USAgainstAlzheimer's NETWORK
we can stop it by 2020.

Alzheimer's Talks Transcript

Important Alzheimer's Blood Test Research with Dr. Howard Federoff

Friday, May 16, 2014

George Vradenburg: Welcome to Alzheimer's Talks and thank you all for joining us this afternoon for a very intriguing and exciting topic. My name is George Vradenburg. I'm Co-founder and Chairman of USAgainstAlzheimer's.

USAgainstAlzheimer's is an entrepreneurial and disruptive organization demanding a more rapid solution to the challenge of Alzheimer's. We are in essence a collaborative web of coalitions and networks changing business as usual and the speed with which we get some medicines to market and to the patients that are suffering around the world.

My own mother-in-law died of this disease about 20 years ago and my wife and I founded USAgainstAlzheimer's out of of a sense of commitment to her but also in the fear that in fact if we don't do something in the next few years and get some means of deferring and delaying this disease that the next generation and then the next generation is going to experience this disease in very very large numbers. So we press for greater urgency from government, industry and the scientific community in the quest for an Alzheimer's cure. We do this by leading industry coalitions and broad-based care coalitions across the entire field and we do it by intersections between government, industry and the scientific community. Even as we lead, we try to do this through collaboration and unity. We like you all want to create a social movement that will create an inevitable momentum against this terrible disease.

This is our most popular call to date, we have over 700 people registered not only from across the country but from a few countries overseas representing the excitement about the possibility of getting a non-invasive diagnostic for Alzheimer's and a tool with which we can measure candidate drugs to see whether they are having a positive effect on populations.

This call is made possible by the generous support of the Zickler Family Foundation. Thanks to their generous contribution, we're able to bring this conversation to you today.

It's now my pleasure to introduce you to Dr. Howard Federoff, the Executive Vice President for Health Sciences at Georgetown University Medical Center and the Executive Dean of Georgetown University School of Medicine. He is a neuroscientist who led the team that has produced this result - the first of a kind blood test for Alzheimer's disease. In his view, this test can predict with a very high rate of accuracy if a healthy person will develop this cruel disease within a short period of time. This has the potential to be a real game changer as we'll discuss this afternoon, the possibility of detecting this disease before a

patient shows symptoms brings us even closer to finding an effective means of intervention which if administered before you get symptoms may have the possibility of deferring and hopefully deferring forever the symptomatic aspects of this disease. And it will enable us to be able to test the effectiveness of candidate drugs by determining whether the blood-based diagnostic itself is being effective. That's why Dr. Federoff's work is so essential to moving forward toward our goal of stopping this disease by 2020.

If you have a question during the call, please press star 3 on your phone. By pressing star 3, you'll be placed into a question queue, please have your question ready to share briefly with the member of our staff and then we will try to get you on the air live as soon as possible when we open it up for questions.

With that introductory material, I'd like to introduce Dr. Howard Federoff. Howard, thank you so very much for doing this today. The excitement I think in the community about your work is palpable and we're looking forward to hearing more about it.

Dr. Howard Federoff: George, thank you and thank all of you who have shown interest in this work. What I'd like to begin with is just to briefly describe the nature of the work that we had undertaken, the results that we had published a couple of months ago, and how we are thinking about those results, both in terms of their implications but then thinking about what additional work will need to be done in the future.

A few years ago, we, along with many others in this community, were interested in answering the question - is it possible to find some measurements by looking at blood among individuals who are cognitively normal that might be predictive of the subsequent emergence of cognitive impairment or Alzheimer's disease. And so together with a number of colleagues, we designed a study that involved the enrollment of a little over 500 individuals in two parts of the United States: western New York and Irvine, California who were community dwelling and who were cognitively normal. We enrolled those subjects with the expectation that, one, they would be willing to participate in serial follow-up, they would be willing to allow for the research team to draw blood serially, and that we understood that we did not, at the time of the study, have yet any way of conveying to that group of individuals whether we would or we would not be able to answer the question that I had posed at the beginning - is there something in the blood that we might be able to identify that would predict subsequent cognitive impairment or Alzheimer's?

