UsAgainstAlzheimer's

ALZHEIMER'S TALKS

January 2018 – Transcript

Welcome to Alzheimer's Talks, a free monthly teleconference presented by UsAgainstAlzheimer's. My name is Brooks Kenny, and I am the executive director of WomenAgainstAlzheimer's, which is a network of UsAgainstAlzheimer's.

I'm so glad that each of you could join us today. I want to share a couple of quick updates about our work, and then I will introduce our very special guests, Dr. Richard Isaacson from Weill Cornell Medical Center and Karen Segal, an advocate and board member of UsAgainstAlzheimer's, who is participating in Dr. Isaacson's current research study.

As most of you likely know, at UsAgainstAlzheimer's, our vision is to stop this disease by 2020, and we have a number of strategies underway to achieve that goal. We thought it would be interesting for this group to share a little bit about our work in brain health given the topic of today's call. Despite the Alzheimer's crisis that we all are very familiar with, our healthcare system and society still finds itself in a place where we are not yet prioritizing brain health awareness, brain-healthy behaviors, early detection of cognitive impairment, and early and accurate and compassionate diagnosis of Alzheimer's disease and other dementias. So as part of our efforts, we are developing a Brain Healthy Ecosystem. We're really excited about it. It's a collaboration that will engage both healthcare and consumer stakeholders in what we hope will dramatically shift how we approach the conversation around brain health and cognition. We're really looking forward to sharing more with you about this important initiative, and we'll be doing so in all the various ways we communicate, through email and through talks like this.

I also want to share a bit about some of the work we're doing at WomenAgainstAlzheimer's in light of the topic today. We realized pretty early on that we wanted to focus on empowering women and empowering women's voices, recognizing that we are more susceptible to this disease and that we are more likely to be the caregivers for loved ones. One of the new projects that we are engaged with is

called the Women's Leadership Council. This council is made up of women executives from a wide range of industries who are committed to taking on women's brain health as a major priority. We're working with this group in order to develop brain health content, to develop speakers and information that women can take back to their companies, to their networks, to their communities—recognizing that we need to be talking about brain health and caregiving in our living rooms and in our board rooms. So this is a new initiative that we're doing at WomenAgainstAlzheimer's that we're very excited about and look forward to sharing more with you about the results.

Probably the best thing to do at this juncture is to turn and introduce you to our very special guests today. We have Dr. Richard Isaacson, who is the director of the Alzheimer's Prevention Clinic at Weill Cornell Medical Center in New York. Like so many of us, he has a personal connection to Alzheimer's, with several family members who've had the disease. In his practice and in his research, he takes a really comprehensive, multi-faceted approach toward Alzheimer's treatment and prevention. He is the author of two bestselling books—his most recent being The Alzheimer's Prevention & Treatment Diet—and he has helped develop Alzheimer's Universe, which has online lessons and brain activities. If you haven't yet, I really urge you to check it out. I'm going to give you the website now, I'll say it twice: It's www.AlzU.org, again it's www.Alz[the letterU].org. Feel free to check that out; I know he's going to speak about it as well.

Many people are not aware that Alzheimer's starts in the brain as much as 20 or 30 years before symptoms appear. Dr. Isaacson sees this as ample time to make brain-healthy lifestyle and dietary choices in order to delay the onset of symptoms. Today we are fortunate to have him talk with us about his work generally in Alzheimer's prevention but also about a study that he is conducting right now, that's looking for the earliest possible signs of Alzheimer's in women. This study's findings could end up really helping both women and men alike. We can't wait to hear the latest news.

We are also very fortunate to have with us Karen Segal, who is participating in this study. Karen is a board member of UsAgainstAlzheimer's. She has Alzheimer's in her family. Her mother was diagnosed in 2002. She really has learned firsthand how challenging it is to juggle family life and caring for someone suffering with this disease. We are humbled and ecstatic that she has joined the UsAgainstAlzheimer's board to help disrupt the conversations around Alzheimer's disease in our effort to find a cure by 2020

through research and through clinical trials. She's going to talk with us about why she decided to join the study and what it's been like, her personal experience, should you all want to consider joining a research study or sharing this information with loved ones.

Before I turn it over to Karen, I do want to share just one quick housekeeping item. When we're done with both of our speakers, as always we will open the lines for your questions. If you do have a question, all you need to do is press *3 on your phone at any time during this call. By pressing *3, you will be placed into the question queue. Please have your question ready to share briefly with a member of our staff. Or if you are listening to us online, you can simply type your question in the box. We will get them coming in, and answer as many questions as we possibly can.

With that, I would like to turn it over first to Karen Segal to tell us about why she chose to participate in this study and what her experience has been like. So, Karen, if you could start, we'd love to hear your personal story about your mom's diagnosis and what some of those challenges have been and then obviously pivoting to your inspiration for joining the research and how others might get involved. So, Karen, thank you so much for being here. I'll turn it to you.

