minds, and he happens to be the nephew of John Kander of Kander & Ebb. I think, on our group some of you will know the composing group of Kander & Ebb. But they actually help put together bands of older people they've called the initial one the "Fifth Dementia", and so that they'll play together, sing together. And I am actually a big believer that there's a scientific benefit, that this isn't soft science, even though we don't know how it's working. I think there's huge improvement from the social interaction, and the music or the dance. Dance in Parkinson's has shown a huge impact.

DR. LAURA BAKER: Absolutely. Oh, yeah.

NANCY LYNN: So I encourage anyone to visit Music Mends Minds website because I really like what they're doing. And there are many other groups doing work like that. Just going to answer Imelda's question and somebody else's question on the multivitamin. Is there a better age to start taking it? And what they asked what dose I think of the vitamin was used. But I think you're saying I would imagine you're saying to use it as

the package recommends.

DR. LAURA BAKER: Yep, and please talk to your doctors. You know, people can overdose on certain components of the multivitamin, and it's just, make sure that your doctor doesn't see any conflict with taking starting that multivitamin. It's super safe. We did not have any side effects, but you just want to make sure you're not taking too much of something.

NANCY LYNN: That was great that you just answered that because someone did write in a question: can too many supplements be bad for you? And I'm going to go out on a limb because this drives me nuts. All the advertising for Prevagen and Neuriva—is there any proved benefit to those? And I'm sorry I'm putting you on the spot, but I'm not going to say, are they bad, but is there any proven benefit to these that we know of?

DR. LAURA BAKER: The only study, the only randomized controlled trials ever been run on Prevagen involved 30 people. And it was conducted by the company that that makes the supplement. And that is a whole other topic for us, conflict of interest. And so it's possible, but the studies just haven't been done in a way that's important. And so when my patients and my participants ask me about that, my general answer is, if it hasn't been tested in a clinical trial then I would not take it. If there's no downside, and it's not very expensive, and it hasn't been tested in clinical trial, then that's up to you. And just check with your doctor, because I do believe in an element of control, too. So you know if there's something you believe in, there's no downside, it doesn't hurt you, and you've talked to your doctor, it's not going to hurt you, but in your mind you feel that you it's going to benefit. I'm all in support of, you know, doing what you think is going to be good for you, but really check to make sure there's no risks.

NANCY LYNN: Yeah, I agree. The placebo effect is just as good as any other effect.

DR. LAURA BAKER: Oh, yeah, I love the placebo effect. It works for humans.

NANCY LYNN: And when people spend lots of money, then you want to make sure that they know whether there's really scientific evidence

behind something or not.

DR. LAURA BAKER: Absolutely.

NANCY LYNN: I'm shocked to see that we're actually only 3 minutes away. Which so I'm definitely going to ask you to come back, and maybe before the summer of 25. But we got some really interesting questions, I thought on the HOPE study which is something that I guess a device that does sensory stimulation, I think with electricity. Any info you can give us on that? I think it's currently enrolling.

DR. LAURA BAKER: Yeah, I'm excited about that. I've met the PI of that study, and we've talked at length about it. And I you know, I'm excited about it. I think there's definitely promising preliminary evidence to support continued investigation. That as strong a statement as I'll make. But I just think when, as we go forward, and we, and especially non-pharmacologic interventions, we all, if we can stay open about what we don't understand. And how you know something seems crazy, but if we can stay open to the possibility that there, you know, if we can continue to do rigor science, test these ideas and stay really open to new ideas, especially in new interventions, new devices, new techniques. When we close our doors and think medicine is the only way, drugs, infusion, or a pill is the only way, I think we are cutting ourselves short. And I don't think that's the direction we're going. So I'm very excited about it. And so the brain stimulation is I think a good example of something new and up and coming, and I don't know, we'll see where it takes us.

NANCY LYNN: I like that answer. And I'm going to throw in because so many people have asked about it, and Susan just did again in the chat. Do we know anything about lion's mane? The effect of lion's mane?

