

Zoom in on Dementia & Alzheimer's

Is Alzheimer's Hereditary? Genetics and Dementia

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Transcript of Zoom with Dr. John Hardy, Chair of Molecular Biology of Neurological Disease at University College London Institute of Neurology

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Please note: This transcript has been edited for clarity and brevity.

NANCY LYNN: Welcome to everyone, my name is Nancy Lynn. I'm a Senior Vice President at BrightFocus Foundation. BrightFocus funds research globally to understand and treat Alzheimer's disease, macular degeneration, and glaucoma. We are delighted to bring you a third episode of Zoom In On Dementia and Alzheimer's, which is supported with some educational grants from Eli Lilly and Company and Genentech.

We received a lot of personal questions. I think you'll find that they will be answered, but more in the abstract. So, I might suggest one or two questions that are typical of, you know, my mother got it, will my children get it? Those types of questions. So, if you have a question to ask that is personal, if you can make it into something more generic, like if a person has x y z and not so specific to you, that would be better.

So, I'm going to start, let's jump right in so I can introduce Professor John Hardy, thank you so much for joining us. Let me give a little bio professor. Professor John Hardy is the chair of molecular biology of neurological disease at the University College London, Institute of Neurology. He is a

world-leading neurogeneticist in the field of neurodegenerative diseases, receiving numerous accolades that include the Breakthrough Prize in Life Sciences, the Brain Prize and in 2009, being elected a fellow of the Royal Society. I wasn't sure whether to call him professor, doctor, or sir, because they all they're all applicable, but we're going to call you and professor today. In 1991, Dr. Hardy's team uncovered the first mutation directly implicated in Alzheimer's Disease, leading to the formulation of the highly influential amyloid cascade hypothesis. Welcome Dr. Hardy.

DR. JOHN HARDY: Well thanks for having me. It's a real honor to be in this series and you know BrightFocus has helped us in the past. It's a real honor to help if any way and help back. It's really a nice thing to be on this call.

NANCY LYNN: Thank you so much. It's so hard for people to get a direct and accurate and information in plain English. So that's what we're going to ask you to do today. And I realized that in titling, this this episode "Is Alzheimer's Hereditary? Genetics and Dementia" I started out with one of the most commonly confusing things. Alzheimer's and dementia are different things. And so today, a lot of the questions are about Alzheimer's, but a lot of them are also dementia. And obviously, we're going to ask you to explain genetically what the difference is. But can you give a little overview? What's the difference in how we're going to be talking about that today?

DR. JOHN HARDY: Well Alzheimer's disease is a disease and so in other words it relates to a specific pathology in the brain which causes specific symptoms. Typically starting with a with problems with short-term memory. Dementia is a general term which covers Alzheimer's disease, but it also covers other rarer diseases. Those other rarer diseases of frontotemporal dementia, prion diseases, vascular dementia. So, Alzheimer's disease is a single disease, but you know, dementia is a general term for people who are losing their cognitive availabilities.

NANCY LYNN: And I'm going to just ask the obvious question. Then we're going to talk about generally, Alzheimer's disease and hereditary and genes associated. Are there different statistics and genes for the different types? If its vascular dementia or Parkinson's related dementia. Obviously,

we can ask specific, I see there are already questions coming in about vascular, Lewy Body. Can you generalize or is it different for every type of dementia?

DR. JOHN HARDY: There's different genes involved in the different forms of dementia, yes different form. So yes, you mentioned Lewy Body dementia that some of those genes are common to Parkinson's disease and some of them but a lot of them are different from the genes involved in Alzheimer's disease. So yes, different genes are involved.

NANCY LYNN: Okay. That's important to know. So, I'm going to start, I'm looking in the chat box here because usually I'll ask a bunch of questions but since you are all asking them, which I'm thrilled. Let me start with one of the most typical and then we can get to some of the more specific ones. I'm going to ask Michelle's question. If a person has three generations of Alzheimer's on the mother's side, two generations of Alzheimer's on the father's side, what testing can be done to know the person's fate? So, you might want to preface this, I'm jumping right to someone's question so that we can use an example. But let's ask you the question: is Alzheimer's disease hereditary?

DR. JOHN HARDY: Well, in response to that question, the first thing I would do was I would ask at what age did they, did the other generations get it? There are rare forms of Alzheimer's disease where the disease is a simple genetic disease. So, the and those in general of onset ages in the, well actually, forties and fifties. And if you're in one of those families you nearly always know it, of course, because it's a, you know, a very dramatic disease. And if your parent in one of those families has it been, you have a 50% chance of getting it at about the same age. Those families are rare and if you're in one of those families, well, by all means email me, but I think that there are specific programs at the Alzheimer's Disease Research Centers for people in those families. Now more generally though what you find is people, and I think this is the question that just texted, to say that in her family, the age was between 70 and 80, and if that is the case, then your chances of getting the disease, let's say your mother or father had the disease at about 70 or 80, and you're at about let's say 50, your chances of getting the disease by about 70 or 80 is

a little bit higher than mine. I don't have it in my family. But it's not the major reason for the problems in your family. It increases your risk, but not to an enormous extent.

