Alzheimer's Talks
What if we could stop Alzheimer's before symptoms begin?
A conversation with Dr. Reisa Sperling
March 15, 2013

George Vradenburg: Welcome to Alzheimer's Talks on this sunny, here in Washington, Friday afternoon, presented by USAgainstAlzheimer's.

Today's call is a discussion with Dr. Reisa Sperling of Harvard, more about Reisa in just a second. My name is George Vradenburg, chairman and co-founder of USAgainstAlzheimer's and I, as many of you know who've been on these calls before, am engaged in this effort with my wife and friends and now thousands and thousands of individuals who have been touched by this disease. In my case, my wife Trish, her mother died of Alzheimer's about 20 years ago and once you've seen it you do not want to have anyone experience it. So thank you very much for joining. This is a teleconference series by USAgainstAlzheimer's - Alzheimer's talks. Today's call is generously sponsored by Jill Lesser who's a board member of USAgainstAlzheimer's Network our C3 compatriot.

So today's call is with Dr. Reisa Sperling. Dr. Sperling is Director of the Center for Alzheimer's Research and Treatment and Director of the Education and Information Transfer Core at Massachusetts Alzheimer's Disease Research Center. She's also co-leader of the neuroimaging program at Massachusetts Alzheimer's Disease Research Center and also Professor of neurology at Harvard Medical School, clearly an under-achiever!

Today she will be discussing with us her ground breaking new study, that she will be commencing in the near future, on individuals whose brain scans show build-ups of beta amyloid plaque but who do not yet demonstrate clinical symptoms of Alzheimer's or other dementias and you will understand from her why working in this particular population is so important. She will be testing the effectiveness of Eli Lilly drug solanezumab which in previous studies has shown might have promise with people that have a mild stage of Alzheimer's.

If you have a question during the call, please press star 3 on your phone. By pressing star 3, you'll be placed into the question queue. Please have your question ready to share briefly with a member of our staff and when we open this up to questions in a few minutes they will get you on the call live as soon as possible. When you press star 3, you will not lose connection with the call. You'll still be on the call even though you will be on our question queue.

With that, I'd like to have Dr. Reisa Sperling of Harvard. Reisa, thank you so very much for joining us today and spending sometime with an audience that is both large and clearly quite interested in your research and so we'd love to hear a bit about your research.

Dr. Reisa Sperling: Well thank you so much George for having me and thanks to all of you on the line who are willing to spend your Friday afternoon this way. It's really encouraging so much interest is developing on Alzheimer's disease.

I've been working in the field of Alzheimer's disease for almost 20 years and although we've had some setbacks and we had some continuing challenges, I have to say I'm feeling very hopeful right now that we are about to get some important answers at least telling us whether we're on the right track or not. So as George mentioned, I am very fortunate to be leading a new effort which is a new type of a prevention trial in which we're trying to find older individuals who are at high risk for developing symptoms of Alzheimer's disease but are still clinically normal. And the reason this is so important is because we know that older individuals unfortunately are at high risk for Alzheimer's disease as they age and getting older remains the greatest risk factor for Alzheimer's disease.

As we've done a lot of research over the past decade, we found that there are markers. We call them biomarkers or imaging markers using PET scans or MRI's, which I'll tell you a little bit more about in a moment, that can identify evidence of the process of Alzheimer's disease. As George told you, the build up of these amyloid plaques that begin in the brain before people have symptoms at all.

So let me just start by telling you a kind of parallel story that happened in heart disease about 30 years ago where people discovered that there was cholesterol plaques that started to build up in the heart and these are very different in the amyloid plaques that occur in the brain. But my understanding is they had lots of discussion and even what they called the cholesterol wars because they weren't sure about what was good cholesterol or bad cholesterol and because when they tried to lower cholesterol at first in people who already had very severe heart disease, they didn't have much success. But they stepped back and they said, well, let's test a cholesterol lowering agent, statins, many of you have probably heard about these drugs in people who have a rare familial form of high cholesterol and also in people who are at high risk for having a heart attack because they've had a little bit of heart symptoms or at risk for stroke because of having a TIA. And although cholesterol was not the only cause of heart disease, by lowering cholesterol and treating people before they have symptoms, we've already decreased death and illness due to heart disease by about 28% in this country and the hope is that we could do the same thing if we could identify people who have evidence of Alzheimer's disease pathology beginning in their brains before they have symptoms. Just like we treat heart disease before people have symptoms. In effect, almost every other disease known to man where we really made a dent such as cancer or diabetes or osteoporosis, we've done it because we treat people before symptoms.

