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

Can Alzheimer's Be Prevented?
The Science Behind Reducing Your Risk
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Transcript of Zoom with Dr. Richard Isaacson, Director of Research at the Institute for Neurodegenerative Diseases of Florida and Director of Brain Health at the Atria Institute in New York

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

NANCY LYNN: Good morning, good afternoon, and good evening. We have people from around the world joining and welcome to our sixth episode of Zoom in on Dementia & Alzheimer's. Today's program is, "Can Alzheimer's Be Prevented? The Science Behind Reducing Your Risk." And we're very excited today to have this information program which is supported in part by educational grants from Lilly and Genentech. And I am Nancy Lynn. I'm Senior Vice President of Strategic Partnerships at BrightFocus Foundation, which is a nonprofit that's been funding innovative research all over the world for the last 50 years for Alzheimer's disease, macular degeneration, and glaucoma. And welcome. And we have a fantastic guest today and a great subject.

I am absolutely delighted to introduce Dr. Richard Isaacson, who serves as the Director of Research at the Institute for Neurodegenerative Diseases of Florida, and is Director of Brain Health at the Atria Institute in New York. He is a renowned neurologist with a focus on the treatment and prevention of Alzheimer's disease. He was also the founder and former

director of the Alzheimer's Prevention Clinic, a first of its kind in the world at Weill Cornell Medicine and New York Presbyterian, where he was also Assistant Dean of Faculty Development, and associate professor of neurology. And Dr. Isaacson, I'm absolutely delighted to welcome you to the program. And for full disclosure, Dr. Isaacson was also the doctor of Lauren Miller Rogen's mother. Lauren Miller Rogen married Seth Rogen. Her mom had early onset dementia diagnosed at the age of 55. And we've all been working on a movie about that. So that will be used to educate young people in high schools and colleges, and all generations about their experience. And so, Dr. Isaacson, thanks for your help with that film as well.

So, I'm going to jump in. This is a question, as I mentioned to Dr. Isaacson, that I argue with people about all the time. The big question on the right, "Can Alzheimer's and other dementias be prevented?" Really, can they be prevented? Our discussion today is about reducing your risk. And I look at this in the context of people saying, don't smoke. Quitting smoking doesn't stop you from getting heart disease or cancer, but it reduces your risk, so I'll turn it over to you to answer.

DR. RICHARD ISAACSON: Sure. Well, first of all, thanks, everyone for joining. Appreciate it. I look forward to a lively discussion. I'm in Las Vegas today at a conference. I wasn't up all night because I was in Las Vegas. I was up all night studying and trying to figure out the answers to all the questions y'all submitted so hopefully, I'm prepared today. If you have any hard questions, maybe, Dr. Rossi, I don't know, Nancy you can do some hard...Amanda, you take the hard ones, but I'll do the best I can. So, I'll tell you a little bit about myself. I'm a neurologist. I'm a preventive neurologist, and if you haven't heard the term prevention and neurology or preventive neurology yet that's okay, because it's kind of a new field in medicine. And definitely a new field within neurology. You've heard of cardiology, of course. But have you heard of the field called preventive cardiology? And actually just calling me a little earlier was Dr. Arthur Agatston. Dr. Agatston was a mentor of mine over 20 years ago in Miami and South Beach. You may know Dr. Agatston's name because he wrote the book The South Beach Diet. But that's just a book that he wrote, and that's a great book, and he's done great work. But he is a really renowned scientist, and really what he did is really help put the field of preventive cardiology on the

map. Where if you identify that a person has a risk factor for a disease like cardiovascular disease, and you intervene early enough to figure out who's going to get it, and what you can do about it, cause that's complicated, it's not always one size fits all. Preventive cardiology is a field that tries to prevent or reduce risk for having a future heart attack.

This is a great slide, because I don't know that anyone can fully be aligned on or fully agree whether we should be calling this prevention or risk reduction. We've actually written papers. We've written research papers on the semantics behind, you know, should we be using the word prevention? Or do we need to be using the term risk reduction? And what I can tell you is for the public, for the lay public, over a decade ago, when we founded the first Alzheimer's prevention clinic in the United States, I kind of put my flag in the ground and said, you know what I'm going to use the word prevention because I think it's a really important word for the public. Because the word risk reduction gets a little bit lost, and prevention is the effort towards preventing any chronic disease of aging. And I agree I mean you can't definitively prevent a heart attack. You can't definitively prevent a stroke. You can't definitively prevent cancer. Sure, you can not smoke or smoke less, or quit smoking, and that'll reduce your risk of developing, you know, lung cancer and other diseases.

But when I think of the term Alzheimer's disease, I personally feel that the word prevention is okay with qualifiers. And I want to be very transparent about what I mean by with qualifiers. So, I'm really, really, really transparent about this. There is no way possible that if someone comes in to see me and says, can you make sure I never get Alzheimer's? Can you definitively 100% sure prevent me from getting Alzheimer's? Absolutely not, like I would never. The motto that we have is, I promise, and in our work we promise not to over promise, and we have to be very, very cautious. I'm going to do anything and everything as long as it's evidence-based and safe to try to promote someone's optimal brain health as they age. I'm going to try to focus specifically if they have a family history of Alzheimer's. I have 4 family members with Alzheimer's. I've seen this disease in my family since I was little. I've seen this disease, even after all my training. I diagnosed my dad's first cousin at a wedding in 2007. So I've seen this disease, I've seen the toll it takes. And you know,

I can tell you, like my Uncle Bob, he was pretty healthy, he exercised, he was strong, but he still got Alzheimer's. And there are people that can do everything right and still get Alzheimer'. And there are people that can do everything right, and actually, because of them specifically, their genes, their biological sects, their specific set of risk factors, I really believe that the right word in those cases may be prevention.

