WEBINAR #2: WHAT'S HAPPENING IN ALZHEIMER'S RESEARCH
20151021 - 1759

2015 ACL/CDC/NIA Webinar Series on Alzheimer’s & Related Dementias
October 21, 2015

JENNIFER WATSON: Okay, good afternoon everyone. It's 2:00 o'clock straight-up. And we’re here together today for Webinar #2 in our Alzheimer's and Related Dementias webinar series, sponsored by ACL, CDC, and the National Institute on Aging at NIH. Today’s webinar, “What's Happening in Alzheimer's Research?” is the second in our three-part series. And I'm so glad you could join us today.

Before our speakers begin, I have a few housekeeping announcements. First, if you have not done so, please use the link included in your email confirmation to get onto Webex. And I'm noticing that many of you are there. It looks like we have over 500 attendees right at the moment. So that you can follow the slides as we go through them, but you can also use the chat and Q&A features on the right-hand side to ask questions during the course of the presentations. We will get to the questions at the very end of the session.
If you don't have access to the link we emailed you, you can also go to NIH.webex.com and click on the “attend a meeting” button at the top of the page and then enter the meeting number, which is 623031136. That’s 623031136. And the event password is 280web2015.

If you have problems getting onto WebEx, please call the WebEx tech support number at 866-229-3239. All of our participants are now in listen-only mode, but we welcome your questions throughout the course of this webinar. So again, use the chat function and Q&A function on the right-hand side of the screen to ask your questions. And we'll sort through them and answer them as best we can when reach our Q&A portion of the program this afternoon.

If there are any questions we can't answer during the course of this webinar, we'll follow up to be sure we can get those questions answered. And if you think of any questions later, you can email me at WatsonJL@NIA.NIH.gov.

We are recording this webinar. We’ll post the recording, the slides, and a transcript on the AOA website as soon as possible. And the link will be at the end of the slide deck
and in the follow-up email you receive. So you will get a follow-up email that will give you lots of information that you're probably looking for. And if you don't find the answer to the question you need, then please just email me at WatsonJL@NIA.NIH.gov.

We’re happy once again to be able to offer free continuing education credits for this webinar, thanks to CDC. All the information about requesting continuing education credit will appear at the end of this slide deck and will be available on the website. You’ll also find a link in the follow-up e-mail that you receive after the webinar.

So in the interest of disclosure, please note that presentations and content today will not include any discussion of the unlabeled use of a product or a product under investigational use. And now I'm really happy to kick off today's webinar.

As I mentioned earlier, this is the second session in our 2015 webinar series, the 4th annual series, on Alzheimer's and Related Dementias for Professionals. This is a collaboration among the Administration for Community Living
or ACL, the Centers for Disease Control and Prevention, and the National Institute on Aging, part of the National Institutes of Health.

The goals of these webinars are to inform professionals in aging services, public health, and research about federal resources available to help people with dementia and their family caregivers [and] to improve coordination of federal resource.

We also have a special focus on encouraging awareness of research and research participation opportunities, which is the focus of another NIA/ACL/CDC collaboration called Recruiting Older Adults into Research, or ROAR.

Just giving you a heads up about the next webinar, the third in our series, will be next month Tuesday, November 17th, Caregivers Supporting People with Dementia: New Research and Technology. And here also is the link to where you can find the detailed agenda for that third webinar and the link to the archived webinars from both this year and the three previous years that we've done this webinar series. So please be sure to look there.
Today’s webinar, What's Happening in Alzheimer's Research, will cover the research plan to cure, treat, or prevent Alzheimer's and related dementias by 2025, engaging participants in studies through the Brain Health Registry, investigating how exercise and diet affect dementia risk, and using technology to monitor, manage, and study dementia and novel early predictors of risk.

And with that overview, I will introduce our first speaker, Suzana Petanceska. Dr. Suzana Petanceska is a Program Officer in the Division of Neuroscience at NIA/NIH, where she oversees research portfolios and programs in basic and translational Alzheimer's research.

Since 2012, Dr. Petanceska has led a number of NIA strategic planning activities related to achieving the research goal of the National Plan to Address Alzheimer’s Disease, and that goal is to prevent and treat AD by 2025. And with that, I'll turn it over to Suzana.

DR. SUZANA PETANCESKA: Thank you, Jennifer. And thank you everyone for joining us this afternoon. In 2012, the United
States launched its first National Plan to Address Alzheimer's Disease. And with that, we joined the growing number of countries determined and committed to curb the crushing socioeconomic impact of the disease.

The first and boldest goal of the National Plan is to identify effective treatment and prevention strategies by 2025. Failure to achieve this goal puts us at risk to live in a world where, by 2020, the number of individuals with dementia, most of them with Alzheimer's, will triple.

Next slide, please. As I just said [inaudible].

Next slide, please. To date, the enormous efforts put toward identifying effective disease-modifying treatments against Alzheimer's has not been successful. This failure is in large part a result of the fact that - next slide, please - that Alzheimer's disease is a disease of tremendous complexity. It is a highly heterogeneous disease with multifactorial challenges.

Decades before an individual presents with the clinical symptoms of AD, the genetic makeup of that individual
interacts with many environmental impacts, and some of these interactions trigger a number of disease processes that propagate and finally result in the clinical etiology of the disease.

Despite tremendous advances in research over the last few decades - next slide, please - despite tremendous advances in our understanding of the disease over the last three decades, we’re still merely scratching the surface of this iceberg, which symbolizes the disease complexity.

Next slide, please. The National Institute on Aging, as the largest funding agency supporting aging research from basic to clinical, was tasked with engaging all the stakeholders who participate in Alzheimer's disease research and [inaudible]. The [inaudible] as well as the research community to formulate a blueprint for a new, bold research agenda that will enable the delivery of the much-needed cures and prevention strategies for all types of aging patients at all stages of the disease.

To do this, the Institute convened two strategic planning research summits, one in 2012 and the second one as recent
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as February of this year, where we brought together over
120 scientists from academia, industry, advocates, [and] researchers on other comparable diseases to rethink how we go about studying a disease, understanding the drivers of the biologic processes, and to develop [an]intervention.

Next slide, please. This is just a listing of the major topics that were discussed at the 2015 AD Research Summit. And as you see, they’re arranged from what kind of research approaches and resources are needed to get a full understanding of the heterogeneity and multiple challenges of AD, putting forward a new paradigm for AD drug development that will be collaborative, participatory, predictive, and productive; identifying the strategies for AD prevention; bringing innovative technologies to advance disease monitoring, assessment, and care; and, very importantly, strategies to better empower patients and engage citizens in the research process and come up with new ways to partner amongst stakeholders to accelerate the innovation that is needed to deliver this.