Karen Segal: Thank you, Brooks. My maternal grandfather had this disease, and my mother has the disease. There are always first signs that something is wrong; we've all been there. And in 2002, which is many moons ago, when I was pregnant with my third child—a baby girl after two boys—my mother was ecstatic, finally after four grandsons, to have a granddaughter. However, each time we spoke, she kept asking me, when is the baby due and is it still a girl? And I knew that something wasn't right. My father, who is a physician, was in denial and unwilling to act. Six months after my daughter Caroline was born, my sixty-two-year-old mother was diagnosed with Alzheimer's disease, and she was completely devastated and would call me multiple times a day telling me that the diagnosis was wrong. In order to help her avoid depression, I lied and told my mom that she was correct, that she didn't have Alzheimer's, and for the next seven years my mom managed to use her outgoing and friendly personality to cover up her illness.

So I, over the last 10 years, have witnessed the relentless and devastating effects of the disease. My once beautiful, energetic, charismatic and loving mother is now a shell of her former self. It's been so

painful for our family to watch. Alzheimer's robbed my mother of her strong and vibrant personality. My mother's struggle, as many of you can relate, breaks our hearts every day. Not only did I lose my mother but my children lost their grandmother, and there are millions of families living this nightmare, slowly seeing their loved ones fade away and often feeling powerless. So I knew I had to turn my pain into action, for my mother, for me, for my family, for all of us. I've put my pain into action and have become a very fierce advocate, a tireless volunteer to support fundraising for Alzheimer's research and to promote clinical trial participation.

In the process, I became a clinical trial participant. I met Dr. Isaacson in 2015, and I go for check-ups every six months to Dr. Isaacson's office, and he is basically using precision medicine to reduce my risk for Alzheimer's. The appointments include blood tests, cognitive tests and brain scans, and he reviews my diet and exercise routine. We know one thing for sure: that we're not reversing my mother's condition but we might have a chance of curing me, and personally I would rather be driving the bus than chasing the bus. I want to do what I can until there's a disease-modifying drug. Until then, I'm going to stay healthy and hope that Dr. Isaacson's prevention strategies are working. So I would like Dr. Isaacson to now talk a bit more about the prevention strategies that he is working to introduce to all of his patients, not just me.

Brooks Kenny: I was just going to thank Karen so much for telling her story. There's so much power in storytelling. It makes it real for all of us. We thank you for doing it, and we thank you for the way in which you share your story. I'll turn it over to you, Dr. Isaacson. We'd love to hear about your work generally in prevention and then certainly about the study and how others can get engaged, so I'll turn it over to you.

Dr. Isaacson: Thanks so much for having me, and, Karen, I applaud you and your courage and your drive to share this message. Just the fact that we're able to use the term Alzheimer's and prevention in the same sentence is really — I used to use those terms in the same sentence and get tomatoes thrown at me 10 years ago, but now it's okay to do that, just the totality of evidence is overwhelming that there is something that people can do to at least attempt to reduce their risk.

I think sometimes when people hear the term Alzheimer's and prevention, they say, 'Oh well you can't prevent Alzheimer's—there's no cure and the treatments aren't great.' But I think, in some ways when people have that visceral reaction, they're not realizing that the word prevention is a concept, it's a philosophy. For example, we all know about heart attacks and strokes, right? Can anyone definitively, 100 percent of the time, prevent a heart attack or stroke from happening? No, not even close. You can take the medicine, you can exercise, you can eat right, you can do all the things, and you will reduce your risk. Semantically speaking, I think it's really the same with Alzheimer's prevention.

Along these lines back in 2012 I was interviewing all over the place. I was in Miami, and it was an amazing time there, but I really wanted to grow the prevention practice, and I got an offer to come to New York City and start really the country's first Alzheimer's prevention clinic. The dean of the medical school at Weill Cornell stopped everything in its track and said, 'oh no, I've got to meet this guy first, I'm not signing this, what the heck is an Alzheimer's prevention clinic?' And I met her, I explained the story, explained the concept, and she let me start it. Since 2013—this is going into our fifth year—we've had this clinic.

We're trying to help people really before symptoms develop. Alzheimer's begins in the brain decades before the first symptom. Okay? And to me, that leaves ample time to make brain-healthy choices, to make specific targeted recommendations on that person's modifiable risk.

Now, we've seen hundreds of patients—Karen, you've just been a true champion—and what we do is, we do research. Because I don't think that it's appropriate in this day and age to say, 'okay we're going to start a clinic, and we're going to treat patients for prevention, and we're going to try to prevent Alzheimer's.' Well, that's fine, but if you have a research component, if you follow metrics, if you follow blood tests, if you follow cognitive function, if you follow all these things over time, to evaluate the effectiveness of the evidence that you're trying to apply in terms of risk reduction, that's when we're going to truly have answers and really that's what we're trying to prove.

So, over the last five years, it's been quite a ride. Sometimes I say, it's difficult—sometimes it's like moving mountains. Other times it's like herding cats, and sometimes it's like doing both at the same

time. Alzheimer's prevention is not simple. There is no magic pill. There's no magic blueberry you can eat. It's just not that way.

As Karen will tell you, we give pages and pages of typed out recommendations for each person. This is confusing, because, you know, when you have high blood pressure, it's 'eat less salt, exercise, and take this blood pressure pill.' With Alzheimer's prevention, this is the brain, and the brain is so complicated, and we really have to figure out why that person may be at risk. These are called modifiable risk factors. Whether it's improper diet, whether it's having high blood sugar, whether it's not exercising much, whether it's having an Alzheimer's-related gene—and genes are not your destiny; you can win the tug of war with your genes—and we take all of this information together. The term here is precision medicine. Precision medicine means we're going to treat the person as that person. We're not going to say, okay, do this, do that, everyone do the same thing. Doesn't work that way.