So the advances I'd like to tell you a little bit about in our trial are the ability now to detect evidence of early Alzheimer's pathology or these plaques building up in the brain. Again 10 and maybe even 20 years before people get symptoms and we can do that now by using PET scans. These are scanners that we often use that are in hospitals for many other reasons. But with a special dye that can pickup the plaques that we used to only be able to see under the microscope but now can see with PET scans. We can also see evidence of amyloid build up using spinal fluid tests as well and both of these suggest again that the amyloid build up begins 10 or 20 years before people develop symptoms. We don't know yet whether amyloid is really the cause of Alzheimer's disease. It might only be one factor. But if it's enough of a factor that we could prevent the symptoms to begin with, prevent people from ever getting to the stage of dementia, I think we'd have a much better shot at really defeating this disease.

Unfortunately by the time people have what we call dementia due to Alzheimer's disease and I suspect this is what many of you who have a personal relationship with someone who's been affected by Alzheimer's disease have seen. At that point in the disease, people really have very significant trouble. They've lost a lot of nerve cells and I think it may be much more difficult with even very powerful drugs at least in isolation to be able to really rescue the brain at that stage. So again, just like with heart

disease and cancer, we've got to go much earlier and try to treat people early on. This trial we call the A4 trial, the anti-amyloid treatment in asymptomatic Alzheimer's disease, that was a mouthful so we came up with this short term nickname called A4. And again we'll find people over the age of 70 who have evidence of amyloid building up in their brain but don't yet have any symptoms and we will do a 3 year trial with this antibody that George mentioned to you solanezumab.

This trial will be a very large trial. A thousand participants who are amyloid positive which means we think we have to screen about 5000 people to find the perfect folks for our study. And this will be done across the United States and hopefully also in some other countries including Australia. This trial again will be 3 years long and the main outcome is really to see whether we can slow the rate of very subtle memory trouble that starts maybe 5 or 10 years before the stage of Alzheimer's dementia. So we're not looking to at this point, prevent dementia altogether that will probably be a 10-year trial. But just to slow the rate of this very, very early decline.

The A4 trial will also run in parallel with two very important prevention studies that are also starting this year in people who are normal but are at risk for Alzheimer's disease on the basis of genetic risk factors. There are these rare forms of what we call, autosomal dominant Alzheimer's disease and that just means that if you have one of these rare genetic mutations, unfortunately you will get Alzheimer's disease with nearly a 100% certainty and often by age 40 or 50. Again, these are very rare forms of Alzheimer's disease only occurring in 1 to 2% of all Alzheimer's cases but are so important to study because of the certainty that these individuals will develop Alzheimer's disease dementia.

So the A4 trial will be run in older people who have evidence of amyloid and will have a very similar design to these 2 trials in the genetic at risk population. One called the Alzheimer prevention initiative which will be run primarily in Columbia, South America because there's a very large family there who carries this rare mutation and another international trial called DIAN or Dominantly Inherited Alzheimer Network which looks at several different of these rare mutations around the world and these 3 studies, we've all gotten together and tried to collaborate. We have a collaboration for Alzheimer prevention so we can learn whether the drug affects in these rare autosomal dominant mutations are similar to the drug effects we observed in this much more common older population who's at risk because of amyloid buildup.

So it's a very exciting time in that all 3 of these trials will start this year. But it's also daunting because we really want to do our best and get the maximum amount of information possible. And one of the real bottlenecks in getting this research done is getting people who are willing to participate, volunteer for these trials as well as trials that are ongoing at the stage of mild cognitive impairment and Alzheimer's dementia. So if I do nothing else today, I hope to convince you to become activists, to consider participating in research. There are studies for everyone from people who are perfectly normal to people who are unfortunately are already affected by this disease and the way we're going to get the answers to whether the drugs we are testing are successful or not is by the generosity and dedication of families and people being willing to participate in this studies. That's how we won the war against cancer and that's how we will win the war against Alzheimer's disease.

So maybe I'll stop there George and then hopefully see if I can answer any of your questions and then any of those on the line.

George Vradenburg: Thank you very much Dr. Sperling and that’s very, very clear and very direct and I appreciate that.

A reminder for those on the line, if you have a question during the call please press star 3 on your phone. You'll be put into the queue and we'll get to your questions at a moment.

There are about a hundred questions submitted in advance and we looked at the categories of questions and actually, some of the questions that are coming up online very much fit into the categories of questions that have come on. So I'm going to actually ask someone on the line to ask the kind of question that I think I would have asked you Dr. Sperling. So I'm first going to go to Jeffrey Pierce who I think has a question that has been asked by a lot of people before and has to do really aside from the rare genetic mutation cases that you described, I think he wants to know what the relationship of genetics might be to Alzheimer's. So Mr. Pierce?

