Alzheimer's Talks

with Dr. Ron Petersen

Transcript from May 24, 2012

George Vradenburg: Welcome to Alzheimer's Talks. Today's conversation is about the groundbreaking National Alzheimer's Plan announced last week by Secretary Kathleen Sebelius of Health and Human Services Department of the United States Government as well as a groundbreaking prevention trial. Today's discussant is Dr. Ron Petersen who served as Chairman of the National Alzheimer's Advisory Council on Research Care and Services and who is the director of the Mayo Clinic's Alzheimer's Disease Research Center.

My name is George Vradenburg, I'm the Co-founder and Chairman of UsAgainstAlzheimer's involved deeply in this movement as the result of the loss of my mother-in-law to the disease. I want to thank you all for joining our call today. It is the third call in a monthly series presented by UsAgainstAlzheimer's.

Today's sponsor is the Alzheimer's Drug Discovery Foundation. The Foundation accelerates the discovery and the development of drugs to prevent, treat and cure Alzheimer's by raising and awarding funds to scientists conducting drug discovery research in this field and specifically in the early start-up stages of new companies. The Alzheimer's Drug Discovery Foundation has granted more than $51 million to fund over 370 Alzheimer's drug discovery programs in academic centers and biotechnology companies in 18 countries. For more information about Alzheimer's Drug Discovery Foundation, visit www.alzdiscovery.org.

I have the great pleasure of serving with Dr. Petersen on the Advisory Council on Research, Care and Services and his leadership on that council was essential in getting the 25 members moving in the same direction and coming out with a clear set of advisory council recommendations which during the course of the preparation of the national plan made a significant impact in the actual content of the national plan as promulgated.

If you have a question during Dr. Petersen's presentation, please press star 3 on your phone. By pressing star 3, you will be placed into the question queue. Please have your question ready to share briefly with a member of our staff and then they will try to get you live on the air with Dr.

Petersen as soon as possible when we open up for questions. Please note that Dr. Petersen is not in a position to answer personal medical questions on this call. Ron, we look forward to your comments about the National Plan and about this new prevention trial.

Dr. Petersen: Well, thanks very much George for inviting me to visit with you and others this afternoon regarding these issues. I think it's really an important, maybe watershed, time in this country for Alzheimer's disease broadly defined going forward. As you mentioned George, the announcement of the plan last week was the first plan for this country. We know that several other countries around the world have plans and we're learning from them. We're going to interact with them but we have sort of a unique situation here in the United States as well and so it's very timely that this plan be put forward. So what I'd like to do briefly this afternoon, just as an introduction to the topic is describe the NAPA, National Alzheimer's Project Act Plan process and also say a few words about the research summit that was held last week at the National Institute of Health to design a plan for addressing Alzheimer's disease going forward at least from the research perspective and then say a couple of words about the two trials that were introduced last week: one the prevention initiative and the second being a trial of nasal insulin for asymptomatic patients.

Just a brief back ground on NAPA. Again, it was supported unanimously in Congress in late 2010, signed into law by President Obama in January of 2011. And the National Alzheimer's Project Act required the Secretary of HHS, Kathleen Sebelius, to provide this plan. Put forward this plan and to do so, she entered an advisory committee to recommend how the plan should evolve. And in the course of that, a 25 person advisory committee with about roughly, it's not half, but about half. Half and half of federal and non-federal members was assembled last summer and the group began meeting both face to face and with numerous conference calls over the succeeding months. After a great deal of discussion input from various stake holders as well as public input to HHS, the plan was finalized in late April, early May and announced last week.

The plan itself has 5 goals and these are rather broad and generic because the committee did not feel it was wise to drill down and get in to too much detail in any specific area but set the stage for others to do that. At the same time be sufficiently specific to put some metrics out there such that we could determine, whether in fact we were making progress with the plan. So the first goal was research oriented and basically stated we wanted to prevent and effectively treat the disease by 2025. And I'll say more about that in a minute. The second was oriented towards clinical care to optimize care quality and efficiency. The third pertained to caregivers to

expand support for people with Alzheimer's disease and their families. The fourth was to enhance public awareness and engagement in the disease process. And number five was to track progress of the plan and drive improvement. That is how we are going to tell whether we're making progress.