I really believe that different people can take different roads to Alzheimer's disease. What I mean by that is: At the end of the road, it's the bad protein called amyloid, it's memory loss, the brain shrinks that's Alzheimer's disease at the end of the road. But what about the roads to get there? As an example, men and women may be on different roads. There are different roads, and maybe women, unfortunately, maybe they're sitting in the express lane. This is the one time when you'd rather be sitting in traffic, on your way to Alzheimer's disease. But whether it's because of the gender itself, whether it's because of the menopause transition, whether it's because of some other hormonal factor, these are the types of things that are intriguing and that we are trying to study today. What we do is, we try to figure out which road a man or woman could possibly be on to Alzheimer's and intervene. And it's not just one thing, not just two things—it's pages and pages. Then what we do is, we follow people over time, we refine or fine tune our intervention, and then we try to study the effectiveness of our approach.

I want to just mention one more thing, and then I'm really excited to take questions and have an interactive program, but I want to mention a study that came out just two days ago. If you follow the news or follow the Alzheimer's space and if you're Googling stuff and trying to learn and stay abreast of the latest and greatest, you may realize that basically every week there's something new, something

exciting. Last week it was: maybe too much salt in the diet can fast forward to Alzheimer's. Two weeks before that, oh, maybe a diabetes drug could put the brakes to Alzheimer's. This is all exciting stuff.

This week, there was a study published in *JAMA Neurology*. *JAMA Neurology (Journal of the American Medical Association)* is an extremely good journal, one of the best out there clinically. I know the editors, I know the team, and they're tough cookies when it comes to getting these articles accepted.

Two years ago, *JAMA Neurology* published a report on something called the FINGER study. And if you don't know what the FINGER study is, it was the first ever randomized trial, where they randomized two different groups of people, about 1,000 people. Half the people did multimodal interventions: they exercised, they ate a brain-healthy diet, they had personalized care by a doctor or nurse practitioner every three to six months, they did cognitively stimulating activities, they watched their blood pressure, and they watched their blood sugar. The rest of the group, they were randomized to kind of a sham intervention, where they just had discussion groups or whatever. That study, after two years, showed that multimodal lifestyle interventions, under the guidance of a clinician, absolutely slammed on the brakes of cognitive decline. That study was published two years ago.

Well, this year, just this week, *JAMA Neurology* showed that whether you have the APOE-4 gene, which increases your risk for Alzheimer's, or if you don't have that gene, both groups would respond to multimodal interventions. Now that's really good news. What's even better news is that people with that APOE-4 gene tended to respond preferentially well to lifestyle interventions. So there's lots of people out there who say, oh, there's nothing I can do, or oh, I have a gene, or oh this, or oh that. Genes are not our destinies. We can win the tug of war against our genes.

One in three cases of Alzheimer's may be preventable if that person does everything right. That's the good news. However, two out of three cases may not be preventable. But what if we can delay it by six months, a year, two years, or five years? And in that time period, that blockbuster drug comes? Well then, through lifestyle and other changes, that person has effectively prevented their own Alzheimer's disease.

The other issue here is that certain people can do everything right and still get Alzheimer's, and I hear this time and time again. Well, maybe that person had a gene that lifestyle couldn't overcome. Maybe lifestyle tried, and maybe it was delayed by six months, a year or two years, but unfortunately certain genes you can't win the tug of war against today, in 2018.

So the take-home point about all of this is that I really think that today and really in future years—the next several years are going to be really exciting. There's just so much a person can do. Know your numbers, don't be fearful, and learn everything you can—knowledge is power. For people that want to go to an Alzheimer's prevention clinic, there's only a few in the country, and we can talk about those.

Really, anyone that wants to learn the state of the art information: Everything that we learn in our clinic, we literally translate within a few week or a few months and put it on our absolutely-100 percent-free educational website. That website was mentioned before. It's called Alzheimer's Universe. The website is located at AlzU.org. It's totally free. It's like the Facebook saying: it's free and will always be free. It's a 10-lesson course—there are activities to track brain activity and link you to research studies—and what this course has shown is that knowledge really is power. People that complete the course are more likely to join research studies, are more likely to change their behaviors, exercise more or eat a healthy diet. We're hopefully going to even have more exciting research results from the site soon. So with that, I will conclude, and I look forward to the rest of the discussion.

Brooks Kenny: Thank you so much, Dr. Isaacson. Before we go to the questions from the group, can you expand a little bit about these specific prevention steps that folks can take? You mentioned that it's multi-faceted, and you mentioned exercise and food. Can you expand on the other aspects of prevention that you encourage people to consider in terms of lifestyle?

Dr. Isaacson: Sure. The way that I look at risk reduction for Alzheimer's disease—and you can insert the word 'prevention' or 'risk reduction;' either one, in my opinion is okay—is the first part of this path is risk assessment. So, risk assessment and early intervention would be the most descriptive way to replace the words 'Alzheimer's prevention.' So, number one, you have to do a risk assessment. What are your risks? For example, you can't change your age. You can't change your genes. But you can change

the environment which interacts with your genes, and this word is called epigenetics, meaning the impact of one's environment on one's genetics.