Question: Yes. I am a 58 year old male and my mother and almost every sibling, parent, grandparent, way down the line on her side has had Alzheimer's, dementia, type reasons for death and I have had 3 strokes in the last year and a half and I only have a slight speech impairment from it, I've recovered all the other problems that developed. But anyway, being 58, I'm wondering if I'm destined to have this right?

Dr. Sperling: Well, not necessarily. It does sound like you have a likely genetic risk factor on your mother's side. The good news is that you also got genes from your father and depending on which genes you inherited from each sometimes one can help protect against another. So may I ask, at what age was your mother and your mother's siblings did they develop symptoms of Alzheimer's disease? Was it in their 60's and 70's or younger?

Question: I know my mother... Physically she started in her late 50's and... slightly more for the next 10 years and now that she just turned 80, she is in...

Dr. Sperling: Really having difficulty...

Question: Yeah extreme stages dementia.

Dr. Sperling: Well so the genetics of Alzheimer's disease I will say we're still learning a lot about it. But these rare forms tend to affect people before age 50. That's not absolute so there are occasional families who have mutations that are these deterministic genes that can affect people in their 50's, and early 60's, but usually it's younger. The other major genetic risk factor though that you might have heard about is something called, Apolipoprotein E or ApoE4 and this isn't really a mutation in the same way it's a variant that there are 3 variants of this gene that we all carry and you get one copy from your mother, one from your father. The E4 gene does increase risk of getting Alzheimer's disease particularly getting it at a somewhat younger age. So one possibility is that on your mother's side of the family, they've got this ApoE4 gene which does increase the risk of Alzheimer's disease occurring in 60's, 70's and sometimes even into early 80's. Again the good news is you may have gotten an E3 or even an E2 from your father, the E2 is considered to be protective and the E3 is the most common gene. So I don't think you should consider that you are destined or doomed. The one thing I would say is you know, we don't at this point recommend genetic testing for people who aren't symptomatic because we don't fully understand what that risk means for people. They're still doing research on that. And the same things I would tell you even if you have this increased genetic risk from your mom, I would tell you to do anyway, which is to keep your heart healthy, keep your brain healthy which I know I'm sure you're trying to do to decrease the stroke risk. Stay engaged, active, exercise, do everything you can to keep your

brain healthy in any case. My hope is that by the time you really enter the age of risk so maybe a decade from now that we really will have made a dent in having treatments that slow the progression and maybe even prevent symptoms. So I'm keeping my fingers crossed that by the time you really need us, we will have made a real difference.

Question: Yeah I appreciate that and I want to thank you doctor for the information.
Dr. Sperling: No problem. Thanks for calling.

George Vradenburg: Thank you very much Mr. Pierce. And so I am going to move now to the environmental risk factors and bring in a question from Debb Clay in Huntington Beach, California. Ms. Clay, why don't you ask your question?

Question: Okay. My first question was already answered. My second one is, my mother... all my uncles and my aunts and my mother, all have died or are dying of Alzheimer's disease and their first cousin and they all grew up in a small town on Long Island in like one or two houses and they were surrounded by nurseries and they with all the pesticides and everything they weren't under control during the 20's, 30's in that area and they all swam in the canals, the run off and all the rest of the stuff, and genetic would be my mother, her brother and sister and all previous generations, they all lived to 98. But the first cousin also died of Alzheimer's and I was wondering, could there be some type of an environmental pesticide issue?

Dr. Sperling: Well that a very good question because we've always been on the lookout for environmental factors. So I just mentioned the genetics but we also know that people who have the same genetic background have increased or decreased likelihood of developing Alzheimer's dementia.

I will say though that most research so far has not shown a clear link with environmental factors other than maybe exercise and mid-life cholesterol. But not yet with pesticides or people have looked at aluminum or other things and these links really have not born out thus far. Pesticides have shown actually some linkage with Parkinson's disease. A different neurodegenerative disease so it's not crazy to keep looking for links with Alzheimer's disease but they haven't been shown so far.

The one other thing I should say is that Alzheimer's disease is very common. So it's 1 out of 8 individuals over the age of 65 or 70 and by the time you get over the age of 80 or 85, it's 1 in 3. So sometimes we see these, what you might think of as a cluster you're saying people all lived together in a small town but the question is, is it really more than you would expect by a group of people living into their 80's and that's why this research gets a little complicated because you've got to really say, well what would you expect with this group and is there more of a risk and could it be the pesticides or could it be other things that they might have in common such as diet or other things. So this is an important area of research that's still ongoing. We call it kind of the epidemiology of Alzheimer's disease. But I can say that we've looked for many, many factors and just don't have clear ones that explains these pockets as you've said is in your family.

Question: Very interesting. Thank you.