I should also say one more thing and that is that treatments are just starting and let's say you're 50 and your mom got it when she was 70. You know what, you're betting on also is that in the next 20 years, we'll get better at treating the disease. So, you're also, without people generally realizing this, betting on research progress as well. So, you both got the risk as it stands now, and also the risk and the benefits of the research over the next 20 years. So, if you're 50, let's say and you're worried about getting it by the age of 70, live your life, enjoy, enjoy your life. I mean, I'm keep your eye on research for sure and support research and all that sort of stuff. But, you know, don't let it dominate. Don't let it dominate your life.

The other thing is that we know now from epidemiological studies that increasing your heart health helps. So, all of those things, which those boring dieticians tell us to do, eat tomatoes, you know, salads low-fat diets, keep your cholesterol low, you know, manage your blood pressure. All of those things also reduce the risk of disease it seems. So, if you want to do something practical, that is a practical thing to do. I have to say, I don't follow all of those, all those things myself, but that, that is what you should do.

NANCY LYNN: Thank you, and Michelle wrote in 70-78, so just to just to restate and clarify. So, there's early, what we call early onset Alzheimer's, which can come on generally, or develop in your 40s, 50s, 60s. And then what we call late onset Alzheimer's, which usually symptoms appear in your 70s. And those two are genetically different. And so, we had a lot of questions about early onset. Can you talk about the genetic situation for those that have early onset?

DR. JOHN HARDY: So the people with the early onset, and this is actually goes for the other dementias too, if you have early onset disease in your family and let's say, your mother or father, got it at the age of 40 or 50 and let's say their parent got it at the same age, then in those situations, well firstly, I'd be very happy to hear from you, but what you should really

be doing, I think, is looking for a specialist center. You know, if you're in one of those families there really are specialist centers now trying to identify such families and help them with experimental and now approved treatments.

NANCY LYNN: I want to mention that we are going to, Dr. Hardy has very generously offered to provide his email for those who have follow on questions. So, at the end of this episode, we will be providing Dr. Hardy's email to you, and we will also be providing you with a general email to follow up if we haven't answered your specific question or if your question doesn't relate specifically to genetics. And also Dr. Hardy referred to Alzheimer's Disease Research Centers, or specialist centers. And we talked about this before the episode today. It's very easy for professionals in the field to say to all of you: ask your doctor or go see your neurologist. Well, a lot of doctors, the truth is a lot of doctors are not that well educated about dementias, Alzheimer's, vascular, Lewy Body. You know misdiagnosis are very common. Sending people home and just saying, "you're okay, come back in a year" is very common because as you know, these diseases are very complex and would take the doctors so much time.

So in an effort to try to begin helping the situation for you guys, at the end we're going to show you where to find out where there are nationally organized Alzheimer's Disease Research Centers, which run clinical trials, and I see there are already some questions about clinical trials in the chat which is great, where there are Alzheimer's Disease Research Centers and where you can call to try to find a qualified neurologist or a doctor near you because we realized that is difficult for a huge swath of populations in the United States.

If someone has a recent vascular dementia diagnosis, can that be connected to Alzheimer's?

DR. JOHN HARDY: Probably not. I mean, there is some overlap, probably not. And I mean, of course, the person with a vascular problem, should be controlling their blood pressure and cholesterol and so on and so forth. And this is something that I think that local neurologists are really you know on top of. If you, if they made the diagnosis of vascular dementia,

they will I hope anyway, be telling you to control your blood pressure and so on and so forth.

NANCY LYNN: Here's a question from Mindy in the chat. My neurologist discourages me from getting genetic testing. I have Alzheimer's on both sides and donated my mother's brain, which was another, we got some questions about that. She said she would do it. What's your take on this? Would you want to know? This is a great question. Would you want to know if you had APOE4 or APOE4 positive?

DR. JOHN HARDY: My view on this is changing. So, if you'd asked me two years ago, I would have said, "no, I don't want to know." But my view is changing and the reason my view is changing is because treatments are coming now. And, you know, if you'd asked me two years ago, I would have said no because there isn't much I could do about you apart from the heart health type things, which I mentioned. But now I might want to know earlier because I might want to get involved with a center, which is starting to do the treatment with the drugs, which are, which are coming on, well, and now on the market, but not yet widely available. So, this is a question where the answer will change over the next over the next few years.