Next slide, please. Some of the key messages that the summit participants put forward are the following: the need
to recognize the heterogeneity and multifactorial nature of the disease and develop research programs that can really take this heterogeneity head-on and develop a good understanding of it.

The need [is] to really understand to a much better and greater extent what healthy brain aging is all about and what are the predictors of how people are doing, which is really needed to inform prevention strategies for AD.

The need to bring new research approaches to the AD field and to ensure that the knowledge that the community generates, the research models, the biological specimens, are shared rapidly and extensively to accelerate the process of discovery and drug development.

The need to build new multi- and cross-disciplinary translational teams, that not only bring together basic professional and clinical researchers, but will also enable a marriage, if you will, between the biologists, the engineers, the mathematicians to work on the [inaudible] disease and develop interventions.
The need to develop strategies to overcome intellectual property barriers that slow down innovative processes in drug development and come up with new public/private partnerships.

And, last but not least, bring patients, caregivers, and citizens forward as more direct partners in research.

Next slide, please. So the summit participants put forward a series of research recommendations that the NIH scientists were able then to translate into research implementation milestones, which in fact is a research framework that is meant to enable everyone participating in Alzheimer's disease research and drug development to band together toward achieving the goal of identifying effective cures and prevention strategies.

These research implementation milestones will be used by the NIH to develop new funding opportunities, new research programs, and new public/private partnerships.

One such partnership - next slide, please. The result of a launch of a number of new programs is a new partnership,
the Accelerating Medicines Partnership for Alzheimer's Disease. This venture brings together government, industry, and nonprofit organizations to work on two big topics and two big problems – bringing new approaches to the discovery of the next generation of therapeutic targets for Alzheimer's disease and, second, testing the utility of new biomarkers as markers for disease progression and markers for drug responsiveness.

This is one of the programs launched in 2012 that aims to – next slide, please – to really lay the foundation for precision medicine for AD, which in fact means enabling us to treat the right disease properly with the right drug in a patient who will respond to the drug at the right stage of the disease. Thank you.

JENNIFER WATSON: Thank you, Suzana. I really appreciate you joining us today. Next up, we have Dr. Michael Weiner, who’s a Professor in Residence in Radiology and Biomedical Imaging, Medicine, Psychiatry, and Neurology at the University of California, San Francisco.
He’s the principal investigator of the Alzheimer's Disease Neuroimaging Initiative, also known as ADNI, and the Brain Health Registry that he's going to talk to us about today. Handing it over to you, Mike.

MICHAEL W. WEINER, M.D.: Thank you, Jennifer. Can you hear me clearly?

JENNIFER WATSON: Yes.

MICHAEL W. WEINER, M.D.: Good, okay. Next slide. Jennifer, if I’m running over time, just tell me to cut it short, okay?

JENNIFER WATSON: Will do.

MICHAEL W. WEINER, M.D.: Okay. So this slide shows my disclosures, which are many because the Alzheimer's Disease Neuroimaging Initiative receives lots of support from the pharmaceutical industry. And my grants are listed at the bottom of the slide. Next slide. Is this slide 3?

JENNIFER WATSON: Yes.
MICHAEL W. WEINER, M.D.: So the Brain Health Registry, what I’m going to talk about, is a website. It’s a website for recruitment, screening, and longitudinal monitoring of subjects for Alzheimer's trials and neuroscience research. This is a website that works, as I’ll describe to you. It's a low-cost way to accelerate the development of treatments for Alzheimer’s disease. And the reason why it does this is number one, it’s low cost. It’s a website. It’s scalable. We can recruit a lot of people at extremely low cost.

It reduces screen fails at sites because we get a lot of information on the subjects before they’re sent to the sites for enrollment into a trial. And this lowers the overall cost of trials and speeds the development of treatments. The idea is that we're going to speed up the development of treatments by speeding up clinical trials, by getting subjects to the clinical sites more quickly, and by reducing screen fails.

Next slide. So our overall goals are to accelerate neuroscience research, especially Alzheimer’s trials. It’s an online registry as I’ve described. By the way, the registry is available to any investigator. For example,
other investigators around the country, if they want to use this website, they can work with us. We can refer them subjects. We have a goal to establish a large cohort of participants who are monitored longitudinally. When I say large cohorts, tens of thousands, hundreds of thousands. In an ideal world, we would have millions of people to monitor longitudinally.

We want to share the data, and we want to provide participants who are interested to other investigators to facilitate their trials. We want to provide prescreened and longitudinally monitored participants for randomized treatment trials.

Next slide. So I’m going to describe the website, talk about how we enroll members, get the information, and talk about how we refer subjects into clinical trials.

Next slide. So this is a website based at the University of California. It’s approved by our IRB. Everybody signs in, and we obtain informed consent online. By the way, I encourage everybody who’s on this phone to go to brainhealthregistry.org and sign up and join the Brain
Health Registry. You’ll see what it's like. It doesn't take you much time. We don't charge you. And you can help speed the development of Alzheimer's treatments by joining the registry.

So the registry consists of questionnaires which are essentially self-report. We ask you questions about yourself. How old are you? Do you have a family history? Do you have a memory problem? Are you depressed? How well do you sleep? What medications do you take, et cetera.

And we are developing what we call the informant or study partner questionnaires. That is that your spouse or your family member or a friend who knows about you could sign up and give information about you, obviously with your consent. Because getting information from study partners, or what we call informants, is very important, especially in the field of Alzheimer’s disease, where the subjects themselves may not be the best judge of how well they're doing.

We use online neuropsychological tests. One is Cogstate and one is Lumosity. And I'll describe these more a little
later. But these are essentially computerized tests which allow us to figure out how well people's brains are functioning. And then we do this longitudinally. People are asked to come back every three months or every six months, and we plot the change over time.

Next slide. So this is what our home page looks like. This is an example. Our home page changes. This is B. Smith, who is an African-American model and a restauranteur and author who’s developed unfortunately Alzheimer’s disease. And you can see, we have some others. Draymond Green of the Golden Gate State Warriors did a public service announcement and so forth. And what we want people to do is click that button that says “join now.”

Next slide. And if you click “join now,” you join. And basically, it’s quick. It’s safe. It really is easy to sign up. You tell us about yourself. You play some games, which are these cognitive tests. And then we ask you to come back longitudinally. And you keep coming back more and more longitudinally.
Next slide. This is an example of what the website looks like. You can see on the left-hand side there, there's the medical history, your early medical history. That is your childhood history, your diet, questions about your everyday cognition, family tree. So you have a choice of which of these you want to take. It doesn't all have to be done at the same time.

Next slide. Cogstate, as I mentioned, is one of our partners. Cogstate provides a computerized, online neuropsychological test.