George Vradenburg: This question triggers a question that many, many people ask of me and that is whether there are non environmental or other things you can do to diminish your risk for Alzheimer's whether it’s diet, whether it’s exercise, whether it’s mental games, whether it’s social interactions. What

is your view and what is the evidence about the ability of these other activities, these lifestyle activities to diminish the risk of Alzheimer's?

Dr. Sperling: Right. So as you know, there's been a lot of work on this on the past 3 or 4 years and I would say it's been a bit controversial because again the evidence, I think there's some suggestive evidence but there's not enough hard evidence to say if you eat this or you do this you can really decrease the risk of Alzheimer's disease.
My own opinion is that the best evidence is around exercise, that both people who exercise in mid-life and in particular people to exercise into late life that does seem to confer some brain protection. That's probably not just against Alzheimer's disease but other forms of dementia. And I think this evidence, although again it's not absolute, I think it's growing and there are some good basic science data and neuroimaging data that suggest that exercising regularly, walking briskly but even doing more than just walking, can help convey some brain protection.

The diet I would say is a little more controversial. I think that there's evidence about the Mediterranean diet and you may have heard diets that are high in olive oil and beans and fish and not so much in meat and dairy, I think that data is promising. The problem is that there are other things that sort with Mediterranean diet such as genetics and exercise and other things that people who eat a hard healthy diet like that might also be doing. So it's hard to know whether the Mediterranean diet is everything. There's also been some very nice work recently about dark leafy vegetables and fruits especially dark fruits. So blueberries and pomegranate, blackberries and strawberries, they have these things in them that makes them so colorful that might have some seanols, some protective effects in the brain as well. So I do recommend that people eat a healthy well-balanced diet and I do recommend exercise. I also recommend a multivitamin once a day.

What I'm a little less keen on are the crossword puzzles and Sudoku and things where people are sitting at home doing lots of mental exercises because I don't think that data is as strong and I'd rather see people outside exercising, social interaction. So what I tell them to take up if they want to do something new is ballroom dancing because that combines exercise, social interaction as well.

George Vradenburg: Thank you. We have a couple questions here related to early onset Alzheimer's disease. So the first one is concerning research on that subject. So I'm going to go to Den Standard to ask her question. Deb?

Question: Hi. How are you?

George Vradenburg: Fine.

Question: I have... I've been diagnosed with early-onset Alzheimer's.

Dr. Sperling: How old are you?

Question: I'm at this stage, I'm 63.

Dr. Sperling: Okay.

Question: So I'm doing pretty well. I have you know some cognitive deficits. My memory is not too bad. But what I'm interested in it, I was wondering if there are studies with people with early onset because it

would seem to me that if we catch it, if we diagnose it very early, you know I was at first diagnosed with mild cognitive until they gave me a lumbar puncture for biomarkers of which came back you know my AP42 was low, very low and my tau was very high. And so they thought that felt you know I had some I guess Alzheimer's pathology going on. Been having some trouble in the past couple of years but I sort of thought it was my learning disabilities changing overtime and so I sort of said oh it's that and I'll just sort of adjust to it but I never could adjust to it which was the reason alerted me to have a neurological cycle done.

George Vradenburg: I think Deb asks an interesting question, that is whether there's any research on early onset victims of the disease.

Dr. Sperling: Yes so there absolutely is research and some of the research is really aimed at the genetic side and trying to find biomarkers again in people who have these rare mutations. At age 63, it's a little more likely that it comes from this other gene I mentioned Apolipoprotein E4. But I also take care of people who don't have a genetic risk factor or clear family history who develop Alzheimer's disease in their 50's or early 60's and I think there is a lot of research going on is the first thing and I think it's terrific that you were aware enough to go and get a diagnostic workup and that you're interested in this kind of research.

I'm not sure where you live but one thing I can tell you about is the Alzheimer's Association has something called Trial Match where you can go on, put in a little bit of information about yourself and where you live and they can tell you about any type of research studies that are within 50 miles of you. So I would encourage you to consider that. A lot of the research is really trying to understand does Alzheimer's disease have the same rate of progression and the same types of symptoms when it affects somebody with a relatively young brain at you know in the late 50's or early 60's as compared to when it affects somebody who is in their late 70's or 80's and there are some subtle differences that may be important in helping us understand how to better treat early onset Alzheimer's disease. But it is a very active area of research. I would highly encourage you to consider volunteering. Some of the research is for clinical trial to find medications and some is helping us in finding more sensitive biomarkers like the spinal fluid you mentioned and imaging studies. So I would encourage you to look that up on the Alzheimer's Association website or call and there's other information online if you can get some and also to help you look for other studies near by you.

George Vradenburg: I think I'll follow up with another question about how to engage in clinical trials so you may have answered this but nevertheless a number of people who have called in are asking this question. So I'm going to turn to Mary Kaiman in Omaha, Nebraska. Mary?