So the first thing is: what are the risk factors? When it comes to risk factors, there are modifiable risk factors and non-modifiable—really important concept. I believe that's lesson two or three on Alzheimer's Universe. In brief, some of the most important risk factors for Alzheimer's are those that are modifiable:

Number one: exercise. Exercise on a regular basis *absolutely* can protect the brain, can reduce amyloid in the brain, in a variety of mouse studies. Exercise is absolutely one of the most powerful things in terms of modifiable risk. Now some people say, 'well, what do you mean by that? Do I walk every day for 20 minutes?' Well, yeah, at the bare minimum, walking 20 minutes a day, 140-something minutes a week, is a whole lot better than nothing at all, than leading a sedentary life. But the devil is in the details here. Exercising three to four times a week for at least 30 to 45 minutes each session absolutely will work better in my opinion, based on the evidence. The other part here is: each person probably needs a different exercise plan. If someone has a high amount of body fat, high body fat messes up a person's metabolism. When your metabolism gets messed up, your blood sugar goes up. When blood sugar goes up, insulin goes up. When insulin goes up, inflammation happens in the brain, and it's like pressing the fast-forward button on amyloid deposition in your brain's cells. So there's a lot of connections here. If you have, say, someone with a belly that's been getting bigger and bigger over time, the larger the belly, the smaller the hippocampus, or the smaller the memory center in the brain. Someone with a big belly may want to try to reduce belly fat, and a great way to do that is exercise that's a little bit more vigorous. Cardiovascular and high-intensity interval training—that's something that I recommend quite a bit. If you haven't learned about it, definitely look it up. There's also advanced content on the Alzheimer's Universe website that goes into extreme detail about all this stuff.

If someone has low muscle mass, well then, maybe the person needs to do something a little different: weight training, resistance training, trying to build muscle—super important. If you only focus on fat burning and you don't build muscle, you know, your metabolism won't be supported over time. So the key here is cardiovascular, resistance training as well as stretching, yoga, walking, and not leading a sedentary life. Those are some of the key points, and I really do believe that these activities need to be

personalized. The more you exercise—you've got to do a solid three, four times a week. Otherwise, you're just not getting as much of a benefit.

When it comes to dietary patterns, there's no, like I said before, magic blueberry that you can eat to prevent Alzheimer's. It doesn't work that way, but if you have to choose one dietary pattern, the Mediterranean-style diet I think is really the most evidence based. Also something called the MIND diet that you can learn about also on that website and elsewhere. When it comes to the Mediterranean-style diet, we really think about plant-derived foods and fruit as the primary source of carbohydrates; olive oil, extra virgin, as the primary source of fat; fish and lean poultry, that's the best source of protein, and less amounts of red meat; low fat yogurt is probably okay, maybe you don't have to go too high, especially full fat dairy products; and wine in moderation, maybe a drink or so per week on average. And is red wine better, is other alcohol better? It's hard to say—again, everything in moderation.

When it comes to other interventions, you know, I could do a whole talk on this, but keeping the brain active, cognitive engagement, learning something new, and lifelong musical experience delay cognitive decline. Learning a new language can build up backup pathways. Really focus on sleep, making sure to get a minimum of a solid seven hours or so—seven and a half is probably better. Reduce stress—lots of deep breaths, mindfulness-based stress reduction—is one evidence-based structured way that a person can really protect brain aging over time. And super-duper important: cardiovascular risk factor modification.

Having high blood pressure, smoking, high cholesterol, or diabetes—those are terrific ways to press the fast-forward button to Alzheimer's disease. High blood pressure and high cholesterol doesn't cause Alzheimer's. It just presses the fast-forward button towards it. Diabetes can double your risk of having Alzheimer's, and diabetes is mostly a lifestyle disease, certainly in certain people genetics are a major cause. You know, changing your diet, lowering the carbs, exercising on a regular basis, intermittent fasting, eating less food overall—lower caloric intake, less than 2100 calories a day—can cut your risk of mild cognitive impairment in half. People that fast intermittently, for example, say they wait 12 to 14 hours several nights a week between dinner and breakfast—that's a great way to press the brakes to aging in the brain. So, hopefully that's a quick overview. Again, I could probably talk for another hour just on that topic, but these are some of the basic tenets.

Brooks Kenny: And I could listen to you for hours on this topic. That was such a great summary, and we're so grateful for it, because you really have an amazing ability to simplify it and to provide those visuals. I think the fast-forward button perspective is really valuable for people to take away with them. And for those of you who are frantically writing down every word that Dr. Isaacson said, not to worry. This is being recorded, and we will make the recording available to everyone on the line, and anyone that registered.

We are going to go ahead and open the lines for questions. Just a reminder that, if you have a question, please press *3 on your phone at any time, and by doing that, you'll be placed in our question queue. Have your question ready to briefly share with our staff. If you're listening online, you can type your question directly in the box, and we'll get to as many as possible.

So, Dr. Isaacson, we had a couple of questions related to women and hormonal changes. Janet from Connecticut asks: Could hormonal changes during menopause be a trigger for brain changes? And Patrick from Georgia asks if the disparity of Alzheimer's in women is related to menopause. So we'd love to hear your latest thinking on those questions.