NANCY LYNN: I think that also, I've been doing this about 15 years, people feel that there's a right answer or wrong answer there, should you get tested or not? And I don't really think, I got tested 10 years ago when I first started to get into the field to see, you know, APOE condition. I'm a want to know type of person. There's a lot of people who are not want to know type of person, so I don't think that there is a definite answer to that. There's a gentleman, you may know him as well, who worked with Eli Lilly as a scientist for many, many years and he found out he was APOE4 positive, had two of the four alleles, and I remember calling him one day and asking him how he was doing and he said, "you know, being APOE4 positive is not a death sentence." It's not, so I think that's what you were just saying. You want to live your life, you want to even if you're diagnosed with a dementia, you want to live your life as best you can and I think that's the message you want to express love, be loved, be loving and live what the way you can.

So for those who are want to knows, and they want, and there's a lot of

them I suspect on this call because they're all asking questions. I have it in my family in some way, I want to know if I'm going to get it and I want to know if my children are going to get it. So if someone wants to get tested, what types of diagnostic tests are available and how do you get them? And well then I'll go into how do you know if they're accurate? And what do they mean?

DR. JOHN HARDY: Yeah, that's a difficult question and there's no simple answer. So, I mean, of course, you can get essentially you can get testing with companies like 23andMe, essentially, you can. And I don't know what the quality of the information they give is. If you have an E4 allele, the risk allele, then your chance goes up by a factor of between 2 and 3 of having dementia. So, if it's 5% at age 70 in for me, for example, then it's 10% if you have an E4. Those are the types of numbers that you can get in. If you have two copies of E4, your chances are maybe 20% by the age of 70.

Having said all of this, I was at a meeting yesterday and to my amazement, there's a study in Holland where they're looking at centenarians. And their oldest surviving person, their oldest surviving person is somebody with an E4 homozygote and they're 103 years old and they are still cognitively okay. So just like you said, and just like the Eli Lilly guy said, you know, genetics isn't destiny, it is not destiny. And also, I absolutely agree, this is a personal decision. There's no right and no wrong answer about whether you want to get tested or not.

NANCY LYNN: And I want to, because a lot of people asked, if they're worried about it and I wrote a little list for myself to try to compile the question. There are brain scans now that will tell you if you have a certain sticky protein called amyloid in your brain, which is thought to be indicative of Alzheimer's. But as Dr. Hardy is saying, there are many people who grow old and are cognitively healthy who have lots of amyloid. There are also people who have dementias that don't have any. So, we're really not clear yet, let's, let's state that. But we can have a scan to find out if there is amyloid or another protein called Tau in the brain. We can now soon have a blood test that sees certain proteins in the blood, which is the cheapest, fastest way to find out where your amyloid protein stand. We can have a genetic screening at a place like 23andMe or someplace more

sophisticated. We can do cognitive tests; we can do lumbar punctures. So, if you're, I think I'm asking a repetitive question, but it's because there are so many questions about this. If you say to your neurologist, I want to know, can I get a scan? Can I get a blood test? Can I, how do people navigate this?

DR. JOHN HARDY: Well, you're pointing out an area where there is confusion with the researchers. So, you know, your confusion and your listeners' confusion really reflects where we're up to. All of those things, so the genetic testing, the blood test at present, the scans, all of them give information which make the diagnosis more likely, all of them, but none of them, reach certainty by any means. A lot of them are not quite ready for even being used in a medical situation. We're very interested and excited by the blood test, but they have not yet been approved. And the reason they have not been approved is because all the quality control work has not yet been done. So, we think, we think we're moving towards greater certainty but we're not there yet.

NANCY LYNN: Which is frustrating.

DR. JOHN HARDY: It is frustrating yes, more research, that's all I have to say Nancy, more research is all we need.

NANCY LYNN: I will support that as well, and along those lines, there have been a couple of questions about participation in clinical trials and I, I would say that this idea of getting scans, which scans are very expensive, \$7-8,000 in the US and they are not reimbursed. If you are a want to know person and or a person who wants to contribute like Anya, who, who wrote in the chat, "I plan to be contributing to the society into my 90's" -- you go! -- "I need to know", you can participate in a clinical trial.

So, there are, we'll do another episode specifically about clinical trials. But when you volunteer to participate in research, if you qualify, if you're able, and that's another very complex area, you will get all of those tests generally as part of your trial. So, you would, for example to participate in a test, let's say for Leqembi, the new antibody that is likely to get approval, you would get a brain scan, a lumbar puncture. You get a lot of testing done and you will get state-of-the-art treatment or attention. So, that is one way for the want to know people to participate and learn

more, and also, a way to give back. And I think the same is true for brain donations, although that also is a comp, you need to live near a place, you need, there are all kinds of conditions. So, if anyone is interested in brain donation, please do email us. And I'm going to go to, I think Mindy was raising her actual hand rather than her virtual hand.