We began the study, and again with many colleagues we made certain determinations that turned out in our estimation to be important. The first is that work that we had done previously had disclosed that it was important if one wanted to look at anything in the blood that we needed to standardize the approach; and so we made the decision that individuals who agreed to participate would be evaluated in the morning at two different clinical sites and that their blood would be drawn, they would have been asked not to eat after dinner the prior day, and if it were possible to withhold their morning meds until the bloods were drawn because we knew that both clock time and eating as well as we suspected medications might alter the ability of the team to determine whether there was a signal in the blood that might be predictive of that future cognitive impairment or Alzheimer's disease. So we enroll these

subjects and we follow them yearly with a neurocognitive battery that was designed by my colleague Mark Mapstone, who is the first author on our Nature Medicine paper. And approximately midway during the study as would have been anticipated, given that the minimum age for entering into the study was 70 years of age, some individuals had gone on during that several year period of follow up to meet the criteria of amnestic mild cognitive impairment or probable Alzheimer's disease. Then we looked at those individuals' blood, both at the time of entry when they were cognitively normal and then we could compare them at the time when they now had amnestic MCI or Alzheimer's disease to ask whether at the time of entry when they were cognitively normal, was there something that we can measure in their blood that would have allowed us to predict that so called phenoconversion. We compared the bloods of those individuals to those that entered cognitively normal and remain cognitively normal. And we used an approach that is commonly called metabolomics, which means that one measures metabolites. Just briefly metabolites are the products of cellular metabolism. Metabolites are the things that our cells either produce or utilize to do their work and metabolites are detected not just within cells but also in extracellular fluids including that part of the blood that's called the plasma.

We analyze blood plasma and through an extensive amount of metabolomic work, utilizing an instrument called the mass spectrometer, we were able to identify among a substantially larger number of metabolites 10 which were lipids, or fats, which were all lower in individuals who enter cognitively normal and subsequently then phenoconverted to either amnestic MCI or Alzheimer's. These plasma lipids represented principally Phospholipids, Phosphatidylcholine but also Acetylcarnitine. Both of those are very well known metabolites, a lipid is a type of metabolite.

And we were then convinced that what we needed to do next since we continued to enroll subjects as part of our longer term study, that if we had the opportunity now that we had discovered these ten lipids that were highly predictive of that phenoconversion that I described earlier that we would like to within the same cohorts in new subjects who would be entered again as cognitively normal subjects and then subsequently phenoconverting to amnestic MCI. Whether those ten lipids, when utilized to examine among a different group of phenoconverters whether they would have been predictive of that phenoconverting event, and we call that the validation phase of our study. And so in the discovery phase which I describe the identification of the ten, we found that it was very highly accurate and then separately in the validation phase, using a different set of individuals who were enrolled subsequently to those in the discovery phase we were able to validate again with reasonably high accuracy that those ten lipids were indeed in this relatively small study able to predict the phenoconverting event.

We were very much interested in trying to understand whether those lipids were related to some cellular processes, either as it might be circulating cells in the body or cells perhaps that lie elsewhere including the brain, and I think our current understanding is that we cannot yet directly link the lowering of those lipids per se to any alteration that we could describe with confidence that is going on within the brain or the central nervous system. And so that is certainly an important piece of work to do. I might comment that previously a number of other investigative groups had described lower plasma lipids, including many of the species that we had identified, as being lower in individuals who have Alzheimer's disease as compared to control in a way corroborating the fact that these lipids are indeed lower when

there is a manifestation of Alzheimer's disease. But the linking of those lowered lipids, what they do, what they mean, is still work to be done.

So let me just summarize what I think are the limitations of the work that we published because it's fueling a lot of interest and being able to extend the work. Number one, we looked at relatively small numbers of individuals and so clearly there is a great need to expand this and to conduct this work and replicate it, not just within our own research group but others as well. Secondly, almost all of the individuals enrolled in our study were Caucasian and we believe it an imperative to look at a more diverse set of individuals to discern whether this 10 lipid panel or perhaps the discovery of any other of set of metabolites might be useful in predicting phenoconversion, it might be different than that which we reported. And then third I've already heralded, we have to understand the biology in so far as: what does this mean and how can we put this into the framework that might be the more conventional framework in understanding the prodromal phase of Alzheimer's disease through the progression of Alzheimer's disease and this is work that's going to require a large number of studies, many I'm sure will be done by great laboratories and investigative teams throughout the world but nonetheless it has to be put onto the sort of biological map as we think about it in order to fit into a rubric an intellectual framework that really defines what is the underlying reason these lipids are lower and how can we relate them to our understanding of either disease risk and/or progression to manifestation.