Well the first goal with respect to research, one of the first items in that was to bring together experts in the field of Alzheimer's disease research to ask them questions about what are the obstacles to achieving success. How are we going to get to a significant treatment improvement in the quality of care of these individuals by 2025? So, last week May 14th and 15th at NIH, about 50 to 60, 57 or so individuals were invited to give presentations or be discussants at a day and half long conference and another 500 plus people were in attendance at this meeting and actually the meeting was oversubscribed with regards to addressing these issues so it was a great deal of time for Q & A and public input on this. The committee then boiled down to about 20 or so specific executive committee members on the second half of the second day and then out of that came a writing committee which was charged with actually just distilling down the recommendations of the day and a half meeting in the course of that afternoon and evening to specify for the country, for the advisory committee and for the secretary as well as for the National Institutes of Health. What are the priorities in this field? So I'd like to just summarize some of the basic findings from that meeting. There were several overarching issues that were discussed across. The six sessions in the summit meeting itself dealing with different aspects of largely therapy development, drug development, treatment development for Alzheimer's disease. That was primarily the focus. The focus was again to find a path to treatment and prevention. Among the over arching issues was the recognition that this is probably a very heterogeneous disease. It's not a single cell abnormality. It's not even a single system abnormality but in fact involves multiple interacting neural networks. And consequently we are going to need a systems biology approach to addressing this disease. It's doubtful that a single silver bullet will come forward to have a significant impact on the disease. There is also an emphasis on rapid and extensive data and specimen sharing. That is the importance that when data are generated, they're made public as soon as possible. They're digested by other groups and other people to be maximally effective. This then is going to take multidisciplinary translational teams to carry it forward. There were concerns about barriers to intellectual property. That is IP at various levels where you're dealing with the private sector or even the not-for-profit sector. There were issues about what's mine and can I share it, should I share it and how important it might be to share these data at the same time there have to be sufficient incentives out there to academic centers as well as to private industry to invest in this and move forward. So that leads to the issue of public/private partnerships. How important they

are and how they're going to evolve with the evolution of the plan. And then finally, the last over arching issue was the recommendation for a national IRB, Institutional Review Board. These are the boards that are required for patient safety and a very big stumbling block to getting therapies out in the market. Revolves around the issue of how long it takes to do a clinical trial. Clinical trials often take much longer than they are projected and that leads to loss of efficiency, economy and may in fact compromise the integrity of the trial. As such one of the elements of getting a clinical trial executed is getting the protocol by the IRB. Well if you're running a study that's going to be carried out in 50 or 60 institutions, that means that we need 50 or 60 review bodies to approve it. Hence, having a single national IRB that is charged with reviewing a specific protocol, all centers, all participants then would apply to that body will be much more efficient. So those are sort of the over arching issues.

The first session then of the six sessions revolved around a lot of the basic biology. It was entitled Interdisciplinary Approach to Discovering and Validating Next Generation Therapeutic Targets. And in this session, there were interesting discussions regarding again the complex pathobiology of this disease and necessity for a system's level understanding. And emphasis on translating genetic findings that have been very prolific in the last few years into mechanistic insights into novel drug targets. With an emphasis on developing more biomarkers and in particular new in-vivo imaging agents. We're pretty good at looking at amyloid these days. We can image it now with a PET scan. We have effective tracers. We can look at it in the spinal fluid. But again, going back to the notion that Alzheimer's disease is a complex entity, not a single target. We're going to need perhaps imaging ability to look at tau pathology, synuclein pathology, TDP-43 vascular pathology. So we really need to emphasize other bio-marker development and imaging efforts. We also need to share the data and collaborative findings and maximize existing infrastructure. The thinking there is that while we'd like start from scratch and maybe do it right this time. If we're going to reach a goal of having an effective treatment by 2025, we really have to maximize what's out there and it doesn't mean that what's out there is ineffective.

The second session revolved around challenges in pre-clinical therapy development. So in specific animal models, animal models are felt to be very important in characterizing this disease but at the same time, we have to realize that we need more robust models. Clearly the mouse models that are out there are very good and very helpful but we may need to expand to other species as well. There was one aspect of the discussions I thought that was quite interesting regarding the pre clinical models and that is that animal model data are often not shared completely. If there's a negative trial for example, therapeutic trial in an animal model,

that often does not get published. Does not get put out in the public domain and consequently other people don't learn from it or about it, don't benefit from mistakes that may have been made and it compromises the utility of those data, in particular negative data. One person actually suggested that here be a national governmentally sponsored website like clinicaltrials.gov, there be a site called preclinicaltrials.gov. Meaning that if you're doing a therapeutic trial in an animal model, you should register it with the federal government and report the results, be they positive or negative. Now, that may or may not come to be but the point being that there's a lot of information that can and should be shared out there.

The third session was more clinically oriented. And really discussed the value of either using existing or developing new cohorts of individuals, registries of individuals if you will, who are asymptomatic but may be at variable levels of risk for the disease. So using bio-markers, using other imaging modalities. Can we characterize populations of individuals out there? Large populations that may be candidates for intervention trials. Be they pharmacologic, non-pharmacologic and to the extent that at least some these trials can be population-based. By that we mean of course that they reflect the actual population out there. A concern was raised that the many good populations that have been assembled thus far come to universities and medical centers but in so doing are self selecting and may not reflect the disease as it exists out in the general community. So some of these trials need to be, some of these cohorts need to be population-based. We need to think also about new neuro-psychological and behavioral measures since this is still the hallmark of the disease. And we need to correlate the biomarkers imaging markers with these behavioral measures as well.