And let me get a little more granular. When you look at the term dementia as a whole, The Lancet, it's a major journal that you may have heard of, in 2020 The Lancet commission came out with a major paper, so a few years ago now that said 4 out of every 10 cases of dementia may be preventable if that person does everything right. It's a lot of qualifiers there. So I want to be really, you know, as clear as possible. Can Alzheimer's and other dimensions be prevented? Yes, I believe that there are certain types of dementias that absolutely can be prevented if that person does everything right. And the person also has some luck on their side. You know, vascular dementia is probably a little bit easier. Alzheimer's prevention is very complicated. Alzheimer's is a very heterogeneous disease, and what I mean by that is different people can take different roads to Alzheimer's. And you know, my Uncle Bob, he did a lot of things right. He did smoke, okay fine. And you know he did some things that you know could have been shored up. But he had a gene that increased his risk. And when you have a gene that increases your risk, that's different.

So I think that is definitely possible for people to reduce their risk. And I think some people I think it's okay for them to shoot for an overall goal of prevention. Now, even if we can delay Alzheimer's disease or cognitive decline by 6 months, a year, 2 years, or 5 years. And in that time a blockbuster drug comes, or in that time you, you delay it long enough so that the person, you know, would have passed away from something else. Okay, well that's sad thing. But you know, I really believe that the term risk reduction and prevention, whether you use it interchangeably, whether you kind of take some deep breaths and just do the best you can. In our scientific papers we often use the term risk reduction, and for the public we lean a little bit more towards prevention.

NANCY LYNN: I got it. And before I launch into the first question, I'll also

note that a lot of people don't have the opportunity to do everything right. Not everybody has the means and wherewithal, if you're in a rural community, to eat a great diet, or get exercise, or engagement, and so on, social engagement, education. So I'm just going to shout that out there. So in a perfect world, with perfect resources, you may be able to practice all of these things I've listed here perfectly, but in the meanwhile we do the best we can, right? So I'm going to read first, Dr. Isaacson, Carol's question: "I have mild dementia and I am trying my best to keep my brain functioning. I'm 65 years old, healthy, and happy. How do I get my brain to survive dementia? It really is so scary. How can I prevent this terrible disease?"

DR. RICHARD ISAACSON: So when it comes to preventing or delaying cognitive decline in someone that already has symptoms, the semantics here, the words and the phrases and the definitions, get even more complicated. So the way that I think about Alzheimer's disease as a disease, you know, can you prevent or reduce your risk for developing a disease? That answer is yes, in some cases or many cases, but there's a whole slew of things to try to prevent disease progression, the pathology. When somebody already has symptoms, even if they're mild, it means the disease, the pathology, started in their brains, you know, at least 5, 10, 15 years, sometimes longer before the symptoms began. So, when it comes to you know trying to prevent the progression towards severe dementia, or when you're trying to slow or delay cognitive decline, that's some of the semantics that I would use.

So how do you do that? Well, you can come to places like this. You can learn more. Staying engaged. Social interaction. Keeping the brain engaged with learning new things, playing a musical instrument. Use it or lose it. So keeping the brain engaged is absolutely critical. Having a sense of purpose. Getting up every day and okay, maybe not every day, but you know, every day you have to get up, but maybe at least several days a week the goal would be to try to do something. Do something for someone else, do something for the world and really staying engaged is critical.

When it comes to the medical side of things, I really give two categories.

One category is a pharmacologic, and that means drugs, prescription drugs. FDA approved drugs for Alzheimer's. For example, there's several new ones that have come out recently that are very complicated that we can talk about. There's also some vitamins, a few supplements, not a lot, but a handful of stuff that in the right person at the right dose for the right duration of time at the right stage, all these qualifiers, you can use different interventions. And the key with these pharmacologic interventions is they have to be personalized. And again, this is the confusing thing, because some of us have heard. You've seen one person with Alzheimer's. Well, you've seen one person with Alzheimer's, right. Alzheimer's is very you know just different. It's convoluted, it's heterogeneous. So what I would say is in a person that already has some symptoms, we should definitely think about the pharmacologic and we should also think about the non-pharmacologic. When it comes to symptomatic therapies, there are several FDA approved drugs that are used for symptoms. A medicine called cholinesterase inhibitors. There's pills. There's patches. Start low and go slow. You know, not taking it with an empty stomach. That will get you some side effects. There's a lot of best practices, a lot of stuff mixed in here. But there are FDA approved drugs that can help. They're not miracle drugs. But they are helpful in my opinion.

NANCY LYNN: And let me jump in Dr. Isaacson and say, we did two of the first six programs were on all of the approved drugs, and you know, both for behavioral symptoms as well as biomarkers. So I'm really interested, though, because we were not able to get to touching on supplements, vitamins, and I even have some questions about that. So maybe while you're there, you could go on that subject.

DR. RICHARD ISAACSON: Sure. So if you've already heard the drug stuff, that's cool, no problem. That's like the most questions I get nowadays are about the drugs. But when it comes to vitamins and supplements again I want to be really transparent. You can't like take a magic B vitamin, or you know, eat a magic blueberry, or, you know, walk around the block 5 times, and think you can, prevent or reverse, or, you know, delay, cognitive decline. You have to do a little bit of this and a little bit of that. It's like making a stew, all the different ingredients, and you have to have it, you know, altogether. So when it comes to vitamins and supplements, the take home point here is that there again, going to hear me say this a few times,

there's not a one size fits all approach.

So, I'll start with one supplement that I think a lot of people have heard about: omega-3 fatty acids. Some people call them fish oil. It's actually a little bit of a misnomer. Fish eat the algae. The algae have the omega-3s, the fatty acids, the brain healthy fats. Then people eat the fish, or you get the oil from the fish, and then you get brain healthy fats. And the terms there are called DHA and EPA. They have long names. I'll skip that. But the devil is in the details. There are certain people with certain genes that may respond preferentially to supplementation with omega-3 fatty acids or eating a diet rich in omega-3s from fatty fish. But those people will do best in terms of a preventative approach if they start the supplements early before symptoms. So that was a lot of information. I'm going to say it one more time because it's confusing. But if someone already has dementia and wants to take omega-3 fatty acids, studies have shown that omega-3 fatty acids after a person has been diagnosed really don't really seem to move the needle. But what the latest data shows is that people, specifically people with something called the APOE4 gene... APOE4 is a variant, if anyone's checked their 23 and me you could get it there. Some doctors check it. I've been checking it for a long time on my patients. When someone has an APOE4 variant that increases their risk of Alzheimer's, it doesn't mean they're definitively going to get it, but when someone has an APOE4 variant and they identify that early omega-3 fatty acids from eating fish, fatty fish like lake trout, mackerel, herring, albacore tuna, wild salmon, sardines, eating a diet rich in fatty fish is helpful. But a lot of times people just can't eat enough and that's why we oftentimes use omega-3 fatty acids, but only before symptoms, and in people with the APOE4 variant. So that's a use case.