So with that, I would love to be able to engage with you in some questions and answers. And again I want to thank George and the invitation to appear here and I'll turn the program back over to you George and we can begin the Q and A.

George Vradenburg: Thank you very much.

Just a reminder to those on the call that if you have a question please press star 3 on your phone. By pressing star 3, you'll be placed into a question queue. Please have your question ready to share briefly with the member of our staff and then we'll get you live on the air as soon as possible thereafter.

I have a question, Howard, what is the next step here in your own work, you mentioned that you are doing some continuing work, you're hopeful that the field will pick up and replicate or move forward that work. I think there are a lot of people out there who would be interested in participating in a trial of this thing if it were available in a trial setting around the country. So what is the next step so to speak in terms of testing this out and seeking a confirmation of your result.

Dr. Federoff: Yeah, we are currently planning three different activities. One, which we hope to be able to begin shortly, will involve the application of the test to a set of samples that have been part of a longitudinal study that have been ongoing in which individuals were followed for decades. We believe that that's an important bit of work to do because it may establish now that we've described the ten lipids. One, can we determine at what age relative to the diagnosis of Alzheimer's disease do we see a lowering? Two, can we distinguish, using the ten lipid panel, what we will call a non-Alzheimer's dementia from Alzheimer's dementia. And three, if we're fortunate enough and our initial review of the distribution of individuals in this longitudinal study, we might be able to begin to ask whether it's relevant other than in Caucasian subjects.

The second thing that we're doing George is we're planning for what will be a prospective study and colleagues together are just about at the point where we're ready to complete the description of that. We will be hopeful to secure funding for it.

And then the third bit which is something that will relate to the study subjects in our original cohort. We've done a lot of additional work in order to be able to ascertain in addition to the ten lipids, are there other signatures, other molecules, that are going to be highly predictive of that phenoconverting event and that work has gone very, very well. We anticipate over the next year that we will be able to contribute several additional papers to the literature and that too will help provide a basis in terms of this biological framework that I was referring to earlier.

George Vradenburg: I think we'll take our first question from a caller Sharon, is it Fratepietro?

Question: Yes.

George Vradenburg: Please ask your question.

Question: Yes. I was wondering what the breakdown in gender was in your study group and also if the results were affected by gender?

Dr. Federoff: The latter is no and approximately 60% of the subjects were women in our study.

Question: Thank you.

George Vradenburg: Let's go to Rhonda Gray and Rhonda, would you ask your question please?

Question: Yes, yes, thank you. My mother has Alzheimer's and I will be 60 years old in November and I was wondering if there is any sort of gene testing that I could have done or do I have to wait until I'm 70 for this blood test you're talking about or is there anything available in the Atlanta, Georgia area where I can go to be tested?

Dr. Federoff: Well thank you for your question and I share the understanding of your concern. Unlike a gene test, the test that we described currently is in its clinical research phase and I was saying earlier, and although this may be somewhat disappointing, we think it's imperative to expand and to externally validate the results that we have before we could imagine taking steps that might result in the ability of this test to be ordered by your doctor. We think that that's still some years away.

Which regard to gene tests, I don't do any work in this area other than we did look at ApoE alleles in our cohorts and I would say just generally in addition to discussing with your personal physician it's overwhelming likely that among the things that can be ordered, you will not find that there is likely a clinically available test that will provide a lot of additional information to manage any risk that relates to Alzheimer's disease unless one is a member of a very rare family that has familiar Alzheimer's disease.

Question: Is there any kind of vitamin combination that I could take as a preventive? You know we hear about D3 and that sort of thing?