Question: Yes. Thanks so much for sponsoring this and doctor thank you so much for taking time to give us so much information. My question is, well, initially, I'm interested in the study that you're proposing and I would like information on participating at and I am 72, I'll be 73 in November.

Speaker: Perfect.

Question: My dear mother passed away about 20 years ago at age 85, 86 from complication of Alzheimer's and she had shown symptoms for approximately 5 to 10 years before that but at that time as you know doctor there wasn't a lot of medication available and so we finally had to put her in a facility care for her. It was one of the first Alzheimer's care facilities in Denver, Colorado at that time.

And I guess for myself and probably many others are concerned about this, is if there is a genetic factor, I know you've been talking a lot about genetics.

And I have one other related question that occurred to me. I am a cancer, a breast cancer survivor, of about 4 years now and I had surgery, chemo, and radiation and my brain was so much affected by the chemo. Although I'm starting finally to think clearly but I wondered if going through that illness and that experience would affect the brain that would make it more prevalent to Alzheimer's?

Dr. Sperling: All right. So let me start with that question because there has been some research on this. So you were right that some chemotherapeutic agents and radiation can have effects on brain and thinking. But as far as we know that really doesn't pre-dispose one to a higher likelihood of Alzheimer's disease.

Question: Oh good.

Dr. Sperling: In fact there's been a little bit of research that suggest the opposite which is that people who are cancer and cancer survivors may actually have a slightly lower incidence of Alzheimer's disease and that might be because of either the treatments that have been applied along the way that may have some effect but also because survivors of cancer must also have some other good genes that help them survive. So that's one...

Question: That's encouraging.

Dr. Sperling: It is and again I am proud of you for going through all that and still being working hard which is great. In terms of volunteering for studies, so this particular study, the A4 study will start in the fall and we'll have more information available on that over the next few months. You will be able to find it on the Alzheimer's Association trial match as well as some other registries, so the Alzheimer's prevention registry which maybe we'll talk about it a bit later. But if you want information even sooner, I'll give you a couple of possibilities. So one, there is an e-mail called brainlink@ucsd.edu. And I'm sorry it's not a catchier name yet. We're actually trying to get the domain name A4 but we don't have it yet. So... So we will.

Question: At the University of California or?

Dr. Sperling: At the University of California, San Diego who will actually be the coordinating center. And also I think if you look online at the NIH, at the National Institutes of Aging, there is some information there. But I hope greatly over the next few months, we'll be able to get more detailed information out to people so that they can start thinking about whether they would want to participate. Right now we've been fortunate enough to get the NIH grant and we're working very hard with our partners at Lilly to develop the protocol because the big next step is getting the FDA to approve the protocol so that we can start enrolling. And again we hope that will happen over the next few months.

George Vradenburg: Thank you very much for your question, Mary. Here's another question that relates to the same subject matter but from another angle, Elizabeth Fahey of Wellesley, Mass has a question about the participation in clinical trials.

Question: Hi, Dr. Sperling. Actually, I have a personal connection because you treat my father and you've been unbelievable. We live here in Boston so thank you for everything.

So I have 3, 4 for my ApoE and I'm in my late 40's. We have a lot of relatives on both sides who are in their 70's and I'd love to encourage them to particpate but I think their questions would be similar to what I am thinking which is what are the risks, what does it actually entail? Can you talk a little bit about that aspect?

Dr. Sperling: So I certainly can and you know a decision to participate in clinical research is definitely something to think about carefully, to talk about with your family and your doctors because it's not for everyone. What I will say is we try to have research studies that are open to people who want to commit to a little bit of time and low risk as well as studies that are more intensive and might involve more risk so that we really hope to have a study for everyone who might be interested.

The A4 trial in particular, I can tell you that part of the reason we chose solanezumab as the drug was because it had a good safety profile. I've been working on other kinds of antibodies for the past 10 years and unfortunately some of the antibodies I was the most hopeful for did have some side effects with brain swelling and although I think those may be tolerable, I was concerned about this in normal people. So for us, we decided to go with solanezumab because the risks were less. Now having said that all drugs, of course, and especially all experimental drugs can have risks and that'll be an important part of the discussion with participants. I think the hardest part though is the studies will be somewhat intensive meaning people coming in to get the antibodies, the infusions, and getting testing, and we know that this takes a lot of people's time. The nice thing is that often, at least at our center, people begin to feel like they're part of our family where they come in every month and see people and there's some benefits to being involved in clinical research and staying engaged. But it is a time commitment and I do try to make that very clear to families and people who are interested in participating because it's really important to us that people who come into the trial are able to commit and stay in the trials for in this case 3 years, which we know is a big commitment but really important to have as many people stay in the trial if possible.