B complex vitamins -- so I'm generally pro B complex vitamins, but I'm going to sound like a broken record, in the right person at the right dose. And here we go again, there's a marker in the blood, it's called homocysteine, these are big terms and big blood tests that you may or may not have heard about. People that take B complex vitamins, if they don't have a high homocysteine in their blood as a marker then the B vitamins are not going to be effective.

NANCY LYNN: Are they going to be harmful? Is there any harm if you're not in a position to go get all these tests done, is it harmful? Should you try it?

DR. RICHARD ISAACSON: So, you know always I would say, check with your doctor. But you know most B vitamins, you just kind of pee them out sort of thing. It's not really that big of a deal, and they're very well tolerated. You know there's even a kind of, here we go again with genetics, but in our program, we do genetic testing. And we practice in this era called precision medicine, where we give each individual person a different, you know, targeted plan based on their genes and their medical problems and things like that. There are certain types of B complex vitamins, B vitamins, that are really biologically more optimized for certain people based on genes. So you know, I think regular B complex vitamins, they're not going to hurt you but you know, talk to your doctor. And if you have a high homocysteine and you want to slow brain aging a little bit and slow brain shrinkage and maybe stabilize or improve memory just a little bit, the VITACOG studies that were done out of England showed that a B complex vitamin can do that in people with mild cognitive impairment. So that was a lot of caveats and a lot of confusion. But that's why vitamins and supplements are confusing, because it's you know a lot of nuance in when to make the recommendations.

NANCY LYNN: And of course we get so many questions about them. And I'm actually going to ask you some more questions about them. Why don't we use your caveats as blanket, everything will not work for everyone. And so to me the important thing is to know if something's going to be harmful and you obviously don't want to go by a bunch of things that aren't going to help. But there's so many questions about what may help. But I want to ask Darlene's question for her from the chat. And the reason I'm going to ask this is because we've had more than one person ask about this. Are you a supporter, and or I will just say, you know, what are your thoughts about Dale Bredesen's ReCODE? Darlene is not a huge fan of the vitamin supplement pathway. And so we do get a lot of questions about Dale's work. So, if you have anything scientific you'd like to share, please do.

DR. RICHARD ISAACSON: Sure. So I think, you know depending on how a physician is trained, what team members they have around them, and kind

of what their interests are, different doctors can take different approaches towards trying to help a person reduce their risk of Alzheimer's and try to help their brain health. You know, it's hard for me specifically to comment about that work, because I'm not as familiar as I could be with it. I've read, I've skimmed or scanned over some of the papers, and I've you know, obviously been asked questions. But the way that our team has approached the field of Alzheimer's disease and Alzheimer's prevention and precision medicine, is just what I would say is just a little different. And what I mean by that is we basically rather than kind of give lots and lots and lots of stuff that is maybe a little bit more one size fits all, or one size fits most, we have the luxury, and this is not, you know as easy, to spend a lot of time with patients, to do genetic testing on patients. We do something called preventative cardiology labs; there's a company that we use called Boston Heart. I have nothing to disclose, but it's a company we've used for over a decade. So we take a really deep dive in specific areas and then really focus mostly in those areas. There are other areas that you know, the recode program I believe they look at toxins and things like that. We don't, we haven't, really gone there sort of thing. We take much more of a vascular risk factor kind of lens. We take anemotional and social health lens. We take a lot of very, you know, we look at genetics and we personalize care based on that. But we're really intentional when we make recommendations. And you know from what I've seen, we tend to use a more targeted, smaller group of suggestions. In our 2019 study that we published, on average people that saw us for risk reduction got about 21 different interventions, and only a handful of those were, you know, vitamins or supplements sort of thing. But we use FDA approved drugs. We use exercise prescriptions. We use very specific diet tracking and sleep tracking and you know, real time feedback. So I guess what I would say is, you know you can take different roads to try to prove something or not, and we've taken just a little bit of a different road.

NANCY LYNN: Well, and the beauty of having you here today is since we're a research focused foundation, a scientific focused foundation, is that you can back up the science behind what you say today. I think I just have to mention this, because I think this is a very funny comment from Don who was told that vitamins just make expensive urine and says we should eat well, or should we eat well? And I've been taking DHA for

over a decade now, and so I hope that isn't just making my urine more expensive, but I guess what would the science say there?

DR. RICHARD ISAACSON: Well, so I'm glad someone brought that up, because you know, I hear that a lot, and I hear that from like, you know, like honestly good doctors. And I hear that there's a reporter for an outlet that I'm sure you all have read. She and I get along great, but we kind of fight a little bit because she's kind of in the camp of, you know vitamins don't do anything. But when you take an evidence-based look and a look from the sense of precision medicine, you know, I guess let's try something else. You have to believe everything the government tells you, right? Okay, well, maybe not. But the USDA, like our government, the dietary, whatever United States, whatever it's called, basically says that at the age of 50 people should take a B vitamin. Why? Well, because as we get older the B vitamins that we eat in food is not as easily absorbed, and it's not as efficiently absorbed, and that can lead to something called vitamin B12 deficiency. And vitamin B12 deficiency is actually not super common, but you know 2-3% of every 100 people that come in to get their cognition checked out, it could be potentially due to a reversible cause, and that could be due to a B vitamin deficiency. So as we get older it's harder to absorb these things. So I don't really agree that all vitamins are garbage. Like personally, I take DHA myself. I take magnesium. I take that for headaches, though not for brain otherwise. I take vitamin D because my D levels are low. So I felt like that was important. And that's kind of like what I take, you know, and everyone's going to need like a different potential thing. And you know, maybe a lot of people don't need them. But about 30% to 40% of the people in our 2019 study went on at least one, sorry one or more, actually two vitamins or supplements in our study. So about a third in our published studies.