The fourth session focused on re-purposing drugs that are already on the market or combination therapy and here we have had some success with this thus far, but clearly taking a drug that's already gone through all the hoops of the FDA to gain approval for perhaps another entity, another indication, another disease may be useful through high-throughput screening techniques to be shown to be effective against Alzheimer's Disease or some of its targets. We should think more about using that because of the efficiency. At the same time, there was caution expressed on the part of individuals saying that we have to maintain rigor in the development of repurposed drugs because just because the drug is on the market for say, an acute indication and treatment of this particular entity, it may behave very differently when you put it into older people and the people who have to take it for years and years. So the safety profile may be quite different. The point being again that we need to maintain a high standard for even repurposed drugs but there's a lot to be gained from that particular approach.

The fifth session revolved around non-pharmacologic therapies. That is while we all are looking for the magic drug or the medications that may have an impact on this disease. There may be important end roads into fighting this disease from the non-pharmacologic lifestyle orientations. The same time we need to correlate what's going in these lifestyle modifications with actual mechanisms and molecular events. Again, how did they interact with some of the underlying imaging and biomarkers? And of course just because you take the non-pharmacologic approach does not mean that you're doing that exclusively. You could combine pharmacologic and non-pharmacologic approaches. This is clearly how we approach heart disease and cardiovascular risks. So I think that type of strategy can be adopted by the Alzheimer's community.

And then finally, the sixth session dealt with the development of public-private partnerships that we need to take into account that the plan for Alzheimer's Disease is a national plan, not just a federal plan. So it's absolutely vital that we engage the private sector. Both the for-profit and the not-for-profit sectors since this problem is large enough, we're going to need to combine all aspects of the research enterprise to make in roads into this. That means that we must consider what are some of the road blocks to this when we're dealing with chronic disease and the development of drugs, do we have to reconsider what is called patent exclusivity for say drug companies? We're dealing with time it takes a molecule to go the market, that extensive time if it involves a considerable period for trials, chronic disease trials that may last years. The patent exclusivity might be quite short with regard to drug development. That's not an incentive to the pharmaceutical industry and so we need to consider, does that have to be modified one way or another. So, those in fact were the main outcomes of the summit and these are now going to be used by the National Institute on Aging. They're going to be used by the advisory committee and other bodies going forward in terms of how to prioritize research in the near future.

George, also mentioned that at the press conference, Secretary Sebelius made the announcement and Francis Collins described the two trials that are being funded with addition of funds for Alzheimer's disease research in 2012 that President Obama released a couple of months ago and there were two trials. One is the Alzheimer's Prevention Initiative and this a study being run by Eric Reiman and colleagues in Phoenix involving a cohort of individuals, a family of individuals in Columbia, South America who have a genetic predisposition for developing Alzheimer's disease. Many of the members of this family have a genetic mutation in presenilin 1 that presupposes them to develop the disease by about age 45. And so the trial of that Dr. Reiman and his colleagues are going to pursue involves an immunological approach to

treating asymptomatic carriers with the disease. They're going to use a placebo for carriers and they're also going to enroll a group of non-carriers in this study and intervene with the immunological therapy early in the disease course, measure a variety of outcomes. Not only cognitive, not only behavioral, but a variety of biomarkers to see whether in fact in those individuals who are genetically destined to develop the clinical syndrome whether or not there will be an impact on that by this intervention early in the course. So this is an exciting time and exciting trial that's going to provide useful, very vital information for the field.

The second trial that was approved is a project by Suzanne Craft at the University of Washington using intranasal insulin in subjects with mild cognitive impairment or mild Alzheimer's disease. Preliminary data had indicated that intranasal insulin may in fact be effective at treating aspects of the disease. There was some cognitive improvement in some of the earlier trials with this; there is a variety of mechanisms regarding insulin insensitivity in Alzheimer's disease may be an interaction with actual amyloid processing that may be impacted by the treatment with intranasal insulin.

So these are two important trials. One in prevention mode one in a symptomatic mode that is moving forward and so I think this is a great jump start to the initial stages of the National Alzheimer's Project Act. And now that the plan is out there, organizations such as USAgainstAlzheimer's, the Alzheimer's Association, the Alzheimer's Foundation of America, and other advocacy groups really need to go now, talk to the Representatives, to Congress, to Capitol Hill to see if in fact we can have an impact on what the plan recommends and what it's going to take to actually bring it to fruition. So, in a sense, a lot of work has been done but I think the larger body of work is about to be embarked upon right now and I think all of us need to be involved as advocates to bring this to fruition. So, long winded. Let me stop there. I'd be happy to take any questions regarding either the Plan, the summit, the new trials or other issues regarding Alzheimer's disease research going forward.