Dr. Isaacson: Yeah, well, this is—how do I put it—I'm shocked and humbled that the answer to this question has actually been clarified by some of the research we published just a few months ago. When I was in medical school, not that long ago—okay, kind of a long time ago, actually—when I was in medical school 20-ish years ago, there were no treatments for Alzheimer's, and now there are some treatments, and we can at least talk about prevention. When I was in medical school, I learned that more women had Alzheimer's because they live longer than men. Then as I've gone through my career, I just didn't think it was that simple. There's something else about the female aging brain that just—I don't know, my gut—doctors oftentimes trust their gut—I just saw different women age at different rates once they hit the menopausal period. I guess, what some of the past research showed is that menopause causes metabolic changes in the brain. And what our group showed—this is led by Dr. Lisa Mosconi; she's just amazing; we recruited her from NYU a couple of years ago—is that these metabolic changes in the brain, in the perimenopausal period and menopausal period, actually increase the risk of Alzheimer's disease. What this means is really—could this help us solve this longstanding mystery that's

surrounding Alzheimer's: why do women get it more often? Two out of three people with Alzheimer's are women. What I'd also like to come out of this is: can we figure out a screening test?

So Karen has graciously volunteered to be in this exciting work, and what we're going to be doing is: we just got some NIH funding—it's a little bit of funding—we have enough funding for 19 women a year for the next four years, so making progress. I'd like to do 300 or 500 women, but we'll get there in time, I guess. What our goal is, is to try to do brain imaging on women even starting in their forties and then follow them over time, from their forties to sixty-five, and try to find out, what is the very first change in the brain—metabolic change in the brain—that may signal that Alzheimer's is beginning.

What we've found so far is that when a woman is premenopausal, the brain looks pretty good; brain metabolism related to Alzheimer-specific areas looks good. When a woman starts becoming perimenopausal—menopause symptoms are just starting—well, guess what? Those women are much more likely to have metabolism changes in the brain similar to metabolism changes in Alzheimer's. Then as the woman progresses through postmenopausal stages, that's when actually the brain metabolism goes down much more and looks even more closely like Alzheimer's.

What if we can detect these changes? What if we have a 45-year-old woman where we can see these changes in the brain? Well, maybe we need to give that woman a therapy. There are studies going on with one of our colleagues, Dr. Roberta Brinton—there's a study of pregnenolone. Maybe that hormone analog can delay or prevent the changes and protect the brain. Maybe certain women should be on hormones during the perimenopausal time to protect brain health. Conventional wisdom says five to seven years, 10 years, may be protective, but maybe longer than 10 years can cause harm. Using these innovative approaches, looking at women at 40 onward and figuring this out, I think is really the next frontier when it comes to Alzheimer's prevention.

Brooks Kenny: Great, thank you, that's really insightful and breaks it down in very understandable ways, so thank you for that. We actually have a live question from Sharon in Charleston, South Carolina. So Sharon, you are live for your question to Dr. Isaacson.

Caller: Yes, thank you, Dr. Isaacson. I've been reading recently that anxiety and insomnia may be precursors to Alzheimer's, and I'm wondering if the medications used to address anxiety and insomnia might be detrimental for a person who has pre-clinical Alzheimer's.

Dr. Isaacson: Thanks so much, Sharon. That is a really, really timely question, important question because brand-new research has really been trying to figure this exact question out. So, let's rewind again, back to when I was in med school. In medical school I was taught that anxiety and depression are risk factors for Alzheimer's, and I think that's correct, I think that's still correct today. But what we've really tried to figure out is: is it a risk factor—meaning, having depression increases your risk later because it's a causative effect; it causes the fast-forwarding of Alzheimer's pathology—or is it just a pre-memory loss symptom, a non-cognitive symptom or a psychiatric symptom that is part of Alzheimer's disease itself? Teasing these things out gets very complicated.

As you said also: is insomnia a risk factor for Alzheimer's? Sure. But does it cause Alzheimer's? We don't know. Is it actually a precursor to Alzheimer's that is a part of the disease before memory loss symptoms begin? This is something that science needs to do a little better job with. We're actually looking at this. We have these biosensor devices that we've given to patients; they are like wrist sensors, and we track their sleep. We're actually trying to figure out: do sleep patterns correlate with cognitive function and amyloid in the brain? I think, by using innovative technology approaches like these, we'll be able to figure this out better. I would say the answer to your question is that anxiety and depression and insomnia are definitely related to Alzheimer's in some way. I think it makes sense for us to treat these things in an effort to reduce risk, but I don't know that we have complete proof that treating these symptoms, these conditions, will protect the brain. What I would say is, that in mice, when you treat depression for example with a serotonin medicine like an SSRI—selective serotonin reuptake inhibitor—common antidepressants like Zoloft and Lexapro and Citalopram—they may have a hint of some protective benefits.

Now, again, this is not proven, and there's no FDA approval for any of these drugs for any treatment of Alzheimer's or for Alzheimer's prevention, but there are some exciting studies going on, starting soon, using Escitalopram or Lexapro to see if that can treat some of the behavioral manifestations of Alzheimer's. I think that study may end up being positive.