NANCY LYNN: Okay, and I'm going to ask one more question on this so we can go to some of the other heart health and exercise and diet and some of those other things that are shown to be helpful. But we get a lot of questions about, and today we for this episode, we got are turmeric, dark chocolate, coconut oil, Lion's mane, you know, asking always are all or any of these things proven to be helpful, useful? Again, I know you can't make a blanket statement, but is there anything that the science shows is

something everybody should be thinking about?

DR. RICHARD ISAACSON: Yeah, so in the right person at the right dose some of these things that you just mentioned are probably helpful or may be helpful and not harmful. So let's talk about dark cocoa powder. So I've been a believer in dark cocoa powder for a long time. What is dark cocoa powder? It's not like a you know, chocolate bar that you get with sugar and butter as the first two ingredients, and then some like, you know, chocolate powder and high fructose corn syrup, and whatever else. Purified dark cocoa powder, there's like a medicinal quality that's actually like scientifically measured. You can actually measure the dark cocoa flavanols in there. So when you take kind of like a medicinal approach, just like when you say, oh eat blueberries, blueberries are good, that's good for the brain. Right but you can take a medicinal approach, what are the properties in the blueberries? Well they're anthocyanins and you can purify that. And wild blueberries have a higher concentration, and then maybe you could do a blueberry powder to have even more. So, what I'm trying to say is, you know, when you think of these little nutrients, and you think about chocolate, dark cocoa powder is very different than the routine chocolate that we get out there. So dark cocoa powder has been shown in multiple randomized studies to have beneficial cardiovascular preventive effects. It can have a little bit of a beneficial effect on blood pressure control, little bit of a beneficial effect on insulin resistance. And a study that was published over a decade ago also showed a little bit of an impact on memory. Some of the follow-up studies haven't really panned out in terms of you know, robustly positive results. But basically, in patients that have vascular risk factors, insulin resistance, high blood pressure who you know what, like dark chocolate anyway, and would do better on a dark chocolate snack rather than a less brain healthy snack. So I do think dark cocoa powder actually could potentially be helpful. Problem is sometimes it has caffeine in it and having dark cocoa powder before bed, that's probably not a good idea. So having it earlier in the day. Also having it with a meal, because a dark cocoa powder can give some heartburn to some people. So again, devil is the details here.

When it comes to coconut oil, coconut oil is really confusing. I'm not pro or con coconut oil. I'm going to sound like a broken record in the right person at the right dose. Medium chain triglycerides, that's the technical term medium chain triglycerides. There's C8 and C10, meaning carbon 8 and carbon 10. Coconut oil is like what you get in a can at store, and you've got to read the ingredients, and there's like a lot of stuff in there that most people don't really need. But purified MCT, Medium chain triglyceride, oil that in certain people with certain genes may be okay. But you have to be a little bit cautious, because if you just start adding lots of coconut oil to your diet and you just kind of go unchecked your cholesterol can go one way, you could gain weight because it's very caloric dense. So again, I'm so sorry that I'm going to continually sound like a broken record, but there's a lot of nuance here.

And I think the good news here is that even though we're just getting a broad brush today, before we end, I want to give you all resources. So if you can, if you say I want to learn more, Isaacson. Thanks for kind of wetting the appetite a little bit. He told me a little bit, but now I really want to learn more and figure out what to do. I'm going to send you to a website where you can get a free course on Alzheimer's disease, risk, reduction, brain health, and prevention. And in about two weeks I think hopefully, by the end of the month, give or take, maybe early November, we're going to be launching a free clinical trial funded by the NIH where everyone from the comfort of their mobile phone, you have to be 53 and above, and basically, if you want to learn about brain health and join a brain health study we've actually tried to take all of these rules and all the learnings that we've done in our Alzheimer's prevention clinic and research work and basically, a person can join through their phone, take a cognitive assessment, take a screening. The software will learn about you. And then the software will give you individualized education and guide you through a 6-month step about brain health and also tracking cognition over time. So I wanted to add these practical things in because I think some people come and they really want like targeted advice. And I'm not giving everyone the best targeted device because I'm being more general because that's the science answer in me. But I promise you will leave today if you want to spend an hour watching videos, I got you. Two hours, no problem. And then if you want to join a clinical research study it's called yourbrainstudy.org or retainyourbrain.com. You can

sign up now, they have, like an email thing, at retainyourbrain.com. And basically you can you know, learn all this from the comfort of your cell phone.

NANCY LYNN: That's fascinating. And I'm going to do one better than that. And we do send all the resources. And a recording of this episode will be emailed to everyone who's participating along with other resources. But also next year we're hoping to do an additional series of "Zoom Ins" that are on clinical trials and research studies. So that we could actually... on our second episode for those of you who are there, you all were saying, how do we know what studies are available to us if we're APOE4 positive? How do we know how to join a clinical study? So, Dr. Isaacson I'm going to ask you now to come back maybe early next year, when this study is up and running, and we'll literally walk through, especially if it's something people can do from their own home, and it involves, you know, observational, you know, behaviors, and so on. That's fantastic. So stay posted everybody who's really interested in that. We'll have him come back and really talk us through how we can participate in that in that trial.