George Vradenburg: Thank you Ron for your summary and thank you for your leadership in getting us to where we've gotten. Again, if you have a question for us, please press star 3 on your phone and we will try to answer as many questions as possible in the remaining 35 minutes of this call.

As Ron indicated, this National Plan in a sense represents the end of the beginning, now the work begins. We have a starting gun on a plan to get us to a place where we have the means of preventing and effectively treating this disease and we have a finish line of 2025. To assure that in fact we get from the starting gun to the finish line, we need to sprint and we need the

advocacy of people that are on this phone as well as we organize people around the country to get them to voice their support for this plan or to Congressional leaders to support this plan and to provide the resources and reforms needed to achieve it and I would say, advocate with industry to begin to step up their game in terms of identifying ways that there business practices might change in order to accelerate the research as Dr. Petersen mentioned the greater sharing of data for example.

Last week as we know, the plan was released and we now need to take the action necessary to execute on the plan. And I would like those people who would like themselves to get involved in the advocacy to press 1 on their phone. You will be put in a list that we will use to contact you to let you know how you might participate in the advocacy efforts that are needed to obtain the support needed for both the resources and reforms to execute on this plan and to get us to the finish line of 2025. So with that background by Dr. Petersen, I would love to open this up for questions and I will start with Raphael Schweri from Kentucky who has a question for Dr. Petersen and I'd like you to go ahead Raphael.

Question: Yes, I want to know if anything is being done utilizing different forms of ketones, I was a chemist in a previous life, to get symptomatic relief or even better. And same with MCT Oil, medium-chain triglycerides and the same with coconut oil?

Dr. Petersen: Right, popular topics Raphael. Thanks for asking them. There have been some studies done recently with ketones and actually there is a, I'll say, a nutraceutical on the market meaning not an FDA approved compound but a drug that is thought to improve glucose utilization in the brain using ketones and in fact improve cognitive function and there was a study on this presented at the American Academy of Neurology and also at the International Conference on Alzheimer's Disease in the past couple of years showing that glucose utilization via PET scan was in fact influenced by the use of these compounds. So at the same time, I don't think they have passed the rigorous test of randomized clinical trials and consequently when this has gone to be considered by the FDA that has not happened yet. So, while I think the theory is practical, feasible. I'm not convinced that the data are strong enough to recommend that as form of treatment for Alzheimer's disease right now.

As for compounds like coconut oil and other fatty acid compounds, I think this is the same as there. It's interesting to observe what happened when there was a great a deal of press, as many of you know, in recent weeks and months on the utility of coconut oil. And I think it stemmed around an individual who treated his or her spouse with coconut oil and the person seem to improve clinically with regard to cognitive function and some tests that the person had

been given but again, when you get to a more rigorous trial evaluation of that in a randomized clinical trial, I think that the data are not there right now and so I always get caught in this bind of individuals coming into the office and saying what about this? Hasn't this been shown to be effective and without sounding like, you know, a stuffy ivory tower individual, I mean I have to back up and say I can't necessarily endorse that because I haven't seen the data that are efficiently convincing that these compounds, these types of compounds are effective either at treating the disease once an individual is symptomatic or at preventing.

But again, like the summit said last week, we need to keep open minds about this because there may very well be other treatment avenues that will be effective and ultimately, you know, one of the things I don't think I mentioned in summarizing the summit findings is that it ultimately may take a cocktail of treatments for individuals with Alzheimer's disease. That is, since it's a complex disease with likely multiple contributing factors; we may in fact need multiple medications combinatorial therapy that would be beneficial. So I think keeping our minds open is a reasonable approach.

Question: Can I ask a question about something you said at the beginning?

Dr. Petersen: Sure

Question: You mentioned that I guess studies are being done to see if ketones affect insulin utilization in the cells?

Dr. Petersen: Right.

Question: Now, I'm not a bio person but, my understanding from the reading that I did was that either insulin or ketones like to get on a starvation diet. Can go in and be utilized as energy sources separately. I thought the insulin thing had to do with some sort of receptor on the cell getting the insulin in.

Dr. Petersen: Right, some people have called Alzheimer's Disease type 3 diabetes. I think that's a rather extreme interpretation but one thought is that the cells in fact in the brain lose their sensitivity to the utilization of insulin and hence get deprived of glucose and, you know, whether ketone supplementation gets around that or not. I don't think that's known.

Question: Okay. Thanks.

George Vradenburg: Thank you very much Raphael for your questions. My next question is from Ken Dychtwald in Northern California. Ken?