MINDY: Yes, sorry I was raising my hand because I can't find the raise hand on the reactions.

NANCY LYNN: No worries.

MINDY: I just wanted to throw out there when I donated my mother's brain. It was quite a...it was a, it was an amazing thing and I'm so glad that I did it and it made me feel so much better about what she went through, but I live in Virginia, and I had a very hard time finding a place to donate her brain. And I would be making these calls, you know, offering and people are like, oh she's not in a clinical trial already, we can't take it. And so I ended up, I just want to throw this out there in case anybody is ever interested, I ended up donating to the University of Miami and they helped pay for harvesting it and transporting, I paid a little bit, but it was worth it because then I got to find out her results were included in what I helped pay with wasn't much.

DR. JOHN HARDY: Oh, that's a wonderful thing, and you're right, I work in an institution where we have a brain bank. It is quite difficult, there's a lot of paperwork, and then, as you obviously realize, from Virginia to Miami, so, you know, it's a lot of the transport issues as well. It is a difficult thing to do, and if you're going to do it, I would recommend you start contacting people very early.

The other thing that I've said, the people here is if you can't, if we somewhere can't take your brain, what you might think about doing is suggesting people give money to a research charity, like BrightFocus, in lieu of flowers. We do that a lot here. I've just done that with my mother-in-law who died recently. People gave to the charity she chose in lieu of flowers to remember. So that's something to think about if you can't do the brain donation. But well done for persevering too.

NANCY LYNN: Thanks Dr. Hardy for that flag of funding research and Dr. Sharyn Rossi, who's on our Scientific Affairs team at BrightFocus, put in the chat that she wanted you to know that we do fund that hundred plus person cohort in the Netherlands that you were referring to earlier.

DR. JOHN HARDY: Oh yes you do that's right, I saw that grant go through a wonderful study, It's a wonderful study.

NANCY LYNN: So, from Anya in the chat again, "What percentage brain shrinkage do you think for sure indicates dementia? It's all my mom shows...vascular. Clog arteries, cells die." But brain shrinkage is something that we also see with Alzheimer's. Is there a percentage that indicates, you know, that a person has Alzheimer's?

DR. JOHN HARDY: No there isn't, but let's but often Alzheimer's, let's say the average male brain is about a kilogram and often you get a male Alzheimer brain which is about 800 grams. So that's a big loss. Having said that though, one of the things that's really, your brain shrinks and grows shrinks and expands all the time, you know, based on your water content. If you start to take things which can make you urinate more, and you'll lose brain volume because it sucks the water out of your brain. So, there is natural variation in all of us in our brain size during the day as well. So, it's a bit, I can't give an exact figure but people with severe Alzheimer's disease have typically lost 15 to 20%.

NANCY LYNN: There was some, looking for it now, a Vimeo question from Steve, "If a person tests positive to have the genetics that can lead to Alzheimer's, does that impact eligibility for health insurance?"

DR. JOHN HARDY: You know, I don't know. I don't know that. I don't know that and that is, of course, a question I've seen debated. And of course, I'm here in England and the regulations I'm sure are different here in England than they are in the US. I think it's a very important question. I'm really sorry I don't know the answer.

NANCY LYNN: And I'm sorry to send one at you while you're there in England. But as most of you probably know the, the issues with health insurance coverage or Medicare or Medicaid coverage for Alzheimer's

related testing and medications is it is in a very contentious and difficult state right now and not settled in the US. So, it's a good question and for those that are interested, you know, keep monitoring what happens with, with Medicare and Medicaid and the Leqembi approvals. And I'll note that the Veterans Association in the in the United States voted to cover use of Leqembi. So, there's different, there's different dances being danced right now about coverage and insurance and where it we're going to have to watch and see how that plays out. Darlene?

DARLENE: I'm in California and just for informational purposes, we have in our caregiver support group a 53-year-old, early onset Alzheimer's patient and in California under Medi-Cal it's an automatic with a diagnosis of Alzheimer's, disability coverage and medical insurance, so progress here.

DR. JOHN HARDY: That's great. That's great.

NANCY LYNN: That's great. It's sure right.

MINDY: I would think that'd be a huge deterrent to get people tested because who wants them to say, oh, sorry we're not going to cover you anymore. You know who wants to take that chance.

NANCY LYNN: Yeah, and Darlene. I don't think that's that, wasn't the specific, is that what you were addressing in your answer?