And I'm just going to take advantage of the break also to say several people have asked questions in the chat. Thank you for asking questions in the chat about APOE4 positivity and status as well as genetics. And so, I just will tell everybody that we did an episode on genetics that's available on demand with Dr. John Hardy and so take a look for that if your questions aren't answered today, or if Sharyn isn't answering it in the chat box. It has a lot of great information about the genetics, where people are asking if my parents had it and do I have the chance? If I'm APOE4 positive, what are my chances? So a lot of that was discussed in that episode with Dr. Hardy. But since there are so many questions about APOE4 specifically I think if folks are interested in our doing an episode specifically devoted to that, would you write it in the chat box so that we'll know there's a lot of interest and demand for that subject, and we can add that in.

So let's go, because you mentioned blood pressure, let's go to the things that you can do for vascular health. Because I think, I don't know if I can say that seems like one of the most modifiable risk factors, I don't know if

there's such a thing as most. But let's talk about why that's important to be looking at your heart health.

DR. RICHARD ISAACSON: Yeah. So a happy heart is a happy brain. And a lot of people say, what's good for the heart is good for the brain. But again, there's a little bit of nuance. There are blood pressure ranges that you know, there's a study called the SPRINT MIND study. And the SPRINT MIND study shows that people with a blood pressure average of 140s over 80s versus a blood pressure average of 120s over 70s, so just a little bit lower, 20 points on the systolic, the top number and 10 points or so on the bottom number, could in a very small three year study could delay the onset of mild cognitive impairment by 19%. So that's a big, big, big number 19%. And just in three years of getting blood pressure down by 20 points on the top number and 10 points on the bottom number. So the take home point with blood pressure is, one has to set individual blood pressure targets based on the person's you know, medical history and what we're trying to treat. You know, there are certain people that have low blood pressure. And we have to be cautious about that. So there's always a balance when it comes to blood pressure. We often recommend people track their blood pressure at home. You can buy a wrist cuff, you can basically track your blood pressure at home. And I don't know if you've heard of the term called white coat hypertension. Basically, you go to the doctor's office, and you get anxious because you have run into the appointment and you see the person come with the white coat and they check your blood pressure, and it's high. Tracking blood pressure from home is a really great strategy, because then you can go to your doctor and say I have been tracking, and you know my last 10 blood pressure readings over the last 4 weeks were this, doc. what do you think? And that's a much more you know, objective, clear, helpful piece of data that your doctor can use rather than one blood pressure reading, when you know, you may have been discombobulated running back and forth, and you may have been stressed out because the doctors you know, talking to you sort of thing. So I think blood pressure is really critical.

Blood sugar is also absolutely critical. People with diabetes have twice the likelihood of developing Alzheimer's disease. This is a complicated topic. Some people have called Alzheimer's you know, diabetes of the brain

type 3. I don't exactly use that term, but I think there's some interesting overlap there. The higher the blood sugar, the more rapidly memory and cognitive function declines. The larger the belly size, as the belly size gets larger, the memory center in the brain gets smaller. And having metabolic problems and visceral or belly fat, slows down metabolism and increases diabetes risk, and increases the likelihood to have what we call insulin resistance. And this problem with insulin where the pancreas has to keep secreting more and more insulin, this hormone called insulin, that causes inflammation and that fast forwards, I believe, amyloid deposition. Amyloid is that bad pathologic protein that builds up in the brain of a person with Alzheimer's.

So insulin resistance, blood sugar, blood pressure, and also cholesterol. And now, having high cholesterol is, you know, if you want to slam the breaks to cognitive decline, get your cholesterol treated that's really critical. And there's not a one size fits all approach to cholesterol management. You know most people have heard about statins. There are other medicines that work on a different mechanism called plant sterols, that's a pill. We look at whether a person needs one drug versus a different drug and that's very unique and usually only preventive. Cardiologists do that, but finding the right drug for the person is really critical. There's a newer over the last 5 years injectable medicines for cholesterol called PCSK9 inhibitors. You can get an injection every 2 weeks or so. And PCSK9 inhibitors really don't go through the blood brain barrier, don't affect cholesterol in the brain. And you know, maybe, and then, honestly, the cognitive data using those drugs have been really spectacular. So, while getting your bad cholesterol down, your LDL down, that's a good thing. There's some nuance there, and I see one question from Dawn, "But doesn't the brain thrive on cholesterol? It needs to function?" And yes, I would say the answer to that is, yes, and I can only say that I can speculate but I think we finally have figured out kind of the key about this. And certain people, especially people with the APOE4 variant, there may be certain people that can have cholesterol over suppressed. Meaning too high, of a dose of a certain type of medication where it could potentially impact brain health and cognition. Now, that's not common. That's maybe 5% of the time, 10% of the time. Definitely not more than 20% of the time. And you know, if I had to make a go/no go decision, should statins be in

the drinking water? Well, I don't want it to be in the drinking water. It's just a kind of a saying. But I would rather it be in the drinking water than not, because they have so much of a protective benefit. But again, it's not one size fits all. So I think our understanding of cholesterol management for brain health and Alzheimer's prevention is rapidly evolving. And it's definitely something that I can update you on in 6 or 12 months from now because we're actively studying this.

NANCY LYNN: And while I'm going to ask you to talk a little bit about exercise because I know that is one thing that's been studied a lot, the effects of exercise on the potential of getting dementias, I'm going to ask Roger to put that slide back up that that had my laundry list, and because since we have 20 min left. I'm going to ask you to talk about exercise. And then I'm going to ask you to look at this and say, okay, which ones of these are the most important for us all to be hearing about from you?