Dr. Federoff: I think that the best answer is that we don't have enough data to know whether any nutritional supplements whether they be vitamins or other supplements will necessarily produce a benefit. I think one of the categories of work that many people are interested in doing now that there may be a way, and it may not just be based on the work that we have described, to identify at-risk subjects is to begin to examine whether any type of intervention whether that be based on a candidate drug or a supplement or other can be configured into a randomized controlled clinical trial to ask the question and answer – 'is it possible with whatever the intervention is to delay the emergence of Alzheimer's Disease?' but right now sadly I don't think that the evidence base is sufficient to be able to make any recommendation to you.

George Vradenburg: Here's a question that is from Bonnie Hawkins but reflects a similar question that a number of people are asking about. So Bonnie, why don't you ask your question which I think represents the views and inquiry of a lot of people.

Question: Hi I'm Bonnie Hawkins and my question is would there be any chance that those of us who are listening to this right now could sign up for the next survey so that we can be part of the next study?

Dr. Federoff: Bonnie, thank you for your question. The work that I refer to that we are just about done planning will involve the recruitment of subjects. I think some of the parameters that would be part of the inclusion criteria for identifying subjects are just being finalized. What I don't know yet is whether we will be able to do this in many geographical locations. We're beginning to believe that in order to be able to start this work and complete it in a reasonable period of time, we probably should be doing it at least in several, but at this point we haven't decided whether we will go beyond the two locations that we are contemplating. So what I would say to you is certainly if it were within your geographical region to be eligible or at least to be reviewed for eligibility for the study, we would be happy to entertain it, but until we've actually put that work forward, we do need to secure funding for it, we're not going to be able to recruit additional subjects into a follow-up study.

Question: Okay. Thank you.

George Vradenburg: There was a question submitted before the call from a man named Ervin Betts and he asks an intriguing question and that is can a blood be drawn at any clinic and forwarded it to you for analysis? I know you have some quality controls in terms of time of day and the circumstances into which the blood is drawn but there are a lot of doctors out there and/or researchers who might be sufficiently trained and understand the necessity for that quality control that you could get doctors or researchers from across the country to take a blood draw and to send it to a particular location. Is it possible to do that kind of, almost a national study of your particular approach?

Dr. Federoff: I think it would not be difficult George, given that very sophisticated clinical centers that do routine phlebotomy to make certain that the approach that we had taken could be adopted and I would believe adopted wholly and so the answer to that is yes. I think the next piece of this is really about the follow-up and the deployment of other health professionals to follow those individuals with regard to the so-called phenoconversion event. The first, I described is probably more straightforward in terms of logistics. The second will be vastly more complicated and so we've been giving consideration, as I was

saying a moment ago, to how we think about our next study, which would be a prospective study, and how many institutions will need to be involved. It is taking into consideration the latter that we're thinking about where and then how many institutions would be involved but I don't want anyone to believe that this first part, the blood drawing, is particularly difficult. It's actually very straight-forward and we're hopeful that as this work grows and that we have others independently validate the work that we have initially published, that the type of study the you refer to George could be potentially enabled.

George Vradenburg: It also might help very much in getting access to larger cohorts of minority participants because in any one site, particularly in Irvine or upstate New York, you may not have large cohorts of minority individuals and minority-serving institutions or minority-serving doctors across the country might be interested in participating and permits you to make a more significant penetration.

Dr. Federoff: Absolutely and we've started those discussions, including here in the District of Columbia and elsewhere. And so as one could imagine at this point, there is so much important work to be done. We have to sequence it just given finite bandwidth but all the points that you've raised in your questions and that George that you have expounded upon are all extremely important and it's just a question of how quickly we can get to the highest priority follow-on.

George Vradenburg: Let me take a question here reflects I think a number of questions. It's from Ara Khachaturian and Ara is himself a prominent researcher and prominent leader in the Alzheimer's Movement. So Ara…

Question: This is Zaven Khachaturian.

George Vradenburg: Oh it's Zaven.