Next slide. The test uses playing cards. They show you different playing cards and you have to remember which cards you’ve seen or you have to react to them. So all of these tests basically use playing cards in one way or another. So, in a way, the tests are very simple. But sometimes they are quite demanding because you’re asked to remember, for example, have you seen this card before? And they show you a bunch of cards and then they show you the jack of diamonds again. And you have to remember if you saw the jack or diamonds three or four cards back.
Next slide. Lumosity Labs. They make Lumosity, computer games which you can play online. They also have online neuropsychological tests.

Next slide. Lumosity has over 60 million users, mostly in the United States, but also, as you can see, in Europe and around the world. Lumosity is a partner, and they have been advertising the Brain Health Registry to their users. So this is a way that we are expanding our members by both using their tests and by taking advantage of their advertising.

Next slide. So, we do a lot of different kinds of advertising. We work with advertising agencies, and we work with sponsors who are interested in growing the registry. Because, for example, a pharmaceutical company might be interested in doing a trial with sites in Texas or Southern California or Florida or the Boston area. So we do Google advertising or Facebook advertising and public relations and emails. And we market the site. We get people to sign up. And that's how we grow the site.
Next slide. So, currently we've only been operating a little over a year and we have 31,000 people signed up. And we continue to grow quite rapidly. About half of the people who join return at six months for repeat testing. So we have at least 15,000 people now who’ve come back at six-month and one-year visits. So we have a huge cohort of subjects already. It's mostly been in the San Francisco Bay area where we focused our advertising, but we are growing in other markets. And I think you can start to see how this could be used for enrolling people into clinical trials. But the next few slides give you a better example of that.

Next slide. So this tells us something about the site. So you can see we're having 75 percent of the people who’ve joined the Brain Health Registry are women. So in this case, males are starting to become almost an endangered species or an under-represented minority.

Next slide. This shows the age distribution of the Brain Health Registry. You can see about half the subjects are in their sixties, seventies, and eighties. We also have a lot of young people we could use for other kinds of studies.
Next slide. You can see that 30 percent of the people who join the Brain Health Registry report a family history of Alzheimer’s disease, which is higher than the general population. So we are getting people who are interested in Alzheimer’s, and that’s why they're joining.

Next slide. And this shows you something about the other kind of medical problems and issues, risk factors, that we capture in our various questionnaires. We get a lot of people reporting heart disease and hypertension, elevated cholesterol, diabetes, and so forth. And we can use this kind of information to screen out people so that they're not referred into a clinical trial, where they would be screened out after they got to the clinic.

Next slide. So currently, we’re focusing on two kinds of Alzheimer's treatment trials, what are called prodromal trials. These are patients with mild cognitive impairment who have amyloid in their brain. And secondary prevention trials. These are cognitively normal subjects who also have amyloid in the brain. The A4 study is an example of a secondary prevention trial. And there are a number of prodromal trials underway.
Next slide. And this next slide shows you the subjects we have in our database who will be eligible for a prodromal trial in the United States or in the San Francisco Bay Area. So if you go over to the far left-hand side, the bar graph, you see there where it says All MCI. You see that there’s 1,513 subjects that we have in the United States who appear to meet the criteria for MCI, meaning that they have a memory complaint and that they score low on their memory test.

If you look in the San Francisco Bay area, that orange bar, it appears that we have about 400 subjects who look like they might have MCI, that is they’d be eligible for a prodromal site in the Bay Area. And then we can apply some additional inclusion or exclusion criteria, depending on how we use the database.

For example, we might want to rule out people who have other neurologic diseases or rule out people with alcohol abuse or rule out people on antipsychotic meds. And if we start ruling out all those people, you can see that on the far right, we’ve got about 1,191 subjects in the United
States and still about 300 subjects in the Bay Area. And there’s only two or three clinics in the San Francisco Bay Area who are doing MCI trials. So having 300 subjects who can be referred to those clinics is a substantial number of subjects. And what we’d like to do is build up our population so that we could refer subject in other areas as well.

The next slide does a similar thing for the prevention trial. And the prevention trials are looking for normal people over age sixty. You can see we have 6,000 people enrolled over the country and 2,600, I guess it is in the Bay Area. And if you look over on the far right, even with applying all of the exclusions, we have still over 5,000 people in the United States and over 2,000 people in the Bay Area who would appear to be eligible for a prevention trial. That’s a lot of people to get enrolled into a trial. It’s far greater than the number that you could possibly enroll in the San Francisco area.

Next slide. But another question you might say is, “Okay, well, you’ve shown that you can get people into your website and you’ve shown that you've got people who are
eligible for trials. But how many of those people actually would go to a clinic if you email them and tell them to go to a clinic?

So we’ve had experience now with several hundred people who have gone to clinics. And we find that for every five people that we send an email to, about one will go to a clinic. That is about 20 percent of the people that we contact end up going to a clinic.

Now, you might say, “Well, gee, that's not so good. That’s only one out of five.” But the point is that with website registration, which is very scalable and fundamentally very inexpensive, we can enroll many, many hundreds, thousands of people in different areas and then refer those to the clinics. So that's basically the way this all works.

Next slide. So it’s a website. Brain Health Registry. I hope you'll go to the Brain Health Registry. It’s a website for recruitment, screening, and longitudinal monitoring of subjects for Alzheimer's trials in neuroscience research. It really does work. It’s a low-cost way to accelerate the development achievements for Alzheimer's disease. It
reduces screen fails at sites. It reduces the overall cost of trials. It speeds development of treatments.

From my experience with doing the Alzheimer's Disease Neuroimaging Initiative, I’ve come to the conclusion that the single biggest obstacle toward finding an effective treatment for Alzheimer’s Disease is simply getting people quickly into clinical trial sites. So the clinical trials can run and reduce their cost. If we can speed up trials and reduce costs, we can test more drugs and we can get to a cure more rapidly. And this website is a kind of a low-cost approach toward achieving that goal.

So there's one more slide. Coming to a theater near you: brainhealthregistry.org. I hope you join. Thank you very much, Jennifer.

JENNIFER WATSON: Sure, thanks. Thanks, Mike, for being with us today. And as you see here, the URL Brain Health Registry is right here on your screen. Thank you all for submitting your questions through the Q&A function on the right-hand side of your screen. We will circle back to those questions at the end of the webinar.
Next up is Dr. Laura Baker. Dr. Baker is an Associate Professor of Internal Medicine, Neurology, and Public Health Sciences at Wake Forest University. Dr. Baker’s been an investigator of over fifty clinical trials related to aging and AD progression, treatment, and prevention, including several trials to study the potential therapeutic effects of high-dose aerobic exercise for adults who are at high risk for dementia. And so without further ado, I'm going to turn it over to Laura.