Question: Hi George, hi Dr. Petersen and thank you for the great work you guys are doing. So my question has to do with the scale of this attack. As we've heard, there are some folks who believe it could take 10 to 20 billion dollars to break this disease, to put it behind us. So how does one rationalize the 80 to 100 million dollar increment?

Dr. Petersen: Very, very good question, Ken. And I think, you know, with the President's gesture of 50 million this year, 80 million put in the budget additionally for next year, you're right. The problem of this magnitude likely will take billions of dollars over years and in fact the advisory committee in addition to making recommendations for the development of the National Plan itself, we're also charged by the law, by the NAPA law to generate a set of recommendations to the Secretary and also to Congress. And in this separate set of recommendations, there were perhaps some more aggressive or bold suggestions made to Congress and to the Secretary as to what's its going to take. And one of those revolved around a large budget recommendation and the budget, the figure that was in the recommendations was actually, that the federal budget of Alzheimer's disease research be ramped to at least 2 billion dollars a year. So extrapolating that over the next 10 years. We're getting to this 10 to 20 billion dollars. Of course, these are estimates and yet the figures have come from the individuals who are out there in research community conducting the research and they have, they were asked the question. What will it take to make significant inroads into this disease over the next 5 to 10 years? And so these figures were generated on that basis. But you're quite right. As we know for other major diseases in this country, cancer has an annual research budget of somewhere in the 6 to 7 billion dollars a year. Heart disease is in the 4 billion dollar range. HIV/AIDS is $3 billion a year. And yet we've made progress in each of those disease fronts in terms of converting HIV/AIDS from an imminently fatal disease to a chronic disease. Haven't conquered it but certainly people are living out their lives. Cardiovascular disease, we've had in-roads there. We've reduced heart attacks. We've reduced strokes. People are actually living longer and similarly in the cancer front, some cancers have a very good treatment record. There's a lot of work yet to be done there but the point being that deaths with regard to all these other entities are actually decreasing on an annual basis and yet it's just the opposite story with Alzheimer's disease. So, on that basis I think your point is very well taken Ken, that we do need an infusion of research funding of that magnitude.

George Vradenburg: Thank you. I would just add as Dr. Petersen has recited the relative annual investments in these different disease categories, it is evident that there are two things that we have to overcome. One is a bit of history. We started our war on cancer back in the early 70's so there's been a long period of time where the resource against that disease has been built. And

HIV/AIDS was a build up of resources in the late 80's, early 90's. And then we shifted in the mid 90's to a commitment to double NIH investments across the board and we have not since the late 80's and early 90's made a significant disease specific investment against the disease. So that's one challenge we have. The other is simply our fiscal situation, as where we have to basically not only look at the resources invested in this disease or in NIH but we have to look at what the fiscal pressures are in the United States Government. But in the end, these budgets are politically constructed. So Congress will in fact, I believe, move when large numbers of Americans make their voice heard that this is a disease that is affecting them, affecting their family, affecting their family budgets, and ultimately affecting the capacity of the caregiver to pursue a career or a job. So I think it is incumbent upon all of us to change the political environment to generate the kind of support to make a disease specific investment in Alzheimer's because of the impact on American families, because of the impact on the cost to America, both to the families as well as to Medicare and Medicaid. And to the fact that competitively, those nations who are able to keep their elderly populations productive and working and not dependent on the public health system will be successful in the 21st century and those countries that do not, are not able to do that, will be struggling. So that's a gratuitous comment from your host.

Our next question, I'd like to take is from Sherrill Nelson in Florida. The way I understand is it's a question about the clinical trials.

Question: Hello? Am I supposed to speak now?

George Vradenburg: Yes, you are.

Question: My husband is in the early stages of Alzheimer's, was losing cognition. I'm a caregiver and I'm wondering how we go about finding out if we can sign up for a clinical trial? And what are the qualifications? I'd be happy to give my name and address to somebody when I'm off the air, but that's my question.

Dr. Petersen: Thanks Sherrill. That's a very important issue these days as I mentioned briefly earlier that a major stumbling block to developing therapies right now is resulting from our inability to do clinical trials efficiently and effectively. And in addition to the several of the other factors that I recounted, one of the main issues is the lack of participation in clinical trials by people who are either affected with the disease or willing to participate. So the disease stage now, either at the dementia stage, the mild cognitive impairment stage, or even prevention trials that are being considered in normal individuals need people to participate. So you and

your husband are absolutely vital and there are some means now available to in fact participate. One is through the Alzheimer's Association and that can be found at alz.org and on their website, look for the link to trial match. Trial match is a program that is designed for exactly what you're asking for. That is you would put in some of the personal information, diagnoses etc. that have been given and you would submit that information and people will then contact you as to whether you would be interested in participating in the trial, they will give you information on specifics of trials, trials within your geographic region if you so desire so you could say here's where I live, what's available within 50 miles. What's available within 100 miles or what's available anywhere in the country. And they will get back to you with specifics and how you can contact those clinical trial sites. So that's one outlet.