DARLENE: Yes, specifically that he had the diagnosis from a neurologist that he has Alzheimer's, then he, he could immediately get on disability insurance and medical insurance. The other thing I would like to mention is well, my mother, I donated her brain to University of the Washington back in 2000, but Science Care also takes bodies and helps with costs.

DR. JOHN HARDY: University of Washington is a great center by the way, great center.

DARLENE: Yeah, I agree.

NANCY LYNN: I am looking through the questions in the chat. And somebody, Michelle asks, do you recommend neurotropics? And I know

this is not your area, but there were a lot of questions about supplements, drugs, lifestyle intervention, and so on, are there any, is there any things that you want to highlight that you do think you're helpful?

DR. JOHN HARDY: Well only what I said before, heart health. Heart health. There is a very good study called the FINNGER study, F-I-double-N-G-E-R, double N because it's from Finland originally, showing that all of those, I'm going to say boring things, exercise, good diet, and blood pressure control really do make a difference. Supplements, I'm not a fan of myself but heart health definitely.

NANCY LYNN: Yeah, I think, and I'm going to go to your next Jill, that we're going to do an episode dedicated to those lifestyle interventions. I think exercise and a certain type of exercise has, is the one thing that's been shown to most help the risk reduction, let's say. People, there's a debate now about you should we use the word prevention or risk reduction and I personally err on the side of risk reduction. We don't prevent cancer, but by not smoking, we reduce our risk of it. So, there are those that will argue that you can prevent Alzheimer's. I don't think we're there yet, but we can definitely reduce our risk with lifestyle and that will involve exercise, eating generally a good healthy and Mediterranean diet, if you're not in a food desert and you can get those healthy foods, getting good sleep, reducing stress, being socially interactive as much as possible. And let's see what else is on the list, not smoking of course, not excessive use of alcohol.

And I think one of the things we're thinking about at BrightFocus, because we also fund research for eye diseases, is hearing loss is an accepted or recognized risk factor for Alzheimer's disease. We believe vision loss is as well. Anything that isolates one as you get older, isolates you from social interaction and the healthy, healthy lifestyle is a risk factor for Alzheimer's. Let's go to Jill.

JILL: Hi, I just had started to zoom in on this and I'm really curious, is it expensive to find out if you have the APOE4 gene? And I don't know if I should do that, my grandmother had Alzheimer's, my mother had Alzheimer's, my oldest sister died of it and my next oldest sister has just got it and I'm scared to death.

DR. JOHN HARDY: Well, you sound pretty well yourself right now, so I wouldn't worry too much. I wouldn't worry too much. You can get tested if you want through 23 and me. But that's up to you, you know, I would just do what we've been saying, which is risk reduction through an active life and judging by where you're calling in from, you're doing that already.

JILL: Yes, I work out and I'm still working actively working and I'm going to be 75, so I'm trying to do everything. But I'm scared.

NANCY LYNN: We got a lot of comments submitted by all of you that said I'm scared, I'm scared. And I think for me knowledge is power and even though there's so much we don't know, participating in these types of forums I think is one way to help with the fears that you feel. So, you feel you have somebody you can ask these questions of.

I want also to point out that we have another series called Brain Info Live. If you go to our website and just do www.brightfocus.org/braininfo we have over 70 episodes all on specific Alzheimer's or brain health-related topics. So, you'll find a whole episode, for example on clinical trials or APOE4. And they're in Spanish and English and the first one we've just done in Haitian Creole. So, and I know Alexa put in here I'm not going to be able to find it that we did a whole episode. I don't know if you can unmute Alexa?

ALEXA: On brain donation.

NANCY LYNN: On brain donation. So, if you are interested in brain donation, we did do a dedicated episode. So please do check out that free resource. We're trying to provide free resources, understandable resources, and resources you can share with whomever you wish.

Let's say, let's go to Atalay. I'm probably pronouncing that incorrectly.

ATALAY: Hello, can we ask scientific questions to Professor Hardy?

NANCY LYNN: I think so and I'll ask Dr. Hardy to make it understandable,

his answer understandable, as much as possible to the rest of the community.

DR. JOHN HARDY: I'll do my best.

ATALAY: It's an honor to listen to Dr. Hardy and he's such a giant for us, all the researchers. And I just want to say, I worked with Professor Nihan Unaltuna in 2014, who was instrumental in 2013 getting the TREM2 paper in providing the Turkish cohorts. I wanted to ask him something related to our understanding of AD and basic sciences. You know, for the longest time, the AD field has had a disease model problem because our models were flawed and it led to failures in trials for the last 20 years, until very recently, antibodies that are out there. In Professor's opinion, does he think we're ever going to reach unified understanding of AD or better models, instead of the current status with different theories, such as amyloid, tau, synaptic dysfunction, mitochondrial dysfunction, and their inflammation are all true on their ends.