DR. LAURA BAKER: I'm going to say, I don't know anything about that. So that's one of my disclaimers at the very beginning. I'm but now I'm going to go look into it.

NANCY LYNN: And Dr. Rossi just put some answer. Maybe we're going to have to do another program about it. And I do want to mention before we end for everybody that in the second episode back in May

last year, a lot of you asked questions about clinical trials, and Dr. Baker has mentioned several of them that she's involved with currently and has been involved with, and we've wanted to do an additional Zoom In series to this one. We're going to keep doing this one for sure, but we're also going to add a series on clinical research, where for each episode, we'll have one trial, and you can ask all the questions about how the trial runs, and who's eligible, and what's informed consent, and what does it consist of? And so I hope you all are interested in that, because I got the sense there's nowhere that people can go. So yeah, write in the chat if you are interested in this because I think they can be for non-drug interventions, they could be for diagnostic. There are clinical trials for diagnostic tools to see if there are better ways to diagnose mild cognitive impairment or Alzheimer's, and of course there are drug trials. There are trials you can participate in from home. But it's so important that we help people be engaged in research, no matter what kind of conditions or no conditions that they have. And I think that it's very hard for people to get real information and be able to feel comfortable asking questions along the way of the people running these trials. And so, I hope you all are interested in that, because we did just receive funding to do that program which I'm very excited about. And so actually, we could have you come back, maybe. Is the U.S. POINTER trial still recruiting people?

DR. LAURA BAKER: No, we've closed recruitment. We've got half of our folks have exited the study already, so we're well on our way toward the end. You know just one more point about what you said. You know that I love the idea that you have to talk about clinical trials and just feature one clinical trial and work through it with the details. It's so important that we all learn how to evaluate and conduct rigorous trials. And so, the goal is not the end destination of what the results are. For POINTER, now we've got 2,000 people. We're busy every single day working. But our goal today, my goal every day is, how can I run, how can I help run the best trial? And so that when we get results, I don't have to look back and say, hmm, I wish I would have done this, or we didn't handle that too well. But it doesn't even matter what the results are right now cause our success, I feel like we've already had a successful trial running the best trial and having a conversation about what does that mean for different kinds of trials. I think it'd be so important for new investigators.

NANCY LYNN: Yeah, that's terrific. Well, good. It seems like there's enthusiasm for that. And I know there will be from the scientific community. So we're just a little over time. And thank you, Dr. Baker, so much. I think we can all give a little round of applause, for sticking with us with your technical difficulties, we really appreciate it.

DR. LAURA BAKER: And I apologize for that too.

NANCY LYNN: It's just not easy to concentrate. So really appreciate it. Really appreciate all of you coming. And if your question was not answered today, and I know there are a lot that we're not, we will hopefully either answer them in future or past episodes, or you can send something specific to reply@brightfocus.org. We're not doctors or scientists in terms of being able to answer your questions directly, but we'll do our best to get you to someone who can answer your questions. And please join us next slide in April, I just want to see what the date is. Oh, and if you want resources, we have a bunch of free resources that we could provide pamphlets and printed materials. These are the numbers to call and emails to email. And April 18th is the next episode. We'll see you then. And I'm actually hoping to do our first clinical trial episode in May or so. So again, thank you all for joining. I hope this is useful to you, and we'll see you next month.

Useful Resources

BrightFocus Foundation: (800) 437-2423 or visit us at [BrightFocus.org](https://www.brightfocus.org).
Available resources include—

- Exercise in Adults With Mild Memory Problems (EXERT) Study
- [U.S. POINTER study](#)
- [COSMOS-MIND Study](#)
- [Eating for Brain Health](#)
- [Diet and Alzheimer's Disease](#)
- [Dementia Friendly America](#)
- [Uri Ashery, PhD](#) studies effects of Hyperbaric oxygen treatment on different Alzheimer's disease
- Alive Inside: A Story of Music and Memory – documentary about the effects of music on dementia
- [Music Mends Minds](#)
- [HOPE Study](#)