DR. LAURA BAKER: Thank you, Jennifer, and thank you for having me today. And so where I want to take us is on a trip that's going to entertain the idea that something that we all know very well, and that is exercise, might actually benefit more than just your body. And so, we all know that exercise keeps your body's machinery working properly, with positive effects on your muscles and your circulation, your metabolism. And it could even improve your mood and your ability to manage your stress.

I think what we did not always know or maybe we neglected to consider is the possibility that exercise may also be
good for the brain. We know that exercise has many health-restoring effects, and it may increase your resilience, not only to physical ailments, but also to cognitive decline in Alzheimer's disease. Alzheimer's disease is a heterogeneous, multifactorial disease, meaning there's many systems and pathways that are affected. This is the beauty of exercise. Exercise also has many pathways and systems that it can positively impact.

And so the question is, can exercise meaningfully restore health to these systems that are compromised with aging and with Alzheimer's disease as it progresses?

So, as Americans, we've picked up some bad habits. Addictive food can be found at every corner at a fairly low cost. We've become much more sedentary, going great lengths to avoid extra walking, from car-assisted dog walks to circling the parking lot many times over to find a parking space for your car.

Our communities, as we all know, have evolved to require some form of motorized transportation to get from point A to point B, thank you to urban sprawl. We are tired. We're
overworked and overtired at the end of the day and would prefer to sit in front of the TV and be entertained than to be active. The latest soundbite that you may have heard is that “sitting is the new smoking,” with very similar effects on health, and particularly for older adults who are more vulnerable.

And so in our search for effective interventions to meaningfully change the trajectory of cognitive decline and Alzheimer’s disease onset, might it be the case that if we can reverse these trends and increase exercise, could we have an intervention that could meaningfully change the progression of Alzheimer's disease?

We know from years of scientific work that exercise has potent benefits for both the body and for the brain. And there’s a host of studies conducted in animals that kind of set the stage for our work in humans showing very powerful potent effects, where we see magnificent changes in the brain in response to very short periods of time of exercise. And these changes in the brain suggest that exercise increases resilience. It reduces the effects of inflammation. It reduces the effects of stress. It
increases the function of the blood vessels. And it may reduce Alzheimer's pathology.

Now, in the last fifteen years, there have been a number of people studies looking at, testing whether this intervention that works so well in animals, can we get it to work also in people? And there's been a few studies completed so far that are showing some positive results to suggest that, yes, we should probably start looking above the neck for exercise benefits that might impact and preserve and protect the brain.

Next slide. So today I’m going to tell you about the results of a study we just completed here at Wake Forest to test whether aerobic exercise might improve cognition and slow progression of Alzheimer's disease for older adults with mild cognitive impairment.

And so what you're seeing on the screen is the study design. And we had about 70 people who are enrolled in our study. They ranged in age from 58 to 89 years old. And they were either assigned to complete an aerobic training, a
high-intensity aerobic training, or a stretching and balance program for six months.

At the beginning of the end of that six months, we tested their memory and thinking skills. We collected cerebrospinal fluid using a lumbar puncture so that we could more directly look at the recycling, the brain’s recycling, in this fluid, which gives us a much better picture than blood ever would in terms of what this intervention might be doing in the brain. We also completed some brain imaging to look at resting blood flow and the structure of the brain before and after the exercise.

So here is a description of our intervention. So, for the six months, each group, the stretching group and the high-intensity aerobics group, they completed 45 minutes a day, four days per week, for six months using our local YMCAs. In the first six weeks, we only recruited sedentary people. So if you can think about this as if you are already an avid exerciser, it may be that you have already reached your peak capacity in terms of a cognitive improvement and other improvements in terms of brain function.
So we only recruited sedentary folks. So it was very important that we gradually step people up from the beginning to the sixth week of the program. They were supervised by a trainer for the first eight weeks and then only once a week after that. But they’re still required to exercise four times a week. And they had many different, we had many different ways to monitor whether they were completing their, taking their exercise medication.

So, the two pictures at the bottom show the two groups. One is the exercise group. And in the high-intensity exercise group, we had people exercising at 70 to 80 percent of their maximum heart rate using a treadmill, stationary bike, or elliptical trainer. And on the right, showing a picture of a quite flexible individual, where in this particular group people were required to have all the same activities. And they had to leave their home. They had to go to the YMCA. They worked with a trainer. But they kept their heart rate at a very low rate, beats per minute, and still completed all the same number of sessions.
So, the first finding I’m going to share with you has to do with the exercise effects on one of the hallmark biomarkers associated with Alzheimer's disease that also increases with aging. What you’re seeing here in the picture in front of you is this exercise-related change in this hallmark that I'm referring to here as phosphorylated tau protein. And this is phosphorylated tau protein in the cerebrospinal fluid that we obtained through the lumbar puncture of our participants, who completed either the aerobic training program, which is the red bars, or the stretching program. That's the blue bars.

And what you can see here is that the red bar on the right, this is going downward. These are our participants who are over the age of seventy who completed the aerobic training program.

So what we found is that high-intensity aerobic exercise, compared to stretching, lowered the levels of this hallmark protein in cerebrospinal fluid for people who are over the age of seventy. For people who are younger, we did not see the exercise effects.
I have not shown this that I’m going to tell you. But what we learned about these people who are over seventy is that when we look at the levels of this protein in their cerebrospinal fluid at baseline, before the exercise, their levels were higher than all the other adults. So it may be that these [individuals] over seventy year olds have higher levels to begin with, and then with exercise, they have more room for improvement.

So the second finding I’m going to show you has to do with exercise effects on blood flow in the brain. And I want to make the point that what I’m going to be talking about is blood flow at rest, not during exercise. What we found is that for the brain as a whole, blood flow is increased for those who completed the high-intensity exercise, aerobic exercise program, compared to those who complete the non-aerobic stretching and balance program. And so that's what I’m showing here in the graph. And the increase bar just reflects increase flow.

So here I’m showing you the specific regions of the brain that benefited the most from the exercise intervention. And so the different colors just simply reflect different
regions. So the blue area is the posterior parietal region. That's typically affected most -- most heavily hit by Alzheimer’s disease. We see the largest reductions in blood flow in that blue region with the progression of Alzheimer's disease. The red region is the area that’s affected most by aging. So in the red area, with normal aging, we see reduced blood flow in this particular region. The green is single area bordering the ventricles. We see reductions in this area both with aging and with Alzheimer's disease.

And so what I'm showing you here in this picture is that all three regions showed increased blood flow at rest following six months of aerobics exercise. And so these are changes relative to people who participated in the stretching program. So on your right are the graphs that just show you graphically the difference between the stretching group on the left and the aerobics group on the right. And the colors just simply correspond to the different regions.