When it comes to insomnia, more sleep is better. Getting to the root cause, whether it's sleep hygiene techniques—not using a screen device before bed, closing the window shade when you go to sleep, the room being a good temperature and only for sleeping, no television, nothing in the room to stimulate you, no caffeine after one or two o'clock in the afternoon—sleep hygiene is probably the best way that we can treat sleep issues in a safe way. Like you said, I don't really love those sleep medicines—the Tylenol PM, the Benadryl, the benzodiazepines, Valium, and Klonopin, and Ativan, even Ambien. I don't know—less is more when it comes to these things. That's the Band-Aid approach where you take a pill, to fall asleep, but you're not targeting the underlying sleep problems. Again, it comes back to this situation of precision medicine. Target the underlying problem. Don't throw Band-Aids on this disease. So great question, and hopefully I answered your question as best as I could.

Brooks Kenny: Great. Thank you so much, Dr. Isaacson, and thank you, Sharon, for asking the question. Just a reminder, if you have a question for either Dr. Isaacson or Karen Segal, you can press *3 on your phone. Staying in the vein of prevention and modifiable risk factors, Lila has asked a question related to alcohol, wanting to understand the interaction of alcoholism and Alzheimer's and whether the risks of developing the disease are higher among alcoholics.

Dr. Isaacson: Okay, well, Karen drinks more wine than I do. Sorry, Karen.

[laughter]

Karen Segal: But I drink a lot of water, too, all day long, eight glasses of water.

Dr. Isaacson: Well you drink more water than me, too, so maybe we're even. I'd love to defer this question to Karen, but in brief I don't know that I'm a hundred percent sure about this answer. I do know that people that drink too much and have alcoholism and alcohol abuse certainly have poorer brain outcomes and smaller brains and cognitive dysfunction. Does that—here's that term again—fast-forward towards Alzheimer's? I would hazard a guess to say yes. I don't know a hundred percent for sure, but I would say the data suggests yes. I think there may be a sweet spot for alcohol, but it may depend on the person, I don't know if it's one serving a day, possibly two in some people. I try to hedge a little bit on the lower side—seven servings a week, maybe seven to 10; 10 to 12 in men, four to seven

in women. Other studies, this one big study in the UK or in Europe showed that actually zero servings of alcohol may be better. So I would say more evidence suggests low to moderate alcohol consumption—meaning one in women, two servings a day maximum in men--may have some protective effects, but I don't think we have all the answers. I think the reason here again: precision medicine. Different people with different genes respond differently to different interventions. That includes alcohol, pills, supplements and whatever else.

Brooks Kenny: Great, thank you. I want an invitation to that glass of wine for both of you, enjoying that. No, thanks for that answer. We have a question in from Laura, Karen, to you. What has your experience been like, being involved in this study, and were there any challenges to getting started?

Karen Segal: There was no question in my mind that, as I go and visit my mom every single month in the nursing home in Los Angeles, that I didn't—I can't reverse her condition, but I had control over my own condition. For me, it was—I wanted to have myself genetically tested, and I wanted to know what I could do to modify my risk. I am a fierce advocate for people participating in clinical trials, but generally they're looking for quite a bit older than I am, and I don't qualify for many of the trials. So I actually sought out Dr. Isaacson because he was studying women 40 to 65, and I really wanted to be able to track my brain health over the next decade. We don't know what, by tracking me, we might be able to identify when there is a change or how. The good thing about Dr. Isaacson is he—I'm very disciplined with my diet, with exercise, and with my lifestyle—but he's fine-tuned that even more for me. I feel like for me, I don't know why I *wouldn't* do it. It's not for sure that it's going to take away the genes that I have or reverse them, but if I can delay it until there is a modifying treatment, you know, I'm up for it. I don't want to sit, as I said before, I don't want to sit and watch. I want to drive that bus; I don't want to be chasing the bus. So that's why I've been involved. I realize that not everyone—I live in Chicago and I go to New York—not everyone can do that. But at the same time, there are doctors in different communities, and if you go online you can find a doctor who can do cognitive testing, blood work, and a brain scan for you in your community.

Brooks Kenny: That's a really great point and it's a nice segue to a question for Dr. Isaacson. You mentioned earlier in your remarks that changes in the brain can happen 20 or 30 years before symptoms appear, but, as Karen just said, many of the trials are not taking people in their forties. Do

you have a sense of how that might be changing, or what women listening to this call who are in their forties might do, beyond modifying their own risk, to get engaged in clinical research?

Dr. Isaacson: Well, this is tricky. We were the first program, in 2013. Then the University of Alabama in Birmingham opened up, not a prevention clinic, but here are the words: a risk assessment and early intervention clinic. That's a little bit more PC in some circles. They started their clinic in 2014— We take insurance, and we lose a lot of money because we don't get a lot of reimbursement. I lose a ton of money clinically, and if it wasn't for philanthropy, and if it wasn't for research grants, we couldn't have a clinic like ours because we lose a lot of money. We spend so much time with patients. —What the folks in Alabama did is, I believe they charge a fee, like maybe $1,000 or something—don't quote me on that—but that's one way they've been able to make ends meet when it comes to the finances of this.

In 2015, a program started at Cedars-Sinai in Los Angeles, but the founders of that clinic, Drs. Dean and Ayesha Sherzai, actually moved their clinic to Loma Linda University Medical Center in California.