Question: I don't know if Ara is on the line or not, but let me take the chance to ask Howard a question. A number of years ago, there were reports by Jay Pettegrew about showing specific differences in various phospholipids using the spectra analysis technique in Alzheimer's. The question I have is the turnover of membrane is very active phenomena that's part of the generating nervous system restructuring after synaptic environment toward what extent your findings maybe reflecting or a measure surrogate of that going on, that being the case, have you included other dementias or other situations where we know there is degenerative processes going on such as recovery from stroke or some other neurodegenerative diseases as well as in the developing nervous system. These are highly fluid kind of situations. It would be interesting to know in what way your measure specifically detects Alzheimer's versus some of the others.

Dr. Federoff: Right. Zaven, always good to hear from you. Thank you for your question. With regard to your initial suggestion regarding Pettegrew's work, I think it's possible that the findings that we have looking at plasma could conceivably be altered either by biogenesis, the rate of formation, or the rate of turnover degradation and there is a substantial amount of work that you are very familiar with which suggests that these might be altered in the setting of injury to the central nervous system. So that is part

of the biological reference that I made to earlier and while we're looking at what might be conceived of as a steady state measure, it's hard for us to deduce from those data whether it is consequent to some single process altered rate of formation or altered rate of degradation or both. However we're doing other work that I think will begin to address that by looking at a variety of other measures, some of which actually you might logically infer from my comment are related to encoding of some of the enzymes that are involved in these processes.

With regard to the second which is very important, we are at the point where we've identified both in this longitudinal cohort as well as talking with a number of other potential collaborators, both here in the U.S. and globally, several other really very well defined either prospective or longitudinal studies where we should be able to answer the question about whether phospholipid metabolites are telling us something that may be specific to Alzheimer's or may be a shared feature among other degenerative processes, those that would be progressive such us Alzheimer's, Parkinson's and many others, frontotemporal dementia, or might be more temporally limited such us a vascular accident such as a stroke with a peri-stroke and recovery period. We have to do that work. And I think that the other analyses that we're doing looking both at enzymes to genes encoding as well as other features coming out of the initial cohort, I think will help begin to focus our attention on what to measure in those other clinical contacts that will allow us to more rapidly answer your question either in the affirmative or perhaps we might learn that this is just a general feature of degeneration. But until we're there we won't be able to comment on it and have a data that we will be able to interpret and share with the community.

Question: Well I have, if I may, one more additional comment or question. I was pleased to hear that you're planning a prospective study. Along the line with that, have you thought or considered piggybacking on other existing longitudinal databases to add your measure to the spectrum of measurements that they are telling, one that comes to mind is the ADNI. I think this would be an easy test to add to the ADNI spectrum although they may not be going as far early as you might be going. But it still I think would be nice to find a way to link up or leverage these other existing ongoing longitudinal studies.

Dr. Federoff: Absolutely, we're in several conversations right now to do just that because we think we can add some additional value and assuming that we can secure the participation of the leadership of the different large collaboratives ongoing to really want to collect the blood in a manner that's ideally similar if not identical to that which we've done. I think we can add additional value and then just extending your point further we can then link these data to those others that are being collected which I think is your reference to potentially adding additional value to that ongoing work.

Question: Sure. Thank you. What's the vice president for research doing getting into the wit and science. Have you come to the light side from the dark side?

Dr. Federoff: It keeps me sane.

George Vradenburg: He's bringing mysteries of life to light.

Here's a question that I'm going to ask one of our online callers to ask although it is reflected in at least 50 questions that we've got before this call and it's from Martha Stettinius and it has to do with how soon all of this may really be available to the public. Martha?

Question: Hi, thank you for having me. This is all really exciting. In a book I wrote about caregiving for my mother, I did some research and my understanding is that an international workgroup of Alzheimer's researchers in 2011 thought that it might be another 10 years or more before we find the definitive biomarkers of Alzheimer's disease. I'm wondering if you think that's still accurate?

And my second question is do you think this research could be done by your group or other researchers so that it could be looked at not just over 3 years but maybe 10 years to see how the lipids change so that someone can be told 10 years ahead of time that they might be at higher risk for developing Alzheimer's disease? So they have a chance to do something about it, even if it's just addressing risk factors, I know there's no way to prevent it.