So it’s a remarkable difference. We've got the right side of the brain and the left side of the brain I’m showing.
But it’s a remarkable difference in blood flow between people who participated in this higher-intensity versus a lower-intensity exercise.

And so what do those regions mean? And why is that important? On the left, what you can see is – what I’m showing you here is the findings of other investigators who showed that with advancing age, the frontal region of the brain shows the greatest reduction in blood flow. So remember I just showed you that this is exactly the region that exercise increased blood flow in this region.

On the right, I'm showing you a picture of brain regions that show the greatest blood flow decreases with Alzheimer's disease. So I’m looking particularly at the blue regions. And you'll see that this blue region in the pictures on the right are very similar to the very regions that we saw increased flow in response to exercise.

And so the third and last finding I’m going to share with you today has to do with the effects of exercise on cognition, something that we all care about tremendously as
we get older and particularly as Alzheimer's disease begins its course.

In this study, we tested both short-term memory for what you see and hear over the past few minutes, days, and weeks. But we also tested what's referred to as executive function, and that is our ability to plan, initiate new tasks, complete what you started, multitask, and focus attention. These are the kinds of tasks that we refer to as your CEO part of the brain. It kind of takes charge of where you need to be at any given point in time.

So what we discovered is that with exercise, we did not see any change in the short-term memory. What we did see is change, dramatic change, in your ability to plan, organize, focus, and multitask. So your executive function was -- a person's executive function was greatly benefited with the aerobic exercise.

In the little red box here, I have this idea that we are entertaining, that executive function, these kinds of tasks, these CEO-like tasks, may be more immediately sensitive to the effects of exercise. And it may be that we
need to exercise longer to see benefits in memory. So remember, our trial was only six months. For someone who has mild cognitive impairment and changes related to age, that's a really short period of time relative to the scope of that person’s adult history.

Okay. And to finish up, what I want to hopefully leave your with is that this regular, what we tested here, this regular moderate- to high-intensity aerobics exercise is worth the sweat. It may slow the effects of aging and Alzheimer's disease in the brain and improve cognitive function.

And I think this is a good segue to the next presentation, and that is this kind of a lifestyle intervention. And what I mean it’s not just a lifestyle intervention, but it's a high-dose lifestyle intervention. It's not casual walking. You have to exercise and with exertion to place a physiological challenge on the body.

This kind of high-dose lifestyle intervention, such as exercise or diet, has numerous health-restoring effects that may be quite a promising way to prevent and slow the
disease. And we are going to take this work into another phase. And this is a new study that was funded by NIA to test whether this kind of an intervention, this alternative, strange, nonpharmacologic intervention, can meaningfully slow disease and improve cognitive function for people who are at high risk for developing Alzheimer's dementia.

So the NIA has funded a new trial that will begin in January all across the nation, this test. It's a much longer trial, but our hope is that at the end of this trial, we will have answers about whether this kind of an intervention could meaningfully slow this disease.

JENNIFER WATSON: Thank you so much, Laura. We really appreciate you being here with us today. And we’re moving on next, moving right along to Dr. Martha Clare Morris, who's also with us today. Dr. Martha Clare Morris is the Director of the Section of Nutrition and Nutritional Epidemiology in the Department of [Internal] Medicine at Rush University. And she’s a pioneer in research on dietary risk factors for Alzheimer's disease and cognitive change with aging. And we'll be talking today about the MIND diet. Martha Clare.
DR. MARTHA CLARE MORRIS: Thank you, Jennifer. You can go to the next slide, please. So this first slide, I’m presenting what we know to date from all of the scientific studies done thus far on nutrients and foods in relation to neurodegenerative changes in the brain.

In the left-hand column are the nutrients and in the right-hand column are the primary food sources of those nutrients. So the top quadrant gives those nutrients that have the strongest evidence thus far. So this means that there has been a number of animal models that have demonstrated the biologic mechanisms by which that nutrient impacts the brain. And there’s also been consistent prospective epidemiological evidence that the nutrient slows cognitive decline and reduces incidence of Alzheimer's disease. And there have been a few well-designed clinical trials that also provide evidence, in particular, folate.

So the nutrients that have the strongest evidence thus far are dietary to tocopherol, which is known as Vitamin E; DHA, one of the omega-3 fatty acids; folate from dietary...
sources and supplements in those with low or marginal status of folate; and a diet composition that is higher in the unsaturated fats compared to the saturated fats.

Those nutrients that have moderate evidence, that means that either the studies are rather conflicting and/or there's just too few studies done, include carotenoids, beta-carotene and lutein in particular; flavonoids; Vitamin D; trans fats; monounsaturated fat; and polyphenols.

Next slide, please. So I thought I would just give an overview for each one of those important stronger-evidence nutrients. And the slide presents the data for prospective studies that have looked at either of these antioxidant nutrients in relation to dementia or cognitive change. And some of the studies that used biochemical levels of nutrients in plasma are serum, but most were obtained through dietary assessment methods.

And the plus signs indicate that the study found a positive benefit of the nutrient, a statistically significant benefit. And what you can see from this table is that
Vitamin E by far has the most consistent evidence of association out of all the antioxidant nutrients. Vitamin C and beta-carotene are very inconsistent. And flavonoids, there's just not enough studies.

Advance please. And this table presents the prospective studies that looked at B Vitamins in relation to incident Alzheimer's disease. Some of them are quite large. And again, the way of assessing the nutrient status was either through biochemical levels or through diet. And here the downward arrow means that higher folate was associated with decreased risk of developing Alzheimer's disease. And you can see that the studies are very consistent for folate and negative for B-12. We do know that B-12 has a neurologic syndrome, deficiency syndrome, that is associated with cognitive issues. But for Alzheimer’s disease, the evidence is null.

Please advance. And in this slide, this presents the prospective studies that looked at fat composition in relation to cognitive decline. Most of them used a global measure of cognitive tests. And again, it’s a mixture of diet and biochemical measures of the dietary component.
So there’s fairly consistent evidence that high saturated fat intake was associated with increased cognitive decline, and less so for the unsaturated fats -- monounsaturated and polyunsaturated fats. But a key issue in the methodological issues with these studies is that that not too many of them simultaneously adjusted for other types of fats. And they’re highly confounded. So this might be more clear if these studies had appropriately adjusted for fat composition.

So we’ll advance to the next slide. And here are the prospective studies that looked at fish intake in relation to the risk of developing Alzheimer's disease. The yellow bar in the middle is a relative risk for a ratio of one. So you can see that most all of the studies are showing a protective relation, and with just one fish meal a week. Perhaps the one study that was not statistically significant, it included that one fish meal a week in the reference category.