So I think for all these studies, the important thing is to talk to the doctors, the investigators, ask all these questions and think realistically about whether this is the right decision for them. But most people, the good news is they like participating once they start and of course we try to do everything and make people as comfortable as possible.

Question: Great. Thank you very much.

George Vradenburg: I'm sorry. Go ahead, you had a follow up question?

Question: No. I was just saying thank you.

George Vradenburg: Okay.

Dr. Sperling: Thank you.

George Vradenburg: Dr. Sperling has mentioned three different potential sources of information about how to participate in clinical trials:

- brainlink@ucsd.edu in order to see whether you might want to and can participate in her trial

- Alzheimer's Association Trial Match
- and the NIA website

and Dr. Sperling, you mentioned something called the Alzheimer's prevention registry, you might just mention what that registry is and how to get to it.

Dr. Sperling: Absolutely. So this is a registry where my colleagues, especially at the Banner Institute which is in Arizona, started to really try to be able to give information to people who'd be interested in learning about prevention trials of all types not just the A4 trial or the genetic risk but other trials that will come up including lifestyle and exercise. So the Alzheimer's prevention registry, which you can easily find online, you go to the website and you give a little bit of information about yourself, but you don't have to give too much, and then you will be asked whether you want to be contacted if future trials come up that might be of interest to you or people you know. So it's a really a great way of getting connected and giving your information so that as future studies become available you could be contacted by e-mail or other sources.

So I would encourage all of you to be active, look on the web, look at your local Alzheimer's Association if you have one, because there are lots of opportunities to get involved in research and there's nothing to say you can't sign up for all of these if you're interested.

George Vradenburg: I'd like to turn now, if I could, to some other topics that people were asking about the relationship between Alzheimer's and other disease conditions and so I'm going to ask Kathleen Emery from Verona, Wisconsin to ask her question.

Question: Yes, Dr. Sperling, I've read some research out of Brown University that is linking heart disease and Alzheimer's to type 2 diabetes and I'm wondering what your opinion is on that.

Dr. Sperling: Yes. So I think the link between diabetes and heart disease and vascular disease and Alzheimer's disease is still a really important area of research. So it is the case we've known for a long time that even having a single tiny stroke in a person with Alzheimer's disease pathology in their brain makes them much more likely to have severe symptoms or progress towards dementia. So that's one link is that they are really 2 different pathologies but they unfortunately work together to cost brain problem.

But the type 2 diabetes link I think is quite interesting even just to Alzheimer's diseases itself through two mechanisms. So one is insulin. We know that there are changes in the way the brain uses insulin that might pre-dispose people to Alzheimer's disease and there is another trial that's starting, I hope soon this year, that will look at a nasal form of insulin to try to treat Alzheimer's disease. That's also an NIH sponsored trial. And we also know that people who have type 2 diabetes unfortunately do have a higher risk of other complications in the brain including cerebral vascular disease. So it may also affect the blood vessels which again in turn interacts with Alzheimer's disease. So I think this is a really important area of research. Certainly if we could decrease the problems that occur in type 2 diabetes, I think we would keep brains healthier and there is some evidence that this would also have an effect in decreasing the risk of Alzheimer's disease. So this is a really important area of research.

George Vradenburg: And if I could ask Tony Jones of Greensboro, North Carolina to ask her questions which relates to another sort of relationship between Alzheimer's and another disease.

Question: Hi. Can you hear me?

Dr. Sperling: Yes I can.

Question: Okay. I was just wondering... My grandmother back in the day, they said that she had hardening of the arteries, that was her problem. That's what they used to say seniors had and my mom had Alzheimer's for about 22 years. So I'm wondering, is hardening of the arteries and Alzheimer's the same?

Dr. Sperling: That's an excellent question. So I do think that a lot of what was called hardening of the arteries, and I can tell you my grandfather I believe had Alzheimer's disease and that's exactly what he was called, hardening of the arteries, and I think much of what was called that in fact was is Alzheimer's disease. It is a case that probably some of those folks did have some cerebral vascular disease or small strokes that contributed and of course it's hard to tell. But we use to think that getting older, it was normal to have some cognitive problems or memory problems and we call this hardening of the arteries or senior moments and I think what we've realized is that, losing your memory or your cognition is not normal. And about 70% of the time, when people have progressive cognitive problems, it is due to Alzheimer's disease and even the other 30% of people, in older people who have progressive, cognitive problems, Alzheimer's disease may play a role even though again cerebral vascular disease or some of these other rare causes of dementia may be the predominant problem. So yes, I do think much of hardening of the arteries is Alzheimer's disease and the good news is now we have ways of being able to differentiate a little bit better what is more likely symptoms due to Alzheimer's disease versus symptoms due to these other causes such as vascular disease in the brain.