Dr. Federoff: So to the first question, you know it's difficult to always predict the pace of progress in any scientific and or scientific/clinical endeavor. I would surmise that if the early observations that we've made are replicated and extended and can be shown to be specific to predicting this phenoconversion and individuals at risk for Alzheimer's disease, then my answer to your question is it could be sooner than 10 years but I think it's conditioned on many things, some of which I've just described.

Now with regard to the second question, if we elected to conduct a study of the type that you've just suggested, it's certainly feasible but it may take quite a number of years to be able to answer and I'll just reframe your question: if this test is able to predict phenoconversion, how early proximate to that phenoconversion would it be able to do so? If we did the study prospectively it would take a large number of years to do and I think that that's certainly a worthwhile endeavor and it's something that I hope would be viewed of as a value in the general Alzheimer's community. But the other way that one could contemplate doing this, which is what I was referring to earlier, is that if we have access to longitudinal studies where individuals were being followed for many decades and if the samples were collected in a manner similar if not identical to that which we have and have been properly stored, then I think we would be in a position just to examine those samples now that some of those individuals have gone on to receive the diagnosis of Alzheimer's disease to answer how early were these lipids able to detect that phenoconverting event and so we're just about to start that work. I'm hopeful that within the next year we can be substantially into that and as soon as we are able to we'd love to be able to share those data with the larger community. But that's the way I see getting to the question a little bit more expeditiously than planning and carrying out a long term what might be a multi-decade longitudinal study prospective of clear value for certain, but that other way that I describe could lead to at least an answer of this type much more quickly.

Question: All right, thank you. That sounds great.

George Vradenburg: Martha, I want to thank you for moderating the USAgainstAlzheimer's Community Support Group. It is a robust and rapidly growing group of caregivers and others who are experiencing Alzheimer's in their families on how best to work through the issues of caring for someone with the

disease. So we're going to send information to all of you after the call on how to join for folks who are interested in that.

I will also make a comment on the biomarker thing. There are right now several, 4, major prevention trials either now recruiting or soon in the next year to begin recruiting to Alzheimer's prevention trials - that is the administration of a potential medicine to those people who are thought to be at higher risk for Alzheimer's but before they have symptoms. And in those trials there are a significant number of biomarkers being evaluated and a recent major, over $100 Million, effort called the Accelerating Medicines Partnership of industry, nonprofits, and NIH is financing the inclusion of additional biomarker measures in those trials. So that we hope in the next 3 to 4 years to have very significant advances in the state of knowledge about the biomarkers that are predictive of Alzheimer's and getting such a biomarker, including possibly a blood biomarker, but other biomarkers as well, or a combination of blood and other biomarkers would be a major game changer in the business so that one could test means of prevention not by waiting to see whether half of your population contracts Alzheimer's symptoms and half does not, but to seeing how the biomarker itself has changed and that would be a much faster way of testing.

There's another question we've had a very large number of people ask, and that is when a blood test becomes available, how much will it cost and is it likely to be insured? I'd ask you that, Howard.

Dr. Federoff: So I think the path to having a test that could be clinically ordered is one that would be available in a local care environment, which has to go through typically two levels of approval: one, relating to the FDA, and the other relating to the Center for Medicaid and Medicare Services. So we've only really just begun to think about that issue given all the other work that I've described and in time we will probably become a bit more sophisticated and we'll probably ask for some help from those who have trodden this path before regarding the transition of a laboratory based observation, a test, into one that might be available in the clinical domain.

With regard to the test itself, we know how much it cost per blood that we currently run, we know something about what is the instrumentation required to do this. We know that this instrumentation is found in a number of laboratories that are so called CLIA-certified and so we believe that the technical and the methodological sophistication required to do a test like this exists in many laboratory environments where other blood test that are ordered clinically are done. With regard to the overall costing of this, I think that it's likely to be far less expensive than certainly ordering a PET scan or a MRI. I really don't know yet about the precise economics but my current guess is that it's probably going to be about 10 times less expensive and that's just based on our current understanding, which as I said before is still a little rudimentary.

George Vradenburg: Thanks. Next question Carole Sawada. This goes to the issue of once a blood test is available who should get it? Carol?