DR. RICHARD ISAACSON: Sure. So, you know, if I had to choose one thing that a person can do today to impact in a positive way their brain health tomorrow, exercise is by far the number one thing that I would say. And you know, exercise is kind of a pretty non-specific word. We put people on pretty detailed exercise prescriptions. You know, walking 10 or 20 minutes a day is better than 0. But you know, can you just walk and reduce your risk of Alzheimer's and protect brain health over time? I don't know that I totally agree with that. I think walking is good but really having a personalized targeted exercise plan for you, based on your own individual risk factors is critical. So, as we age, after we get past our thirties and forties, we're losing muscle every year. You get to a point where you lose 1% of your muscle every year. I just don't really think it's feasible for people to expect that they can optimize or maintain cognition as we age without paying attention to muscle strengthening. Strength training, you know, obviously don't want to get hurt. Strength stretching, and you know, resistance. You can do bodyweight exercises but when in doubt, work with a personal trainer. You have to do something. The more muscle you have, the higher your metabolic rate is, and the more metabolically active you are, the more calories you burn. So I think a lot of people out there, they'll walk and they think that's enough. Maybe walking is helpful to maintain cognition in some ways, but it's not going to be in the

category of preventing or you know, reversing pathology, I don't believe that. Exercise is the number one thing that anyone can do today to have a positive impact on amyloid. I think many people are unaware that exercise on a regular basis actually has been shown to have less amyloid build up in the brains of people. So that's something that's, you know, talk about anti-amyloid drugs, and how expensive they are, and how the how many side effects there are. Exercise right now can slow down accumulation of the pathologic amyloid protein.

Doing exercise where you get your heart rate into the fat, burning mode, I think like, I hate to say it probably 7 or 8 doctors out of 10 doctors may not be totally familiar with this. It's not the doctors' fault, the science has changed, and you know it's hard. And you know it's tricky because doctors don't have time to do this type of exercise counseling. But you know our program does. Getting your heart rate to high enough to where if you're talking to someone on the phone, they can tell that you're exercising, but you can still maintain a conversation, that's a good proxy for what we call Zone 2 steady state cardiovascular exercise. And if you keep your heart rate low enough, you could put the treadmill on a little bit of an incline, get your heart rate up. You know my Zone 2 is in the low 100s or so, other people's, you can get it measured. Sometimes it's in the high 80s or high 90s, or 110s, or 120s, it depends on the person. As a person gets older, their Zone 2 target, their steady state target pulse will be lower. And what I'm trying to say is, fat burning is a specific type of exercise, and most people don't learn about that. And I think some people go on the Peloton, and they get really sweaty. And they're moving, moving, moving and they go all out and for 30 minutes they're sweating. If you go too fast and too hard, you kind of lose the fat burning aspect of the exercise. And also, it honestly really takes 45, 50, 60 minutes of regular cardio, of a steady duration of cardiovascular exercise to burn the stored carbohydrates. The glycogen, the stuff that the carbs that really are stored in your liver cause that's where people have it stored in case of starvation. If you can't have food, your liver stores the glycogen. If you want to burn body fat around the midsection, you have to do lower intensity, steady state cardio. You have to do strength training several times a week. You know, for people that have one or more copies of the APOE4 variant, those people actually tend to preferentially benefit from the more higher intensity exercise

as well called high intensity interval training. So again, this exercise prescription is very nuanced, and it's very personalized.

Everyone here, just like I say you should know your blood pressure, you should know your fasting blood sugar. You should know your LDL, your bad cholesterol. Everyone out there should know their resting pulse. Everyone out there should know their percent body fat, and everyone out there should know what their muscle mass is, and if it's declining, or stable over time. And you know, a lot of women get something called a DEXA scan. A DEXA scan is a thing that you can look to get your bone density analyzed, and when you're looking there you can also look at body fat and muscle mass, and every year or so it's a good idea to get that checked out.

NANCY LYNN: Someone's asked, is there a best time of the day to exercise?

DR. RICHARD ISAACSON: Yeah. So almost mentioned this, but I think people sometimes that are really busy, kind of just got to take the exercise when you can get it. So I don't, want to you know, quibble over it too much. I think when people are really trying to lose the stubborn belly fat, because belly fat around the midsection is really hard to lose it gets stuck there over years, fasted exercise in the morning is sometimes a way to jump start belly fat loss. So you know 8 o'clock in the morning, 9 o'clock in the morning, 7 o'clock in the morning. Whatever time you do your 45 minutes to 60 minutes of fast walking, or steady state cardio. And if you don't have any glycogen on board, and don't even have any sugars on board, you can sometimes kind of get fat burning. That being said after the exercise you should eat because when you do strength training, or when you do other exercise, the muscles need some degree of carbohydrates as well as protein to really survive. And if you starve yourself during exercise, you can even break down more muscle then you had to begin with, and that's not a good thing. So you know, I think some people get activated by exercise where they if exercise after 5 or 6 pm, it interferes with their sleep wake cycles. But honestly, I think this is really an individual decision.

NANCY LYNN: And William also asked about light therapy. I have noted a bunch of other things here on the left. I know hearing loss and isolation

are very closely tied to risk of dementia. It's really important to get as much sleep as possible, or I should say the right amount of sleep for you each night, because that is when amyloid is cleared out of the brain. Again, since you can't go into each one of these perhaps today, is there anything important we should know about light therapy since that was just asked?

DR. RICHARD ISAACSON: So I think there's different types of light therapy. Making sure that someone has good sleep hygiene and basically, tries to go to bed the same time every day and gets up at the same time. And you know, doesn't do stimulating activities before bed. Doesn't have alcohol before bed or caffeinated beverages. You know, you only use the bedroom for sleeping, and you have a cool environment. If there's a light that's creeping in from the window, you've got to figure out a way to get rid of the light. You know, really making a proactive plan to get good sleep is really critical, and as we age getting good sleep and long sleep is very hard. It becomes like almost impossible in fact, after we get past a certain age. But we just have to kind of do the best we can. If someone is exercising and not sleeping, you know, at least, 6 plus hours, you know, 6 to 7 hours ideally. 7, 7 and a half is even better than that. But again, that that's challenging as we age. You can't just burn the candle at both ends. If you're exercising, but not sleeping well, people don't lose body fat. And if someone is sleeping well and prioritizing sleep as well as exercising on a regular basis, eating a healthy diet, green leafy, vegetables, Mediterranean style foods, mitigating their stress, meditating. And you know, managing stressful things and not ruminating before bed. There's really what we call the biological principle of synergy, one plus one equals three. So you really have to do all of these things together to have the best chance of success. It doesn't mean everything has to be perfect.