The year after that, we opened up a satellite clinic in Puerto Rico, in San Juan—an amazing opportunity. We really branched out. Everything was going great. We had 106 patients enrolled, and then the hurricane hit, and it has been a terrible, terrible, terrible several months. Unfortunately the clinic does still not have power—unbelievable.

Those are the main clinics. There is another brain health clinic. It doesn't use the term Alzheimer's prevention, but they do focus on brain health. That's at, I believe, North Shore Medical Center in Chicago. There is something called the Cognitive Cardiology Clinic at Rush University Heart Center for Women, and there's a neurologist who works there. There's another program that's starting at Florida Atlantic University in Boca Raton, Florida, by an old and close colleague of mine, Jim Galvin. These are the ones that are most on the radar.

I've had visitors to our clinic—literally every few weeks, I've had people from Barcelona, from China, from Brazil, from different parts of the country. I think in a few years this will change, but for now, aside from going to Alzheimer's Universe and taking the full course, which literally has a ton of information like I've been talking about today—you know, starting a conversation, going to the primary care doctor

and say, 'I'm learning about brain health, and I heard there's things you can do; I took this course online; what do you think?' Eight out of 10 will say you can't prevent Alzheimer's, but two out of 10 may say, yeah, I heard about that, too.

On Alzheimer's Universe, there's also a health care provider course, a free course for physicians. It's over two and a half hours now of content—again, all free, different lessons. There's actually a live patient on there that let me record her entire visit. We do lessons, we have all the journal articles there, and hopefully next week we're going to get accreditation, CME accreditation, so doctors can get licensure credit for taking the course. So if your doctor is interested, tell them to take the course, not because I'm trying to get more people to take the course, but so they can help their patients. We actually have just over 1,200 health care providers who have joined Alzheimer's Universe, and that's a whole lot better than zero. But there's hundreds of thousands of health care providers out there. So I don't think we're there yet. And if a person tries to go to a neurologist for Alzheimer's prevention, good luck. It's just not there yet in most physician practices.

There's also a specialty of medicine called Lifestyle Medicine. There are preventative health doctors—I actually did a fellowship in preventative health—these are physicians that spend more time with patients because you can't do this in 10 minutes per patient. You need a solid 45 minutes or an hour per patient. We spend an hour and a half for new patients, an hour for follow-ups, so . . . Sorry, that was a long answer, but that's where the state of the science is, and hopefully five years from now, we'll have 10 or 12 or 15 Alzheimer's prevention clinics. We're just not there yet.

Brooks Kenny: Wow, no. But you certainly are a disrupter in this space, and you're really paving the way for other clinics to follow. So as a woman and as an advocate on behalf of the women on the line, we thank you for that because you're really pushing the envelope, and it's very, very exciting to see. One of the things we talk a lot about at WomenAgainstAlzheimer's is having courageous conversations—courageous conversations with our providers, asking the tough questions even if it's not being asked by them, having conversations with our family members and in our communities. So we're really grateful for that perspective.

We have a couple questions that are overlapping that I wanted to highlight while we have you. One is from Carsten, related to vitamins. Are there certain vitamins, like B12, or other supplements like turmeric that are proving more effective than others as it relates to brain health? And then a follow-up question related to caffeine and wanting to understand the impact there. I think it's interesting, the nature of a lot of the questions that are coming in—and they keep rolling in, so, thank you, for those of you on the line—a lot of them are related to these modifiable lifestyle behaviors. People seem to be fairly enthusiastic to understand which ones they can control. So can you speak a bit to vitamins and to caffeine, if you would?

Dr. Isaacson: Sure. I'm not a one-size-fits-all kind of person because the reason studies have failed in the past is they've put 1,000 people who are very heterogeneous, meaning they're very different, and they put everyone on the same B vitamin or omega-3 fatty acid or curcumin or whatever else, and then they look at the results and it doesn't work, so people say, 'this stuff doesn't work.' The confusing part here is, with all of these supplements and vitamins, depending on your genetics, depending on your blood test results, and depending on other factors, they may or may not preferentially work or not work. So that's the qualifier I'd like to start with.

We'll talk about B vitamins. I am a very big advocate for B-complex vitamins, including folic acid, B12, and B6. Wait, pause, hold on. I'm a big advocate, but I don't mean to everybody. There's a blood marker called homocysteine. Homocysteine is an amino acid that can be checked in the blood. If someone's over the age of 50, maybe 55, maybe older—we don't really know, depends on each person—and their homocysteine is high, then B-complex vitamins have been shown to delay brain shrinkage and improve cognitive function. In people that didn't have the high homocysteine, it didn't work. So: precision medicine.

The other part of this is that people that had the B vitamins and it worked, also had optimized omega-3 fatty acids levels in the blood. So, you also have to have regular intake of fatty fish—like lake trout, mackerel, herring, albacore tuna, sardines, wild salmon specifically—at least once or twice a week, preferably twice, and/or you may need to take an omega-3 fatty acid supplement. Oops, here we go again. Supplements, Omega-3s: Better from food, but some people need them—depends on your blood level. Depends on what your cholesterol is. Confusing stuff. Depends on which omega-3s. There's DHA,

there's EPA, there's ALA. ALA doesn't seem to help much with brain health, but DHA and EPA probably do. What amount, what type, from algae, from fish, from this, from that? Super confusing stuff. This is summarized on Alzheimer's Universe but, super confusing stuff.