Advance please. There aren’t a large number, but there are five studies that have looked at vegetable and fruit
consumption separately, in relation mostly to cognitive change. And what's interesting to see is that the studies that looked at vegetable intake consistently show a protective association, but fruits are not associated with cognitive change. And MCI was one of these studies.

Advance please. There have been three large studies now that have demonstrated that green leafy vegetables in particular are associated with slower cognitive decline. This is data from the Rush Memory and Aging Project of 960 individuals followed between two and ten years and adjusted for all of the more important risk factors. And you can see the top quintile of intake [had] significantly slower cognitive decline than the lowest quintile of intake of green leafy vegetables. That top quintile was just over one serving per day of green leafy vegetables.

Advance please. So moving onto dietary patterns. There’s been a number of studies now that have looked at the Mediterranean diet in relation to cognitive decline. And about half of them show significant association with either cognitive decline or risk of developing Alzheimer's. There’s been one randomized trial in Spain called the
Predimed study that looked at a secondary outcome and also cognition and found that the randomized group to the Mediterranean diet did better on cognitive tests.

The DASH diet is another -- this is a diet that was developed to reduce blood pressure and prevent hypertension. And also a secondary outcome of cognition in a small randomized trial found that the DASH diet was [linked to] slow cognitive decline.

So we had decided that both the Mediterranean diet, which is a cultural diet, and the DASH diet, which was developed and tested to reduce cardiovascular conditions, they’re focused and studied in relation to cardiovascular disease. But they do not integrate or consider the vast body of research now relating nutrients to the brain.

So our investigative team here at Rush developed a diet called the MIND diet that takes as a basis the DASH and Mediterranean diets, but then integrates the nutrients and food groups that have been shown in the literature to be protective for the brain.
So in this first slide, I’ll just highlight what some of those differences are. So the Mediterranean diet you see in the second row, they eat quite a few potato servings, about two a day. So we don’t specify any potatoes because that’s not been demonstrated to be good for the brain or protective for the brain.

You see in the next row, both diets have quite a few servings of fruits per day, the DASH and the Mediterranean diet. But in the dementia literature, fruits do not have association with slowing cognitive decline. I didn’t have time to present it, but there is a literature on berry consumption in particular being protective of the brain. So we do specify berries. So those are just some of the highlights of the differences of the MIND diet.

Please advance. And this slide present there are fifteen components to the MIND diet, and those are listed in the left-hand column. And we have scoring ranging from zero to one for these fifteen components. And we tested this in our Rush Memory and Aging Project.
Next slide please. So in this study, we had MAP participants that were included in the study because they had at least two cognitive assessments so that we could look at change. And they had diet measured at the first cognitive assessment. The cognitive decline measure was based on a battery of nineteen cognitive tests, and we took the Z score of those tests and averaged them.

And the mean period of observation was four and a half years, which ranged from two to ten years. We had a comprehensive diet questionnaire of 144 food items that we had validated in an older population in Chicago. We also looked at incident Alzheimer’s disease in this study population, and there were 114 incident cases over that follow-up period.

Advance please. So here’s the data looking at the global cognitive scores, the outcome, on the Y axis. And we have here the tertiles of the MIND/diet score. The top tertile, that big dash at the top, had the slowest cognitive decline. And in fact the rate of decline for that group was approximately equivalent to being seven and a half years younger in age compared to the lowest quintile. The second
quintile was also significantly slower than the lowest quintile of scores.

Advance please. We also ran similar models for the Mediterranean diet score and the DASH diet score. Then to be able to compare the estimates of effect, we used standardized beta coefficients. And as you can see, the MIND diet score had almost double the effect size than either the Mediterranean diet score or the DASH diet score on cognitive decline. But all were statistically significant.

Next slide please. So here’s the data looking at incident Alzheimer's disease as the outcome and relating the MIND diet at the baseline to the risk of developing Alzheimer's. So the first tertile of score is the referenced category here in this table. And you can see that even the second tertile of scores had a statistically significant reduction of 35 percent compared to the lowest group. And the highest group had a 53 percent reduction in the risk of developing Alzheimer's disease compared to that lowest group.
I was not able to include the slides for the Mediterranean or DASH diets. The top tertile of those scores was also significantly associated with lower risk of Alzheimer's, but in neither one was the second tertile associated with a decreased risk. So this diet being specific to the brain seems to, you know, even moderate consumption seems to be protective.

Next slide, please. So in summary, this MIND diet score that's specifically tailored to the literature, nutrients and foods that protect the brain, was strongly associated with a slower rate of [cognitive] decline and also a lower risk of developing Alzheimer's disease. It was more predictive of dementia than either the Mediterranean or DASH diets. I think that this is an important step to moving toward developing or specifying a diet that's specifically tailored to keep the brain healthy.

And I see this as the first step. Because as the literature develops, we learn more about new foods and nutrients, we can modify this to get an even better diet. And, of course, these findings need to be replicated in other studies,
other populations. And the ultimate would be to conduct a randomized clinical trial. Thank you.

JENNIFER WATSON: Thank you, Martha Clare. We’re next going to move to Dr. Jeffrey Kaye, who’s a Professor of Neurology and Biomedical Engineering and the Director of the Layton Aging and Alzheimer's Disease Center at Oregon Health and Science University, as well as Director of the Oregon Center for Aging and Technology, also known as ORCATECH. I’m going to flip control of the screen over to Dr. Kaye. Go right ahead. We still don’t have any sound from Jeff. Jeff, you might need to take it off mute.

DR. JEFFREY KAYE: All right. I’m going to start in. I don't know if people heard what I said. So I’ll start it again to say good morning and good afternoon, depending on where you are in the world. And I’m going to barge ahead in the interest of time here because we had some brief technical challenges.

So, I hope to present the role of some new technologies and approaches to assessing and understanding how people age and develop cognitive changes in the real world. And
hopefully, this will translate into better clinical research as well as treatments.

I want to start by framing this discussion by reminding us all that we have a lot of challenges in our research that, really, it’s not the fault of anybody. It’s just the natural condition of being human and being intra-individually variable.

So what is shown on your screens are the individual test scores of individuals who had been in the ADNI protocol, going from left to right, a group of people who are normal, [people with] MCI, and then people with Alzheimer's disease followed over thirty-six months. And then the top panels are their scores on a memory scale and on the bottom are their scores on a composite executive function. And what you see is how it’s challenging to really look at a group and with great precision determine whether there is a particular degree of change, and particularly difficult is to be certain about an individual’s change.