Another is through the federal government, the site of clinical trials.gov. It lists all of the clinical trials that are out there for a variety of diseases and this is another opportunity and then just announced last week through HHS in part of the initiative of NAPA is Alzheimers.gov. And that site also will give you information that you may need with regards to the disease itself and how you can participate in clinical trials.

So, I applaud your interest in doing that because it is absolutely one of the most important pieces in the funnel, if you will, with regard to therapeutic development.

Question: Well he's 80 now and played football with not much protection on his head. Was unconscious several times and now with the new research on head injuries, it's kind of interesting whether that leads to Alzheimer's or not.

Dr. Petersen: Yes, that is very interesting. There are several initiatives that you've certainly have heard about in the press but there was also a meeting in Washington a couple of weeks ago with regard to what's called chronic traumatic encephalopathy, CTE. And this is thought to be the disease involving cognitive and behavioral problems that results from head injuries and the Department of Defense has a particular interest in this entity and they sponsored that particular meeting because the individuals coming back from Iraq and Afghanistan with a variety of head injuries as well as certain other conditions like post traumatic stress disorder may be predisposed to develop cognitive impairment. Now whether it's Alzheimer's disease specifically or not, remains to be seen the initial pathologic evaluations of some of these individuals have indicated that it's more of tau based pathology, tangle formation rather than amyloid itself. But in an individual who is 80 years old, there may very well be a combination of resulting factors from previous head injuries and perhaps an element of Alzheimer's disease itself. So again that meeting that was sponsored by the Department of Defense and the

Alzheimer's Association is bringing light to the importance of these factors in subsequent cognitive impairment.

Question: Thank you very much

George Vradenburg: Thank you very much for questions Sherrill, and our next question is from David Heywood from... David, I don't know where you're from but please ask your question.

Speaker: Yes, I'm in the Seattle, Washington area, Kirkland a suburb. And I have some comments about myself. I have Alzheimer's. I'm a retired internal medicine physician and about 5 years ago, I told my internist that I think I have Alzheimer's because one my older brothers had Alzheimer's and my mother had Alzheimer's. So he referred me to this specialist who did testing and he said oh no, you don't have it. So then six months or so ago, I had my internist refer me again. At first, he says oh I don't think you have it, I don't think you have it, but maybe 5 months... he did put me on some medication, several months ago. And he says I'm doing better and he's now says, oh about 5 months ago, you have Alzheimer's. So anyhow that's kind of why In my e-mail, I got the message about this program and why I'm calling. And I could mention to the doctor the medicines that I'm on and the specialist that I'm seeing said that I'm doing better. So my main problem is not remembering names of people. Whereas my wife, she's phenomenal, she remembers everybody, everybody. You know, she seen them once, she remembers for some years. That's my major problem right now, is this...I have trouble remembering names. And I could give you a name of the medications I'm on if you know anything about them ... This specialist I'm seeing says I'm better.

George Vradenburg: Your comment that leads to the question is whether Dr. Petersen, aside from those people like the family down in Medellín, Colombia whose genetic predisposition is actually determinative they are getting the disease. Is there any indication that your Alzheimer's risk goes up if your mother or your father or other family member has had the disease or has the disease?

Dr. Petersen: Yes, there's certainly, there are generally two genetic tendencies for Alzheimer's disease. One is what we're seeing in Medellín in Colombia with the causative genetic mutation such that if you get that gene, you in fact will get the disease. Fortunately, that's a very rare form of Alzheimer's disease. Maybe 1% or less of all Alzheimer's disease is transmitted in that fashion. Nevertheless, very important as we're going to be seeing in this drug trial to tell us about the biology of the disease and treatments for the disease. The other vast majority though are individuals who get late onset disease, meaning 70s and 80s. That's the bulk of the disease

but even there, there is a sort of a familial tendency sort of "runs in the family", if you will, but that's not peculiar to Alzheimer's disease. That certainly is true for heart disease, for diabetes, for forms of cancer that they tend to run in the family. So if a person has a first-degree relative with Alzheimer's disease - mother, father, brother, sister. In general, their risk of developing the disease is probably elevated 3, 4, 5 fold over the general population. Now what's the general population risk, well that too is very age related. And we say that somewhere in maybe somebody 65 and older, the general risk would be 8 to 10% over one's life but that goes up rather dramatically. It's quite different in 65 year olds than it is in 85 year olds. But whatever that age is, the risk would be increased by 3 or 4 fold if you have a positive family history with a first degree relative having Alzheimer's disease. But, it's important not to overestimate that by the same token because just because mom or dad or brother or sister had Alzheimer's disease, does not mean that you're destined to get the disease. Your risk is up but still, there's a very high likelihood that you're not going to get the disease as well. So it's worthwhile to pay attention to it but it's not deterministic.