Question: Right. My grandmother had what's now called early-onset Alzheimer's with symptoms showing up in her mid to late 50's and being totally disabled before 62. So naturally it's something I'm alert to and I wonder if it became available, I'll be 54 in two weeks, at what age, if it were available,

what age would you recommend that people start getting tested and particularly in regard to their family history. And thank you for doing this.

Dr. Federoff: Yeah, well thanks for the question. I think that the answer still is unfortunately we don't know enough. I think we have to establish, and some of this is going to be in the context of family history, if there is a time window when the test might be predictive, again with all the assumptions that I'd made earlier that will require external validation, then I think it will be important in that context to look at family history. Would it be relevant in the setting of a family that has for example multiple individuals who may have presented you know 5 or 10 years earlier then would be on average. I think that would be a relevant question, initially I think it would be a research question because I think we know too little right now to know that.

And then finally I think the other thing that's always important to mention and I think that we're at the early stages of beginning to think about the work that we're doing and beginning to compare it to the way one thinks about genetic testing. I think there will need to be counseling for both families, the loved one, the patient, and I began to build part of our team to help me do that. So I've added a clinical bioethicist to help us think through a variety of these issues assuming that our work is going to progress and we will be able to have others externally validate this work.

I wish I could be more concrete with you and I know that this is an important question but I think we're just not at the point where any precision can be brought to bear on saying if it were even available, would it be reasonable for it to be ordered for you because of all of the uncertainties that we've been discussing.

Question: Alright, thank you so much.

George Vradenburg: Our next question is from Reverend Ada Criscione and we very much appreciate her work as a Founder of ClergyAgainstAlzheimer's, one of the newer networks in the USAgainstAlzheimer's family. Reverend?

Question: Yes, hi. I don't know if you can hear me. I'm hoping that you can.

George Vradenburg: Yes.

Question: Okay great. So the question is this, when the history was done on the individuals, were there any significant stressors that were suffered be it hormonal changes in women and were they classified separately in the group?

Dr. Federoff: So in the individuals that were enrolled, the 525, there wasn't any historical feature that stood out among a subset of those individuals that might have been identified and perhaps potentially have been put into the category of being a putative risk factor, you know again it's a relatively small number of people. It's really great question and certainly with regard to antecedent events, you know that might include head injury, concussive illness or other, would want to be established since it has been frequently discussed as a potential risk factor and some epidemiological data would suggest that

prior head injury may be a contributory factor. But nothing stood out in our study that would allow for any discernment of the type that you've just referred to.

George Vradenburg: Thank you for your question Reverend. Next question is from Jack Carter. Jack, would you please ask your question?

Question: All right, yes, Dr. thank you for taking my question and for undertaking this research. My question is, are any of the ten phospholipid metabolites that you have identified in your study, are any of those among those that are typically altered by the cholesterol lowering medications?

Dr. Federoff: Yeah, great question. So right there are several major classes of drugs, those that are called the statins they inhibit the enzyme HMG-CoA reductase but also fibrates are prescribed widely. We have not, Jack, directly answered that question as to whether this lipids would be lowered consequent to the administration of either class of agent. We did have patients not take their morning meds but the way that the levels of drug oscillate and the effect that they have downstream, it could even be the case that drugs taken more than a day prior could have affected blood levels of lipids. We were not able to establish that that was the case in our study - this is a very important question. It's been raised repeatedly when I have and my colleagues have talked about our data and there's only one really good way to answer it, is just to study it directly and so we're going to plan on doing that.

Question: Great, thank you.

George Vradenburg: There's a question here from Cynthia Peill. Cynthia, I think you ask a question which is a good one for everybody on the call.

Question: Hi, thank you for sharing so much information with us. I was wondering, first where the results of the study are published, if it's something we could look at online? Just to review and get some more information?

Dr. Federoff: Absolutely. The paper appeared in a medical journal, it's called Nature Medicine. It was published online on the 9th of March of this year.

Question: So Nature Medicine, March 9, 2014

Dr. Federoff: Right

Question: ... and you are the author of the study?

Dr. Federoff: I'm the senior author, the first author is my colleague Mark Mapstone, the neuropsychologist I mentioned earlier, Mapstone. If one goes online and does a search to find PubMed, which is an NIA supported mechanism to collect publications in the medical and the medical scientific literature you'll find it there.