DR. JOHN HARDY: Yeah, well, I think we're moving, you know, I might be just be optimistic, I think we are moving every year closer to a more, a greater view. So, just to give a couple of examples, people used to argue about whether amyloid was important. Well showing that we, if you remove amyloid, improve clinical, slows down the progress, that tells you that amyloid is important. So that argument is over. There are trials now of anti-tau drugs and those looked hopeful too. So, I think the people are getting a little less, the researchers used to as you kind of indicated in your question, just used to focus on one thing each. And I think that we're really moving to researchers having a more general view of the disease and taking multiple factors and recognizing that multiple factors are important. So, there's real progress and I think there's much more of a consensus now than there was before these trials started to show positive benefit. So yes, I think we will get better, and the models are getting better too. You're a scientist and so you know that the animal models have not been perfect by any means but now we're beginning to learn how to use the models more effectively to translate into the human situation.

ATALAY: Yes, thank you very much.

DR. JOHN HARDY: And thanks for those compliments as well. By the way, of course, I appreciate them.

ATALAY: Thank you.

NANCY LYNN: Dr. Hardy I am, oh let's go to Arnold.

ARNOLD: Can you hear me?

NANCY LYNN: Yes.

ARNOLD: In my particular situation, my father was 90 years old, 89 or 90, when he was diagnosed with dementia in 2003. And so, I'm getting to that same age, I'm now 86. You haven't talked about people like me who are in their late eighties, early nineties. And what that tells me, should I start worrying about? I don't think I have it now, except for the old age problem, with forgetting words and names and that kind of thing.

DR. JOHN HARDY: Well, I would say the second one, but first thing my mum is 93 and she's still a pain in the ass. So, you know she's still as feisty. You seem pretty feisty too, I won't call you a pain in the ass but you're a pretty good too. You know, I would just enjoy your life, enjoy your life. You know again, control heart health, don't smoke, but, you know, do those things? But no, I don't think you need to worry.

ARNOLD: Ok thank you.

NANCY LYNN: Dr. Hardy, someone wrote in, does medically controlled heart health like high blood pressure controlled by well, a medication that I can't pronounce. Does that count or do you have to do exercise?

DR. JOHN HARDY: Well, I'm on a blood pressure drug and I'm on a statin and you know those things are all good for this, they're all good yes.

NANCY LYNN: I'm going to ask you a question Dr. Hardy because it came in several times that I know I know what you're going to say but, coconut oil?

DR. JOHN HARDY: No. Nope. No proof, just no proof.

NANCY LYNN: And wine, red wine?

DR. JOHN HARDY: Actually, I don't, I mean believe me I'm going to have a glass of red wine when I get home. But I'm going to have a glass of red wine when I get home because I like it. I don't think it does anything to do, I actually don't think it does anything for Alzheimer's disease. So, I'm not going to use that excuse, I'm going to have a glass because I like it.

NANCY LYNN: But I think there's a deeper message in that to its which we started to refer to, is live the best quality life. A dear friend of mine quotes I think it was Swanson, who is asked why she was doing all kinds of things when she was older to stay healthy and she said "Darling, I want to die alive". And then I think that's a wonderful lesson, in a sense.

We also did a Brain Info Live episode and thanks Martha and others for the kind comments about Brain Info Live. There's a lot of information in those episodes. We did one with a caregiver from Boston who had taken care of her mother through the whole course of Alzheimer's, was her only caregiver. And then, after her mother passed away, her father was diagnosed. And this is unfortunately, not unusual. And the host asked her, "what did you do differently with your father, then you did with your mother?" And I just loved her answer so much because she said, well, with my mother, I worried, we argued. You know, and somebody actually wrote in a question, with where they said their spouse had been diagnosed and that their spouse is doing a lot of things intentionally to annoy them. And I hear this all the time. When your spouse or your loved one or your parent is asking you the same question over and over or getting irritated, this is not on purpose. This is a disease, it's part of a disease. And so, the person asks, you know, what do I do? And I think the thing to do, first of all, is to first understand they're not doing it to annoy you and try to have compassion and try to answer the question or deflect or ignore the question. Be calm. Deflect or redirect I think isn't it and I'm sure there's people on the on this call, I know there's a lot of professionals who have, I'm sure a lot more to say on that. We can do another episode of that, but living your best life, love it.

So, I'm sorry back to the story. So, she said what she did differently with her father was she would just sit out on the porch with him. And she said she would just be with him while he was still able to be present. And that was how she changed. Her behavior is a caregiver. And I just found that really fascinating. She just tried to enjoy being in his presence and giving him love and feeling love from him.