George Vradenburg: Thank you very much for your question. Next question is from Lynda Everman from Tennessee. Lynda?

Question: Yes, Dr. Petersen. I was wondering if you would address the value of autopsy as it contributes to our research efforts.

Dr. Petersen: I'm glad you brought that up Lynda, because it's still, even in the era of bio markers, sophisticated imaging techniques, its still vitally important to get the answer at the end of the day. So when the person passes away with a form of cognitive impairment or dementia an autopsy is still very vital because what we're finding is that... and some of this is age related, that the older a person is the more likely that the underlying causes of that Alzheimer's disease syndrome, the clinical picture of Alzheimer's disease is due to a multiplicity of factors. So if someone dies with the clinical syndrome of Alzheimer's dementia at age 85, the odds are there's likely a contribution of amyloid pathology, tau pathology, the hallmarks of Alzheimer's disease, maybe synuclein pathology, which we see sometimes in movement disorders like Parkinson's disease. There may be an element of vascular pathology there as well. Over time, blood vessels become... you develop hardening of the arteries so to speak and you develop atherosclerosis in small and large blood vessels. So in an 85 year old, the syndrome is likely accountable by a variety of factors. At the same time, if you see somebody at age 65 who dies of the same clinical syndrome of dementia of Alzheimer's disease, that's probably more likely to be due to a single factor and here, amyloid may be the predominant causal factor in

that individual. So, the only way we know that for sure is with an autopsy and after death, we actually examine the brain and look at the multiple contributing factors. So, even though we're very sophisticated these days at pinpointing the cause of the disease in life, it really takes that final confirmation through an autopsy.

Question: Thank you.

George Vradenburg: Thank you very much Lynda. Next question is from Jeane Johnson in Michigan. Jeane you can go ahead with your question.

Question: Yeah, thank you doctor. My husband... we had moved to another state and our doctor of 20 some years had even tried to get him long term health insurance and we were denied twice and nobody suspected anything, so we went ahead and moved and got into this housing situation and we went to a new doctor and immediately he said my husband had short term memory loss and he wanted to send us to a neurology. So, not to be labored this but we sold our house and move back to our old home so we could... so when we got back we went to our doctor for some 20 years and this was a 5 month span only and he came out into the waiting room and said that my husband has short term memory loss and he would do the prework there and then send us to the University of Michigan. Now we hadn't noticed it, the doctor obviously even tried to get him long term health care and so then we were in a clinical trial at the University of Michigan with Dr. Henry Paulson who is a neurologist that's gone on to some more fields than just seeing patients and so forth. But they diagnosed him with Alzheimer's and frontal lobe dementia and I'm wondering what the association is there and also if not only head injuries which my husband has had numerous with football and different things. But also infections, they've talked about, you know and he has had some severe infections, a couple of severe infections if that had anything to do with it.

Dr. Petersen: Okay. Complex questions Jeane. I think maybe what we should do is drop back and say how do we define dementia in general and what can cause dementia. Dementia basically means I'm not thinking as well as I formerly did. Usually my memory is not as a good and some other cognitive functions may be impaired as well. And that's of sufficient severity to now affect my daily function. That constitutes dementia. Now we ask the next question, what is causing the dementia? And here, in aging, again 70s and 80s, the most common cause of dementia is Alzheimer's disease. But there are other causes of dementia. It could be due to vascular disease. Could be due to trauma. Could be due to other medical problems, medications, a variety of things. And so for your husband to be diagnosed with the features of Alzheimer's disease and features of frontal lobe dementia or frontal lobe degeneration, it might

mean that there is more than one process going on. Frontotemporal lobar degeneration as it's called, is also a degenerative disease of the brain but it's not thought to be due to Alzheimer's pathology. By its name, it involves the frontal lobes of the brain, the temporal lobes of the brain and there often is a different clinical profile for individuals with FTLD that is different from Alzheimer's disease. It tends to affect people younger in life. Younger than age 70, FTLD is much more common than after 70 where the reverse is true with Alzheimer's disease.

You mention that your husband had traumatic brain injuries previously. That can affect preferentially the frontal lobes of the brain, the temporal lobes of the brain because of the parts of the brain that are opposed to the skull itself and they can be injured preferentially with head injuries so you may get features of frontal lobe dementia that may be due to trauma rather than a degenerative disease as well. So this goes back actually to Lynda's previous question, and we hope not soon, but at some point in time, it might be relevant to consider an autopsy because the autopsy again would tell us what is exactly going on in the specific individual. But the point being that there are multiple cause of a dementia and while we often think about Alzheimer's disease and dementia being one and the same, it's true later in life but earlier in life, there can be multiple causes to the dementia syndrome itself.