Question: Could you say that word again? PubMed?

Dr. Federoff: Yeah, PubMed. So if you search PubMed you'll get to the PubMed website and then you could just enter the name of the first author or my name and his and you'll find this paper.

Question: Okay, thank you very much.

Dr. Federoff: You're welcome.

Question: Secondly and that's part of an answer to the second question. What are some of the best sources to keep us informed to allow us to enroll in studies that might come out?

Dr. Federoff: Well I think there are a lot of mechanisms and I'm sure that the organization that George and Trish have established USAgaintstAlzheimer's would be one. But certainly some of the other foundations the NIH operates a website that has clinical trials there are either active or have just been completed, it's called clinicaltrials.gov, so if you search that you'll get to the website and you could search on the website for Alzheimer's trials. They tend to be usually for me trying to look at what's just beginning to enroll the best place to go initially.

George Vradenburg: Last question, we're running out of time, from Wayne Philpott. Wayne?

Question: Okay I'm not sure was I muted?

George Vradenburg: You're on.

Question: Okay, hi. Thank you doctor for your presentation today, for your efforts, it was very interesting. I guess my question is I'm very passionate about this disease, my mother died of it, I have two aunts right now who are suffering from it, I had a fiancé that died of it at 57 years of age. For me and those of us that might be on the call who had been involved with other Alzheimer's efforts for like 6, 7, 8 years now but don't feel that they are with a group that are as aggressive as the one that you are representing here today and we want to redirect our efforts and resources. How do we go about doing that?

Dr. Federoff: Well, I thank you for that. The work that we've done as I mentioned has been a collaborative. It is centered around a large number of people, my self-included here at Georgetown University and it's Medical Center. So that would be the entree to explore whether you and others might have interest in helping to further enable our work.

George Vradenburg: And of course you can go to USAgainstAlzheimers.org and join us but if you will give me a call after this call … or actually I have your number, Wayne because you called in on it, so I'll call you after this call.

Question: Thank you very much.

George Vradenburg: Wayne raised an interesting issue. At the end of this call, you can please stay on the line if you'd like to leave us a message with a question or a comment. We are particularly interested in how you heard about the call, what you would like to hear on future calls, but also any comments you

have like that of Wayne, about how to get more involved in the movement and have some passion and some urgency and some desire to upset business as usual in this field.

Howard, Dr. Federoff, thank you so very, very much for your time today and even more than your time, the time that you invest in research on this disease. It is, as all of us know, touched so many of us. And it is so important that we get at a means of detecting, diagnosing this disease, and then treating it. And so, you're been at the forefront of this, Georgetown has been at the forefront of this and we thank you for your research and thank you for your time.

Dr. Federoff: It's my pleasure and thanks for the invitation.

George Vradenburg: We are also grateful to the Zickler Family Foundation for sponsoring the call.

I'm just going to give you a little tease for those of you on the phone about our next Alzheimer's talks. It's on Friday, June 13th at 1:00 pm Eastern with renowned Alzheimer's researcher Dr. Reisa Sperling. Dr. Sperling is conducting, and now recruiting for, a major clinical trial in this effort in trying to discover a means of treating this disease. And she's going to describe the status of that trial and indeed I will try to evoke from her the status of other trials that are in late stages where we believe that in fact we'll get the results in 2016 and have at least a shot at getting something before the FDA in 2016 or 2017. But Reisa Sperling is one of our best researchers in the same class as Dr. Federoff and she is going to offer up her report on the current clinical trial that she's doing with respect to a treatment for Alzheimer's and she'll answer your questions about her study and about clinical trials and late stage trials more generally.

Thank you all for coming today. Thank you for being on this. Thank you for your interest, your curiosity, your passion, your commitment and I know so many of you, we were not able to get to your questions but we have them here and I know from the questions, how many of you have been touched personally by this disease or how many of you actually are deeply engaged in trying to understand the research around this disease. And so we very much appreciate your participation today and again Dr. Federoff, thank you. And please stay on the line if you like to leave us a message and with that I hope you all have a good afternoon. Thank you.