But I think people that have hearing loss really should get a hearing evaluation and get a hearing aid. 8%, I'm going to say that one more time 8% of dementia cases are attributed to hearing loss. 8%. That is that's just a really important risk factor. When people can't hear and people can't see, they retreat. They don't interact, they lose social stimulation, and it turns the brain off and that accelerates brain aging. You know, everything on this list is really critical. Excessive alcohol, you know, fast

forwards cognitive decline. Smoking, that's not very good for the brain or otherwise. So staying engaged and doing all of these lifestyle factors is really critical.

NANCY LYNN: Somebody has asked here, I see cannabis on your list, can that be helpful? Edibles, do we have a science on this now?

DR. RICHARD ISAACSON: Yeah. So I often defer these questions to my colleague, Professor Seth Rogen. But Professor Rogan doesn't seem like he's here today. So oh, well, thanks, Seth, not going to bail me out today. So let's start by saying that...

NANCY LYNN: I know Seth's opinion, but we need the scientific opinion.

DR. RICHARD ISAACSON: Cannabis is a word I think that people associate with marijuana, and marijuana is basically a plant that has different chemicals in it. So what I want to say about that the topic of cannabis is there's different substances. So one is called THC, tetrahydrocannabinol, THC is the psychoactive substance in cannabis. That's the high that people get, and that's the really the psychoactive part. There's another agent or part of molecule called CBD, cannabidiol I think that's how you say it. And you know, when people smoke it, or eat it, or drink it, or whatever the different types of things. I'm in Las Vegas and they have these dispensaries here. I've never seen anything like it. It's like a shopping mall for this stuff. So basically, depends on the type that you get may have differential effects. Do I think cannabis is bad for the brain, and does it cause Alzheimer's? I wouldn't say that, I don't think there's clearly any evidence on that do. I think cannabis is protective? Do I think CBD may be more protective? I don't know. Possibly, but I don't really know. I don't know that we're really ever going to have high quality studies. And you know, as my mom says, everything in moderation. I think if someone is, you know, dependent and using a cannabis every single day and every minute of every day, I think maybe that's different. But you know, if it's used recreationally, you know, cannabis is confusing. But I think in the next several years we're going to have a lot more hard science data.

NANCY LYNN: Craig, from Vimeo, asks about short sleepers. Do those who only need 5 hours or so of sleep have a greater risk for Alzheimer's?

DR. RICHARD ISAACSON: Great question. We in 2017 started a study where we put these wrist trackers on people. It's called the WHOOP device. I still have one. It's actually charging over there. And basically, we actually tried to look at this a little bit and WHOOP devices, you know, fitness trackers can track sleep. They can track exercise patterns. And you know it's interesting. There was a magic number in our cohort that the people that got greater than 7 hours and 11 minutes of sleep tended to do better on cognitive testing. And the people that got less than 7-11, 7-11 is easy to remember with the convenience store, people generally speaking, 7-11, and less had poorer cognitive performance on cognitive tests the next day. There were 2 of the 40 people on that initial study that slept very short. That's what they said, they were short sleepers their whole life. 5 and a half, 6 hours. Sometimes 5, sometimes less. And interestingly, one of those patients tracked with the sleep deprived group in terms of cognition that didn't look as good and sleep deprivation is a very specific finding on a cognitive assessment. Their processing speed is slower and attention is less. And the other person that had short sleep was rocking and rolling, and did great on the cognitive test. So what I would basically say is, I don't have enough personal clinical data. And I think the data is a little bit murky, cause it's really hard to, sort out what do we mean by a short sleeper. What does that mean physiologically and how can we generalize, based on the on tricky answers?

NANCY LYNN: I want to ask a question that caught me. My mom was diagnosed at 79. Her sister now has dementia and since Covid and was 95ish, I know that she couldn't be social anymore because of the pandemic. It seems being social and part of a community impact the brain more than we realize. How can we as seniors keep active when we become immobilized, due to physical constraints, and no community to be with us, especially if we live alone? So if people are living alone. If they don't have all these abilities to do all this other stuff, what are ways they can stay engaged?

DR. RICHARD ISAACSON: Yeah, great question. And this is something that I think our society as a whole needs to sort out and do a better job of. You may have heard of Dementia Friendly Communities in the United Kingdom and the Netherlands, and you know, our society here is just not attuned

to kind of how we need to age gracefully and age healthfully. So, that's a caveat. But what I would say is, staying as engaged as possible is key. You know, to help with that hearing assessments, vision assessments, joining adult education classes, taking zoom stuff, trying to get out of the house as much as possible. Picking up the phone and calling a friend. Having friend circles. You know, there are a lot of strategies. We work with a dementia care social worker that's really helped guide me on these topics. And you know, working with a social worker that is more familiar with the resources, the individual resources and the communities around you. You know the aging affairs divisions, the Department of Elder Affairs. There's a lot of resources that that people may or may not be aware of. So I would say, first of all, you know get educated, get informed, make a phone call, find a social worker, or go to the Department of Elder Affairs on, you know .gov and call and see what resources there are. But I think one really has to make much more of a concerted effort right now. And I think that's unfortunate. Hopefully in the next 2 to 4 to 5 to 7 to 10 years some of the stigma of aging will be addressed and we won't have to be so proactive and reliant on that.

NANCY LYNN: Yeah, I think we've been talking to BrightFocus Foundation and SCAN Foundation, which is a California based foundation, about really trying to maybe do a film again to encourage the grassroots movement to have communities inter-generationally and communities go back to that idea of our taking care of each other in our communities. And yes, it's definitely about people trying to reach out and not be stopped by stigma, and so on. But it would be we think, a really wonderful thing to promote this idea of our children and our grandchildren going back to trying to care for our families and other families in community. And I know it sounds awfully simple and old fashioned, but it's something that seems quite lost these days, and not a lot of attention is paid to in different cultures, and so on.