To illustrate this point further, I have this diagram here - actually, I’m going to backup. So if you were measuring
people every day, you would see this kind of change. However, in the conventional way that we measure people -- so if you look at a memory score on an almost annual basis, you might get data points that look like this. And really what you'd say is, if you only had those data points, you would say, “Oh, well, maybe this person is getting worse.”

But in reality, they aren’t getting worse. You just picked data points that were a particularly good day or a bad day.

And so this difference, this ability to look at people over every day provides the opportunity to even look at the day-to-day variability, which itself maybe an opportunity to look at change that is presymptomatic or telling us that somebody is going to be developing symptoms of dementia at a later date. And so the conventional data points are difficult to pick out what's happening, whereas, if you had much more continuous, frequent data, you would have a much better opportunity to determine real change.

With that in mind, this is a model that we have been using to say how we might make this change. So if you look on the left side, you see the characteristics of the current way we look at change, that is, we use clinic appointments that
are brief because we only spend so much time in evaluation. They tend to be episodically spaced, so there’s long periods where we don’t have any information. They’re often clinic-based, or even if they’re home-based, they still have this brief episodic characteristic to them.

They’re largely subjective. So we rely a lot on self-report, which is very difficult to be accurate about. We have shown that 25 percent of entirely healthy, normal, cognitively intact individuals can’t tell you accurately what they were doing in the last two hours. So somebody will say I was at the gym or I was in bed or whatever, but in fact they really were not. So it’s very hard to relate all of these things that we ask people over long periods of time about.

And we also are relatively intrusive, or intrusive in the sense that we’re taking people out of their home environment. We often are using some tests that are not very much fun, such as actual cognitive testing itself, and therefore inconvenient.
On the other hand, if you go over to the right side of this slide of this figure, the idea is to look at real time, continuous, ideally home-based, and more objective measures that are unobtrusive and ultimately ambient, in that the measures come from everyday living. So whether you’re sleeping, using your computer, taking medications, all of these things are derived from your natural activity.

The way to go from the left to the right is what I'll be describing in the next few slides, and that is to use the advantages of some recent technologies that are actually now well-established, the technologies around pervasive computing. What's meant by that is simply the use of computing capacity, sensing capacity, that's embedded in the environment. The best way to think about that it is, for example, our current automobiles are really in some ways computers on wheels. They do lots of things because they literally have computers in them to monitor and understand what the car is doing, obviously driven by you. But these kinds of technologies are now, as you'll see, available for use in the home and in clinical research.
The wireless capacity untethers people, untethers the data, allows us to move the data around seamlessly. And then, because the data is continuous and multi-domain, it’s classically what might be called big data. And so there’s a lot of analytics around this that we now have the capacity to employ and get really much more effective answers.

So using these technologies, we want to build evidence that we think will lead to actually new observations and discoveries about what's really happening in the real world for people who are challenged with cognitive change. Obviously, the ultimate goal for those who will have change or have it already is to have treatments and more effective research leading to those treatments that would have better outcomes for patients and families.

In the next slide, what you're seeing is how we do this or how this might be done. We are doing this. There are a few other places in the U.S. and around the world that are taking this approach now. What you see on the left side is a floor plan of a typical home or apartment. And around the home, I’ve placed various technologies that exist and that we use in volunteers who agree to have these technologies
installed in their home and turned on. And their instructions are to live their life as they normally do. And we call these volunteers members of a life laboratory. And the laboratory is their home and their lives.

In these homes, we install a number of simple technologies, ideally passive-activity sensors that tell us where activity occurs and how much activity. So we can look at nighttime or sleep activity, walking speed, and very important mobility measures.

On the top, we also are able to look at simple physiologic measures such as weight, body composition, heart rate, using, for example, wireless scales. Looking at medication taking is a very important skill. It’s actually important just because it's important to understand what kinds of medications people are taking, whether they are in fact able to adhere to a medication regimen. That task itself, though, is also a prospective memory test, so it becomes a measure of memory function as well.

Going down to the left bottom, we look at phone activity. We do not monitor phone use. We do not monitor phone calls
in terms of the content. We do not want to know what people are saying. But the amount of phone activity and the number of ingoing/outgoing calls turns out to be a very potentially powerful marker of social engagement and activity. Similarly, whether people are coming and going from their home is another measure of how much outward social activity an individual may have.

And then on the bottom, here is a person using a computer. Computer use is a very important portal or sensed measure. At a number of levels it’s important. So first of all, just the amount of time an individual spends on a computer is a measure of their cognitive engagement. There are also levels of use that one can look at -- so how a person uses a mouse or a keyboard as well as higher level kinds of use.

What we have been doing over many years, we have been pushing to an individual a computer questionnaire once a week that asks them questions such as rate your pain on a scale of one to ten, whether you've fallen. Tell us about your mood. Tell us if you change your medications. These questions turn out to be very powerful measures in themselves that are collected very frequently. And the time
that a person actually spends just filling out the questionnaire is a sensitive measure of their cognitive function.

More recently, we’ve also been looking at driving as another measure because again, the car has a data port that can be used to look at that kind of function. The system is designed to install other sensors or measures. We think it’s important to be technology agnostic. It’s not about the cool gadget. It’s about what you can use to just get the information that's most meaningful.

This system is, as I mentioned, installed in a number of homes and settings. We’ve had over 1,000 people installed. At any given time, we follow about 100 people in the Life Lab. We have up to seven years of continuous data on these individuals.

What can we see with this information? What you see in front of you is a spiral plot. This is an activity plot or fingerprint of an individual. The colors indicate, the dots indicate, where the activity occurred. And the time is indicated by the clock, which this is really representing.
So at the top is midnight. At the bottom is noon. The concentric green circles going outward are weeks. So this is an eight-week record, spiraling outward over time. Typically, you see that people will go to bed at a common hour for them, and then they get up at a typical hour. There’s lots of activity at nighttime, particularly among older people.

If you follow individuals overtime, as this individual has been followed, and developed mild cognitive impairment, you see these patterns clearly change, the nighttime patterns as well as the daytime patterns. And these can be quantified. I don't have time to give you too many examples, but just a couple quick examples is looking at nighttime behavior. So here I’m showing on the left, I’m using the path of sensing the record of over a twenty-six-week period of continuous nighttime activity.

In the normal group on the top compared to people with non-amnestic or amnestic, two different kinds of mild cognitive impairment. On the bottom is simply the number of times up at night. And there are statistically significant differences in these measures and other measures of sleep,
as well as walking around the home and room transitions, time out of the house, and similar measures.

On the right side, I’m showing a similar kind of monitoring, but looking at the computer use over time, in this case over thirty weeks in a group of normal folks. So cognitively intact individuals compared to an age-matched group, who have been followed originally with MCI, using a computer. But over time, they clearly drop off in the number of days typically they use the computer in a week, as well as the typical time of day or time in a session. There are other measures on the computer that have also been shown to be different in MCI versus intact people, including mouse movements and time to complete the questionnaire as well.