DR. JOHN HARDY: It's no good having an argument with somebody with Alzheimer's disease. It's just no good because they won't remember and it's just upsetting for you and for them. And like you say, they're not doing it deliberately and you correct them, and they won't remember necessarily the fact that they've been corrected, it's just yeah the disease.

NANCY LYNN: We have 10 minutes left. I'm going to leave five minutes to go through the resources for you. So, if you haven't asked a question and really want to but are being shy, please, I can't see everybody's so I can't necessarily see you if you're doing that.

MICHAEL: Can you hear me?

NANCY LYNN: I can hear you, yep.

MICHAEL: This is Michael. I'm sorry I can't put my camera on, but for some reason with that camera on, the volume doesn't work. So if I can ask my question now and I know it's a little bit late, but...

DR. JOHN HARDY: Fire away.

MICHAEL: Thank you again for all this. And what I want to touch on, when you were talking about clinical trials, and I think we're really missing a great opportunity today with clinical trials. We think of clinical trials in the sense of drug testing and other things similar to that. But with the technology that we have today that people can wear wearable that monitors in the house, why are we not starting to think of following people who are living with dementia within our home? And start seeing how we're progressing that might help out in clinical trials.

DR. JOHN HARDY: Oh, you're totally right and I don't know the American

situation too well, but here in the UK, we have a center at Imperial College in London, which is exact doing exactly what you suggest. And I've seen Grant applications from America's, I don't know what's going on exactly, to do the monitoring of people with Alzheimer's disease in the house, in their homes and all this sort of thing. So, what you say is I'm going to say beginning to happen. It's a very good way of using technology. I absolutely think it's one of the ways we can improve things in the future. Nice car by the way in your picture.

NANCY LYNN: Thank you, Michael. And I'll mention Michael is someone, he's said it's okay to say, that he is someone living with Alzheimer's and really participates with the community and research and advocacy, and every way possible, so thank you, Michael. And let's go to Laura.

LAURA: Thank you Michael too, because that's the line of what I'm saying. I was in a clinical study I guess I would call it and was told that I had APOE4 as one of my genes studies, and also was in the clinical trials for nicotine and would like to do more. I don't really want to take any medication or that kind, but as Michael is suggesting I'm just keeping track of what's going on and if there are any brain scans or anything else that could be done, I would like that too.

NANCY LYNN: It sounds like we should do an episode really about specific trials that people can participate in because, as the point is being made here, and it's one we talked about a lot not every clinical, there's something called research studies rather than clinical trial that can be a lifestyle intervention. That can be on sleep. It can be on exercise. It could be on diet. It could be many different factors of lifestyle intervention. So, you're not taking a drug or if you don't qualify for a trial that where you're taking a drug, there are alternatives. And somebody has written, how do you know, Mindy wrote, "how do you know if clinical trials are safe or on the up-and-up? I see ads and emails all the time." Or Deborah saying, "I was in a drug trial study and was kicked out because I had no Tau tangles". Some of the recruitment centers, if you don't qualify for one trial or, you know, get kicked out along the way, as Deborah saying, will actually take the time and care to say okay you didn't qualify for this study but there's another one you can participate in. So, I think as I say, you know we

wouldn't be able to address everybody's individual situations here but we could we can if you all are interested, do something that talks more about specific trials are types of trials and how to get informed about them. And I just want to ask if you know Dr. Hardy because I don't know off the top of my head, but we can find out, are there specific active recruiting trials for people with the APOE4 homozygotes?

DR. JOHN HARDY: That was, I don't know if the recruitment finished, organized out of Boston and I'm blocking on... called the, I think it was called the E4 trial, I might be wrong with that. There was one in the past. I'm sure that there will be others in the future because we know about that E4 for generally causes amyloid deposition and there are now a lot of pushed to do to test things against amyloid, deposition based upon the success. So, I don't know the details, but I'm sure there are trials, specifically aimed at that population.

NANCY LYNN: Yeah, I'm pretty sure as well. So, we will, we will do an episode about this. And while we can't exactly endorse specific trials over other trials, I think we can provide information on those that are available and perhaps help you do some due diligence. Susan?

SUSAN: Yes, I'm participating in a longitudinal study here at NYU in New York and part of that is besides going in and doing all this memory testing thing that feels like your brains pulled out, run dry and stuck back in, but they want me also to do a brain scan and MRI. Now I had understood that this may be a little off your topic, but I understood that if you have artificial joints as I do and my shoulders that that interferes with a brain scan, do you have any information on that?

DR. JOHN HARDY: Well, I'll give you unreliable information.

SUSAN: Oh, better than nothing!