I should say also that its sounds like you've had good care. Hank Paulson is a pre-eminent Neurologist at the University of Michigan and I'm glad that you participated in the clinical trial there. That's again what we need. Thank you.

George Vradenburg: Thank you for that question. And I think we have one more question left from Laura Arnold in Florida.

Question: Hello? Am I on?

Dr. Petersen: Yes you are.

Question: Okay. Well, I'm a caregiver and I'm just, you know, there's been a lot of research on trying to find out what causes the Alzheimer's but about the need for support for caregivers is my concern and how we have to handle our patients with the different types of personalities that they have with this disease. What are they going to be doing for the caregivers?

Dr. Petersen: Very good point, Laura. Goal 3 in the national plan is focused directly on caregivers because we realize how important they are to the overall function of, not only the caregiver themselves but the patient. And there's a great deal of emphasis in the third goal on caring for caregivers because they are so vital. We are very concerned about their health, their

welfare because if the caregiver becomes ill, the Alzheimer's disease patient then suffers as well. So there is a great deal of emphasis being placed on the education of caregivers, providing supports for them, culturally sensitive materials so that we know that in a particular culture or ethnic group what the peculiarities are to caring for individuals in that particular setting. We want to be sure that in fact the caregivers are properly educated and are handled in the system. Respites for caregivers is one example. That is, this is a 24-hour, 7-day a week type of job so we need to be mindful of the welfare of the caregivers. Patients often in the care giving system get transferred from one setting to another. From a nursing home to the hospital to the hospital back to the nursing home. We're trying to make that transition as smooth as possible taking into the account again the needs of everybody. So, care giving is absolutely vital and it's a central feature of the plan. One of the 5 goals focuses directly on that. The Agency on Aging is holding meetings on that aspect of care giving right now and so there will be several recommendations. In fact some of the resources that President Obama has put forth as part of the $156 Million that he has suggested in 2012 and 2013, $26 million of that is intended for care of patients and caregivers. So the Agency on Aging again has that squarely in its sight. So, keep your eyes and ears open because we clearly plan to take care of caregivers going forward.

Question: Thank you very much.

George Vradenburg: Thank you very much Laura for your question. I would like to try and sneak in one last question from Sue Halliday in Sacramento. If Sue you could ask a brief question, we get a brief answer. We can finish up here in a few minutes.

Question: I do have a brief question. Thank you. It's regarding the IRB. And what you think of likely of that happening might be and then what some examples of the public private partnership that you think it might take to put something like this together?

Dr. Petersen: Short question, long answer. So I'll try to be brief. As for the National IRB, there is a great deal of momentum behind that and there are some examples. I mean, it does exist in certain areas of say cancer. For example, they have National Cancer Trials approved at a national level. It really is going to revolve around some of the local institutions, medical centers, and universities relinquishing their local control of IRB to a national body. But I think there's a great deal of momentum and that may very well happen.

With regard to public-private partnerships, I think there's a good deal of talk going on between the federal government and between, say, pharmaceutical industry, imaging companies as well as to how in fact we can make investigations in the pre-clinical space more advantageous for

everybody as an example. So, sharing data from private studies as well as publicly funded studies, putting them all in a central repository so that everybody can benefit from them. That's going to take input from the companies as well as from the federal government but there is a great deal of talk going on promoting that already.

Question: Okay.

George Vradenburg: Thank you very much for your question, Sue. And as Dr. Petersen mentioned earlier, this plan is the product of the Bipartisan Act of Congress. It was passed unanimously back in 2010 signed by President Obama in 2011. And it's in essence an American plan. This is a bipartisan American plan and it's going to require all of us to get behind it. And so I am urging any of you who wish to join us in this fight to find a cure to press 1 on your phone now and we will get in contact with you as to how you can get involved.

Thank you for participating in Alzheimer's Talks. We are so grateful for the support of the Alzheimer's Drug Discovery Foundation that made this call possible. They're a great partner in the fight to find a cure.

This is the third call in a monthly series where we will discuss all kinds of topics, from genetics to politics to international coordination, to gender differences in the disease, to ethnic and minority differences in this disease. I hope that you will participate in these calls and share information with your friends and colleagues about these calls when you get the alert.

Please stay on the line if you would like to record a message for us or have any ideas for future topics. In a few days, we'll have a copy of the recording and a transcript on our website for you to share with your friends at usagainstalzheimers.org. Thank you Dr. Petersen and thank you for all the participants on the call for participating in Alzheimer's Talk this afternoon. Take care.

Dr. Petersen: Thanks George.