Interestingly, we have data that suggest that these measures, for example, the computer-use measure shown in this left panel on the bottom, are associated with the regions of atrophy most commonly associated with the pathology of Alzheimer's disease, that is, in the medial temporal lobe structures. So the highlighted colors indicate pixels or brain regions that have the most
atrophy, correlated most highly with less computer individual use.

I've shown you individual uses, individual correlations, and how you can use this data. But the real power of this data is really to put it all together. And what I’m showing here is how we build these models to take all of the data.

So on the bottom of this diagram are what might be called the conventional data, the person’s demographics, their age, their education, their socioeconomic status, their annual clinical assessments, their cognitive function, their reports of physical function or even measured clinical function in a clinic, their genetics, biomarkers, and so forth. These on the bottom are conventional measures.

On the top, the other three groupings are the new kind of data that I’ve just been describing briefly. So [there are] the weekly self-report data of things like mood, pain, falls, doctor or ER visits, and so forth, the 24/7 continuous activity behavior, such as computer use, time out of home, sleep activity. And then other data which I
haven't actually shown, but it’s also very important, in that you get, so to speak, for free the daily weather, the consumer confidence index. These measures actually also provide another level of information that you can then put together in models that might predict the things that are of most interest to us, such as going from being cognitively intact to MCI.

And we’ve begun to build these models using this data. And here I’m just showing one of these models plotted out in what's commonly called a receiver operating curve. It's a way of looking at how close one is to using the model to predict your outcome of interest.

So here we use this model to predict a transition from normal to MCI within the next 24 months. And the models, what's in this table, are really behavior one and behavior two are just using the activity data that I described to you a moment ago. Clinical is basically the conventional way that we look at things, using the demographics, the baseline kinds of measures of cognitive function and so forth.
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But putting these all together gives us a very high so-called area under the curve or high predictive capacity of this transition, which is significantly better than any of the current measures that we have. So that's what this orange line is essentially showing. If it was just chance, it would track along this diagonal here.

Finally, I want to also point out that these kinds of measures are inherently functionally meaningful, so the use of a computer, the use of phones, cognitive challenging tasks, medication adherence, sleep, and so forth, these can then also be looked at relative to other measures of interest.

So, for example, we all know that we’re going to have lots of new imaging studies which will better show whether a person, for example, has amyloid in their brain, which is of concern. But how might those relate to these very common activities?

So one can look at individuals based on their amyloid status and then develop what you're seeing here, a plot of a fingerprint, if you will, of how a person with amyloid
(in the blue in this case) or without (in the red) might relate to having more or less of these activities. And these are just going outwards, the likelihood high or low of having more or less of these kinds of activities.

Putting this all together – this is my last slide. We think that the large value of this kind of approach really will help us to improve our ability to really run much more effective clinical trials. I think we've heard throughout the morning or afternoon today [that] we clearly need to identify people either at risk or clearly know the underlying brain pathology that individuals have when they enter a clinical treatment trial.

So this is often called biomarker enrichment, where we might look at an MRI scan showing a particular amount of atrophy or as shown in this little image here, their amyloid positivity. And this then would identify people who have amyloid or Alzheimer's pathology to go on to a clinical trial.

But we can now begin to behaviorally phenotype or begin to look at those individuals who may actually have more sleep
or behavior change, less cognitive ability based on functional, real-world activities. And this then allows us to further subtype the individuals to those who may be progressing more rapidly or not in the real world. And since the technology, once it's installed, is turned on for as long as the batteries work, you can then go on and continue to follow individuals who have been randomized to a particular treatment or not and look at that change over time.

So hopefully, we'll see more of these kinds of approaches incorporated. I’m going to end there. And thank you. I want to mention that we’re very fortunate and thankful for the support we’ve had from the NIA in most of this research that I’ve described today. Thank you.

JENNIFER WATSON: Thanks to all of our speaker presenters. And I want to take a moment to appreciate all of them for the time they've taken today to present. And unfortunately, of course, because there was so much information, we have very little time for questions, and I really do apologize for that. But please feel free to type your questions into the Q&A portion of the Webex, and we can make sure that those
questions get answered. I think some of the questions that I saw earlier were, Dr. Morris, if you could clarify - I think there was some confusion in your early summary slide about saturated and trans fat foods, that there was strong evidence for those foods. But I think it was probably in a negative sense rather than a positive sense.

DR. MARTHA CLARE MORRIS: So the question is whether saturated fat was good or bad for the brain, is that the question?

JENNIFER WATSON: Yes.

DR. MARTHA CLARE MORRIS: It was bad.

JENNIFER WATSON: I thought that was probably the case.

DR. MARTHA CLARE MORRIS: And what is the diet composition that is positive for protecting the brain is a ratio of unsaturated fats to saturated fats that’s higher. So it’s not that you exclude saturated fats from your diet, but your diet is higher in unsaturated fat.
JENNIFER WATSON: Great. Thank you. And I think there were a couple of questions about whether shellfish is included or excluded, perhaps mercury risk.

DR. MARTHA CLARE MORRIS: So the data that have been published from studies, it's just not - there’s too limited evidence to exclude shellfish. So the answer to that question is we would have to have more data that's published on it. It's just not there.

JENNIFER WATSON: Okay, great. Thank you for addressing that. For Dr. Baker, Laura, there was a question about whether doing a study of people who start doing moderate- to high-intensity aerobic exercise in their forties compared to those that start in their sixties, would there possibly be even greater benefits the younger one starts? Or does it even matter? Maybe Laura’s not with us anymore. So I see that we're really at the end of our time. And I really appreciate everyone participating. We will be posting, as you see on the slide here, the slides, audio, and transcript, and we will also post answers to any questions that are in the Q&A chat here at the link that you see there.
There are CEs available for webinar two, one and two, for the next two years. And I’ll give you a little bit of information about CE credit right now. This particular webinar series is accredited for CNE credits for nurses, general continuing education units authorized by IACET, and then continuing education contact hours for health educators, as you see on this screen.

Next is you can download the slide deck. You'll be getting links to the slide deck from today and instructions about how to get continuing education credits. I would just draw your attention to this verification code right here. The verification code that you'll be asked for is ADWeb14, and there are full instructions in the material you'll be receiving. And there's also contact information for any problems with accessing the continuing education units.

And finally, I’d like to thank you again for participating today. Please join us again November 17th for our third webinar in the series on caregiving. And if you have any further questions in the interim, please feel free to
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contact me at watsonjl@NIA.NIH.gov. Thanks everybody, and have a great day.

(END OF TRANSCRIPT)