DR. RICHARD ISAACSON: I just want to also mention, I saw some stuff going by in the chat with Sharyn and Anne about blood-based biomarkers. I eat, sleep, and breathe the blood-based biomarker field. That's what I've been working with for years now. We have frozen plasma on most of our patients in a freezer in Boca Raton. We have3 little milliliters of all of

our patients in Sweden on ice. We shipped it there on dry ice. We send it to St. Louis and a company called C2N, which some of you have heard about. We are very, very, very active in the blood-based biomarker kind of thing. And in about, let's see an hour, I'm in Las Vegas giving a lecture and then in about two days in San Francisco, giving another lecture, I'll be presenting for the first time some really, I think it's actually really cool, I think it's pretty cool. We've just launched in September at home finger prick testing for Alzheimer's biomarkers. And we're just trying to validate that now as we speak. Now, let's talk about the good, the bad, and the ugly with biomarkers. I think most people don't realize this, but when you all go to your doctor to get your LDL cholesterol checked, there's like nine different tests out there. Different assays, different validated methods to calculate LDL cholesterol. And actually LDL cholesterol is a calculated measure. It's not even directly measured in most of the Quest and Labcorp, and whatever else. We use a direct lab that actually measures it in a direct way, because we're a research-based operation. It's the same kind of paradigm with some of these other blood tests. Amyloid blood tests are not all created equal, and I can't underscore that enough. Also, because the science is so new, every biomarker that we order and we look at on a patient, we get a second opinion from different labs, and we look at everything together. There's, I saw in the chat, and I have nothing, I don't have too much detailed information on the Quest test but the Quest test from my understanding is just not anywhere in terms of as accurate or valid as some of the other tests out there. You know the two assays that we use are the C2N assay and then the folks our team in Sweden. When they did a head-to-head test of 8 different amyloid blood tests, those were the two best ones, so those are the ones we're going to use.

So what I'm trying to say is, I am very bullish and excited about blood based biomarkers. The thing that I'm really excited about them isn't really like diagnosis. I think diagnosis is helpful. And I think you know characterizing disease is helpful. But the data that we're going to be presenting over the next couple of days is when someone goes on an anti-amyloid drug or someone goes on one of these diabetes drugs, you know, for weight loss, or when someone starts exercising and eating a healthy diet, what were their blood-based biomarkers before? And what were their blood-based biomarkers after? And what can we learn about

that to better refine a person's care. You've heard of cholesterol tests. Well, our team is working very, very, very hard on what we call colloquially a cholesterol test for the brain. And we have a panel that I think is pretty close. You know, we have validation to do, and we'd like to do it at home through finger pricks rather than through blood draws and dry ice samples and all the craziness with shipping. But we're closer. We're nearer than further with having a cholesterol test of the brain sort of thing where people can hopefully, before symptoms, as well as once early symptoms begin, can track their brain health measures and then use those numbers to more effectively evaluate the response to the risk reduction therapies that they're doing. I have very, very, very provocative data that I can't get into right now. But it's the future, and the future is now. The stuff that we can do now is just it's like, couldn't even have these conversations months ago, let alone years ago. But the field of Alzheimer's prevention, like just leaps and bounds, just growing by leaps and bounds. So I think if we have to end, and I'm happy to stay on if helpful, I think we have to have hope. No, we don't have a magic cure, a magic potion. You know, a definitive way to prevent or cure Alzheimer's. No, we're not even close, but I really think people can grab the bull by the horns and take active decisions, work with their doctors. Watch me blabbering online. There's a website you can go to called brainmind.org/alz. Again, brainmind.org/alz for a course that I that I taught about this stuff and then retainyourbrain.com or yourbrainstudy.org, and you can sign up for a totally free track your memory, track your risk and learn about Alzheimer's from the comfort of your phone in a free six month kind of simulation study. So, with that, I'll stop blabbing. But I'm happy to take any final questions or do whatever

NANCY LYNN: We absolutely love your blabbing. And I want to thank you so much for being here today, but also for all of this very pioneering work that you're doing. And I think you'll have to not only come back to talk about the retain your brain study, but so that we can get more deeply. There were a lot of questions like, what type of exercise is best if you're over 75. I mean, it's interesting, because what you talked a lot about today is that everything is precision. Everything is what works for you with your genetic makeup, your age, your you know, physiological predispositions. And it's such an interesting time. It's such an exciting time in the Alzheimer's field with all this information we're getting in precision, but

there's the precision, and then there's well, if I can't go, get all this testing done and be part of a trial, what are the general things that are most important for me to know? And I do think we touched on that today. But basically, that's my call for you to come back. And but since Dr. Isaacson has so generously asked, any last burning questions that somebody would really like to ask him before we let him go back to the casino?

DR. RICHARD ISAACSON: Excellent! I heard Casino. I'm going right now. I can go back. Is that what you said? I can go back to the craps table. That's good for the brain.

NANCY LYNN: You can go back to the craps table, only if you're winning. And one other, one last thing I'm going to say is, I'm really glad we talked about vision loss today, because, being a foundation that funds macular degeneration and glaucoma research, hearing loss has been accepted by the CDC as a risk factor, but no one ever talks about vision loss, but that is also keeps one very isolated and is important. And even I know there's a lot of talk now about dental hygiene and things, and I think you called it some kind of a hygiene earlier, heart hygiene. I think whole body hygiene is maybe one general way of looking at what's best for all of us. So let's see, did any last question come in? Nope. We will send the websites. We will send the names of the trials. And we will send a recording of this of this session, so that you can play it back in slow motion and hear all of the great wisdom of Dr. Isaacson before he goes off to gamble.

I want to thank everybody for their time today, and especially Dr. Isaacson. Thank you so much for your time. And we will see you next month. We will be sending you all of these resources. Standing ovation to the doctor. I agree with you, David. And standing ovation to the audience who got really engaged this time. I really appreciate your getting engaged. We'll see you back next November 16th for the next episode. Still deciding on the topic. We may be trying to focus on the use of AI in early detection and diagnosis. All of those cool things that are coming down the path to help detect and diagnose Alzheimer's before it becomes less treatable and less manageable. So, thank you again to everybody, and have a great day.