DR. JOHN HARDY: But that is that MRI, the M stands for magnetic. If you have metal in your shoulders, that that is a problem with the magnets. So, if it is an MRI, yes it is something that you might not be able to participate in because it's a magnetic, you know, it picks up the magnets on so that that's the possible reason. Having told you it's unreliable, you should

check that with them rather than listen to me on that.

SUSAN: Okay, thank you.

NANCY LYNN: And thank you also to Dr. Sharyn Rossi, again, from BrightFocus Scientific Affairs. She's put in the chat, a link to the AHEAD study. So, for those that are interested, you can do that link. Or let's see. It's www.aheadstudy.org. And I am assuming since Sharyn put that in there that this looks at your APOE4 condition. And we're pretty much out of time, but I'll ask just a last question Dr. Hardy. The new drugs: Leqembi, donanemab, that are aducanumab, will they potentially act differently for people who are APOE4 positive then for those that are not?

DR. JOHN HARDY: Well, the danger is that they are and that they do. If you're E4 positive, well you always, you always need to be monitored in these trials, you always need to be monitored. But I think that they basically work in all genotypes, but you need to be monitored. And that's going to be the key, the key answer really.

NANCY LYNN: That makes perfect sense. I could go on forever here, but I'm going to wrap up. First of all, thank you Dr. Hardy. It's really an honor and there are not so many, I think scientists as accomplished as yourself who can also make things very understandable for the rest of us and has a really cool accent. So, thank you for participating with us today and thank you to all of you and especially for asking questions and really interacting today. It's very meaningful to us. And thank you for the questions that you sent in advance as well.

Let's bring up the closing slides here. Thank you. Sorry, they're blurry, at least they're blurry on my screen. But it says, if your question was not answered today or if you have suggestions for future topics, you can email, reply@brightfocus.org. And as I promised, Dr. Hardy has offered to answer questions by email, and you see his email here j.hardy@ucl.ac.uk. And if you're listening online and didn't catch that or anyone who's registered today is going to receive an email with all of this information and all of the resources.

And just let Just let's go to the next slide, please. So BrightFocus. In

addition to the study that we mentioned earlier, BrightFocus funds a lot of research on lots of different topics. So, we decided that we would email to everybody links to BrightFocus funded research that specifically relates to genetics and dementia. There are several. So rather than try to put a whole bunch of links here in a resource page, we will email that information to you. Or again, you can write to us at reply@brightfocus.org.

The little map at the bottom of the slide, if you can see it, shows where the Alzheimer's Disease Research Centers in the United States are. Shows the state, doesn't show where within the state they are. But so, if you're in one of those states, there is an Alzheimer's Disease Research Center, and if you go to the link shown here, and again, if you're seeing this and want to take a quick snapshot with your phone of this slide, please feel free to do that. We will again, we will e-mail this information to you but at www.nia.nih.gov/health/alzheimers-disease-research-centers you can find where the Alzheimer's Disease Research Centers are.

And there's also a link here to the NIH Alzheimer's Disease Genetics Fact Sheet that has a lot of information, basic information. And then, so if you are trying to find a neurologist, you are meant to first ask your primary care doctor. But if your primary care doctor doesn't have a good recommendation for you, I would say to try to call the nearest Alzheimer's Disease Research Center and ask for their referrals. There are, there's the American Association of Neurology. There are a lot of associations and so on but it really, we know it is very difficult to find these resources. And so, again, if we can help in any way, please contact us.

I think that's it. If we go to the next slide. Our next episode is Thursday, July 27th, and we're going to go back to the topic we started. Our first episode was about Leqembi specifically, the new Alzheimer's drug. What is it? What does it do? But with so much happening in the approvals space, we thought we should go back and broaden that to a Dementia Drugs Town Hall: What's New? What's Old? What's Approved? What's covered? And I think after that we mentioned in September will try to do something on lifestyle interventions and certainly thanks to your interaction today will focus a quite a bit also on clinical trials. What clinical trials are available for and how to find them. How to know whether you qualify,

you're not all of those all of those things.

So again. Thank you, Dr. Hardy, and thanks to all of you for participating. And we look forward to seeing you again on July 27th.

DR. JOHN HARDY: Thanks for having me. Thank you very much.

Useful Resources and Key Terms

BrightFocus Foundation: (800) 437-2423 or visit us at [BrightFocus.org](https://www.brightfocus.org). Available resources include—

- [Across the Research Spectrum, Expanding Our Innovative 360° Approach](#)
- [2022 Alzheimer's Disease Research Projects](#)
- [Alzheimer's Disease Research Centers \(ADRC\)](#)
- [NIH Alzheimer's Disease Genetics Fact Sheet](#)
- [AHEAD Study](#)
- [Link to clinical trials focused on APOE specifically](#)
- [Brain Info Live](#)