Speaker: Okay, the plaque in our veins from cholesterol, is that the plaque that collects in the brain when it goes through the blood and runs through the body?

Dr. Sperling: You're asking such great questions. So believe it not, they are not the same plaques. They are both called plaques because of this thing that they kind of form on the surface like that. But the plaques that occur in arteries, you're absolutely right they are due to cholesterol buildup and the plaques that are occurring in the brain are due to this abnormal protein called amyloid and they are different. They share the idea that they kind of clog up the system but they're quite different the plaques that occur in the brain are not in blood vessels, these amyloid plaques and they're not even in the nerve cells. They actually sit between the nerve cells and probably affect the way the nerve cells can talk to each other. So they are different than cholesterol plaques in the artery although there is a link that perhaps keeping your cholesterol low, especially in mid-life, may have some effect in decreasing the amount of amyloid plaques you form. But again they're different kinds of plaques.

Question: All righty. Well thank you so much.

Dr. Sperling: You're welcome.

George Vradenburg: Thank you for your question. You mentioned earlier Dr. Sperling that you do not now recommend screening for Alzheimer's because you don't necessarily know what to do with the information. So I am going to ask two people to ask sequentially. I’m going to ask them to speak to that and ask questions about it. First, to Karen Kaufman. Karen, would you please ask your question.

Question: Thank you. My mom has Alzheimer's now and her mother had Alzheimer's. I did in the last year have my mom tested for the ApoE4 gene mutation because I am convinced that I too would get Alzheimer's and she tested negative. Now I know full well that I won't get Alzheimer's disease. But I had mentioned it to my rheumatologist and that is, you know that if my mother had tested positive, I would have been tested and she said why would you want to know? And I've had lupus for over 22 years. And I participated in many trials and I believe that, that's one of the things that we need to do in order to get treatments for these diseases is be active participants and I think that there's more of that feeling among medical professionals than we think.

Dr. Sperling: So I agree with what you've said and again, I think that the idea of having people who feel they're at risk for Alzheimer's disease because of a family history participate in research and potentially get screening tests including genetics or imaging tests as part of research I whole-heartedly support. And I think that's the best way to do it, so we can really understand what these genetic risk factors and biomarkers and scans mean. What I am not recommending is that somebody who does have a family history but doesn't have any symptoms, I, for the reasons you just said would not recommended at this point that they get ApoE4 testing because it wouldn't change what I would recommend to them right now in 2013. Because if you're negative for the genes, but your family has a strong family history I'd say there might be some other genes that is a less of a risk gene but one that we're not screening for or a gene we haven't discovered yet and you should still do all the things we discussed before: exercise, stay healthy, and active and engaged, whether or not you have the E4 gene. And I feel the same way about, I get asked a lot about people going to get a PET scan to look for amyloid even though they don't have symptoms, and I really think the right way to do this right now is in the setting of a research study because we don't fully understand what having a positive scan means for that individual. We know overall it's a risk factor but we need to study what it means for them. So I think again, participating in research is a fabulous thing. It is the way we'll get the answer. I just don't recommend screening for people who are still normal right now in a clinical situation until we have more information for recommendations to tell them.

This may dramatically change over the next 5 to 10 years, which is if we find in these studies that having amyloid in the A4 study or in other genetic risk studies that we really can offer a treatment to people at that stage and prevent dementia, I'll feel very differently and we'll need to go out and find safe ways of screening large numbers of people. But that's why we have to do the research to figure out how to do that safely and be able to give the best information possible to people at an individual level.

Question: Thank you very much. I do and have always lived by that nutrition, I'm a nutritionist, and exercise and especially since I developed lupus. But I don't think you mentioned anything about the tau protein and I do a lot of reading and there seems to be a lot of talk about that one as well.

Dr. Sperling: Absolutely. I'm glad you brought that up because I get accused of living in amyloid land or being amyloid-centric and I actually think tau is a very important protein as well.

So just to tell folks who may not get the chance to read as much as you have, tau is another protein that accumulates or forms clumps. But in this case, it forms these things called tangles inside nerve cells and a lot of people think that the mechanisms that cause amyloid plaques outside the cell and tau tangles inside the cells, probably have something to do with each other. Because in Alzheimer's disease, invariably, you have both amyloid and Cal tangles. The difficulty has been that we don't have quite as a good marker for tau, so we can see tau going up in spinal fluid but it's not quite as specific. It also goes

up with aging and there's lots of people working on PET scans for tau so that we could see it in the same way we can do PET scans for amyloid, and I think that will happen this year even.