Vitamin D: doesn't have super strong evidence, but if you're low, take that Vitamin D or get some sun. Do whatever you need to do.

Caffeine: no issues there. Everyone should probably be drinking caffeinated coffee, one to three servings a day. In the morning is probably okay. Caffeinated coffee probably has the best benefit as long as there are no issues with sleep, or heart, or blah blah blah.

Curcumin: there was a tremendous study done by Gary Small and colleagues that showed that a specific type of curcumin called Theracurmin—and that's the problem here: 10, 20 different types of curcumin imported from different people in different doses. Just so you guys are aware, I have no disclosures. I have nothing to disclose. I don't work for the fish oil companies. I don't take money from any of these. I have no commercial (I wish I did; I could pay my student loans back), no biases to disclose. But curcumin probably works. I know a cardiologist that actually imports it from Japan and bottles it up himself because he knows it's going to work for his patients, and that's the one I buy. So these are the tricky things. The devil is in the details. It's complicated.

Brooks Kenny: For sure. And you know, there's a lot there that gives us reason to be so optimistic with so many things that we can do in our own lifestyles, and simultaneously, I think it underscores the need for more awareness in the provider community as well as with consumers around these opportunities. Because precision medicine, taking that to scale—a lot more research dollars are needed to ensure that everyone has access to that information and to those opportunities. I know we only have just a moment or two left with you, Dr. Isaacson, so I did want to ask: We had a lot of questions about people getting diagnosed and assessed, and I know it's a big topic, but if you could leave the listeners on the line with any advice on how they may address questions with their provider—whether it's their primary care provider, their OB—the worried well, those of us that are maybe noticing some changes or feeling concerned, and are looking for some support, they're not going to a neurologist but they're going to their regular doctor, any advice for those folks?

Dr. Isaacson: If someone is realizing that something is changing, or there's been a change in any way shape or form, don't delay. Don't be fearful. Whatever it is that's holding you back, whatever it is, if you're noticing something in your family and say 'that's just normal aging,' just take a deep breath. I empathize. I understand a person may be scared or worried but, not today. Today we can actually do something. And the earlier you intervene, the more effective the interventions are. Join a clinical trial. There are Alzheimer's prevention clinical trials going on right now for people above the age of 60. There are doctors out there, primary care doctors, that can at least have a conversation with you about your blood pressure, blood sugar, cholesterol. You can talk to them about exercise. You can see a nutritionist. Start the conversation. Whatever it is, don't be fearful. Go take a course online. Go read a book. Go do something. Anything is better than nothing, and grabbing the bull by the horns today—not tomorrow, today—making an incremental change literally today, an incremental small change in your eating, in your exercise, taking the stairs instead of the elevator, or getting a stand-up desk instead of sitting down all day for eight hours. Whatever those incremental changes are, one plus one equals three, okay? Karen, you're better than me at math.

Karen Segal: I'm going to interject here. Here's the deal. What I started saying at the beginning was my dad, who was a doctor, denied that my mother had Alzheimer's and hid it under the rug and kept the family, kept it away from all of her friends. I am not doing that. I am going to do everything I can, proactively. And I encourage everyone to be proactive because the first person cured of Alzheimer's is going to be in a clinical trial. So if your loved one, if you're noticing signs, sign them up, get them involved in a clinical trial. They might be the first person cured.

Brooks Kenny: Thank you so much. I think we will end it there, with my deep thanks to both Dr. Isaacson and to you, Karen, for joining us today. I can say I'm so personally inspired by both of you. Your tenacity and your passion and your commitment to this fight are really inspiring to all of us. Thank you so much for sharing your expertise with us today.

To those of you on the line, I really hope this conversation was as fascinating to you as it was for me. I do apologize that some of the questions we couldn't get to or that we needed to combine some of them. We simply ran out of time. As Dr. Isaacson said, I think we could spend hours on many of these topics individually.

Again, I do want to encourage you to visit the AlzU website, www.alzu.org, for information. There's great content along the lines of what Dr. Isaacson has shared with us today. Additionally, if you've not already joined USAgainstAlzheimer's, please go ahead and visit our website, it's UsAgainstAlzheimers.org. You can sign up to receive our regular updates. We have a monthly update that comes out. We have a daily roundup of news that we distribute. We also can give you access to information about clinical research and about the work we do in various communities, for women, for African American populations, for Latino populations. We have a clergy network. There's just a lot happening at USAgainstAlzheimer's, so we welcome your review of that website and your questions moving forward.

I really want to thank everyone on the phone or online who participated in this talk today. In about a week or two, we'll have a copy of this recording and a transcript on our website for you, and we encourage you to share this with your friends. If you're looking for one thing to do after this call, don't delete the email when it comes your way. Let it land in your inbox, and take a moment and forward it to 10 of your friends. Let them know you were part of this conversation. Maybe they'll listen to it as well, and we can continue to have these courageous conversations.

Please stay on the line if you want to leave us a message. We're particularly interested in your feedback about the call or any ideas you have for upcoming calls. We're really here to serve you, our community, and we welcome your feedback on an ongoing basis.

So with that I'm going to sign off and just thank each and every one of you for joining us today, and I wish you a very good afternoon.