But the ultimate thing of course is to have a drug that would reduce tau or at least decrease the tangle formation that seems to make nerve cells sick. There are some very promising molecules or treatments that are aimed at tau but they are earlier in development. There are a couple that are in larger scale trials but I think the really exciting ones are just starting in very early human trials. So in 5 years from now, I think we're going to treat people with an amyloid drug and a tau drug just like we treat cancer with multiple drugs or heart disease with multiple different mechanisms. So tau is very important and it's coming. I just want it to go faster.

George Vradenburg: So with apologies to all those who remain in the queue. I am going to just ask one final question that's drawn from multiple questions that we received before this call. And it's a tough one. Dr. Sperling, when will we have the first disease-modifying drug on the market and what is it that we can do to accelerate the time when we'll have an effective treatment for Alzheimer's?

Dr. Sperling: So I think unfortunately the earliest we will have a clear disease-modifying drug on the market is probably 3 to 4 years from now and that is if one of the trials that are ongoing right now with antibodies, the ones that are already going as well as the solanezumab trial that new one that will hopefully confirm the signal or the little bit of a positive effect that was seen in the previous trial are successful and again, most of these trials are 18 months or 2 years long and if they're ongoing now, it really is going to be 3 years before it gets to market.

I think though, I'm hopeful that one of them will make it and even if one of these isn't quite ready I think the fact that we're moving and testing these drugs even earlier in people who have milder forms of disease or who are asymptomatic, I think this might be the key to really getting something on the market sooner rather than later. And there are some other mechanisms we didn't talk about today that are starting large scale trials right now such beta secretase inhibitors, again, they are likely 3 to 4 years away from finishing their trial.

The real bottle-neck, there are 2 of them actually. So one I already mentioned, which is it takes so long to enroll these trials. We need people to volunteer, to come in and be willing to participate in the trial that lasts for 18 months, 2 years or 3 years. People who have symptoms and then again, in these new trials, people who don't yet have symptoms. And the second thing is really funding because people often think, oh these trials are done by big pharmaceutical companies. They should have plenty of money and when these drugs get to the late stage trial, that's true but unfortunately the research that gets them to the stage where we can get them out into big company trials, we're losing funding from the government and from philanthropy right now because of economic times and so there are lot of promising studies that I hope would start this year that aren't getting funded because there is not enough resources going to Alzheimer's research.

So I know George you have said this many times, but we spend 180 billion dollars a year on caring for people who are unfortunately suffering from Alzheimer's disease dementia. If we just took 1 billion extra of that 180 billion per year and put it into Alzheimer's research towards treatments and ultimately a cure, we'd get there a lot faster.

George Vradenburg: Dr. Sperling, I can't thank you enough for spending time with us today and I just have a couple closing comments. To Dr. Sperling's last point about the need to generate additional

resource to this field, to enable Dr. Sperling and all of her research colleagues to generate more trials, to develop more candidates for drug development, and thus have more sort of shots on goal as it were to get us an effective treatment. I would urge you all to join USAgainstAlzheimer's. Go to usagainstalzheimers.org and just join. And by joining, what you will get is something that you can do each week to actually move forward this movement to try to get more resources into the hands of Dr. Sperling and all of her research colleagues. So that's number one.

Number two, I would urge you all to continue to consider participating in clinical trials. Dr. Sperling has laid out 3 or 4 different avenues but I'm going to give you an easy one and that is just stay on the line after this call is completed and leave us a message if you are interested in finding a method to participate in clinical trials and we'll talk to you one on one and help guide you through whatever the best mechanisms might be for you to find out whether you might qualify for a clinical trial and whether there is a clinical trial that's being undertaken in the community near you. Not only you, but all of your friends. So please stay on the line if you are interested in participating in clinical trials so we can help you find a path to a clinical trial that might work for you.

Thank you again for participating in Alzheimer's talks. We're grateful for the support of Jill Lesser, one of our board members, for making this call possible. In about a week, we'll have a copy of the recording and a transcript of the call on our website so you can share it with friends and review it if you wish.

Alzheimer's Talks is a teleconference series. Where we'll discuss a wide range of topics in the coming months. We'll be highlighting: gender differences in the operation of Alzheimer's between men and women; minority health disparities, why it is that African-American and Hispanic-Americans seem to have a greater incidence of this disease; and research into concussions and traumatic brain injury and how that relates to Alzheimer's. I hope that you'll participate on those calls and share the information about these call with your friends and colleagues.

Again, please stay on the line if you'd like to leave us a message with a question or a comment or if you'd like to ask us how best to help you participate in clinical trials. Dr. Sperling, thank you so very, very much for your time this afternoon. It was a fascinating call and I think the listeners on this call got a tremendous amount of information. We deeply appreciate not only your participation on this call but what you do everyday for the patients out there, those people and families who are experiencing the horror of this disease and those who are at risk. Thank you very much and to all of you have a great Friday afternoon and a good weekend.

Dr. Sperling: Thank you very much.