



## CONTACT US

If you have an idea for a story or have questions about the information in this newsletter, please contact the editors.

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All participants make a vital contribution by their dedication to DIAN research: from engagement in the DIAN EXR (webinars, conferences, surveys), completion of smart phone cognitive testing (ARC), interaction in MyDIAN (research portal), long-term commitment and diligence in completing DIAN Observational study and DIAN-TU trial measures, to the ultimate gift of brain donation. Without fear of exaggeration, DIAN research would be impossible without the energy and commitment of our participants.

Like any solid and enduring partnership, communication is key to advancing our common goal of finding a preventative treatment and ultimately, a cure for Alzheimer's disease. As we strive to better our studies and improve the information coming from our team to you, it is important we receive your feedback. In this edition of the newsletter, we highlight ways in which you can contribute your ideas and thoughts, in addition to physical participation in research. You'll hear valued perspective from a younger family member considering life-changing decisions, insight from family members and a DIAN professional on brain donation, and new options for participation for Spanish-speakers. Also provided are links to the initial publication of results from the first DIAN-TU trial, which featured Solanezumab and Gantenerumab, and to other research articles from DIAN and recent news pieces on AD. We welcome your ideas for future

newsletter topics and questions about DIAN research in general, as mentioned by our family members below. Our eternal thanks for the time you have given and continue to give!

-Ellen Ziegemeier, DIAN EXR

## Participant Representation of the DIAN Steering Committee

As a study participant, have you ever wondered who to contact if you have questions and/or feedback about DIAN, the DIAN-TU or the DIAN Expanded Registry? Have you had challenges

with your study visits, scheduling or travel, and are not sure how best to address them? Ellen Ziegemeier or Jen Petranek are your first contacts for questions related to current participation in any DIAN-related study or inquires about joining the research. They can be contacted by [email](#) or by phone at 844-DIAN-EXR (844-342-6397). If your questions or concerns are related to the DIAN EXR, but you aren't comfortable sharing them with Ellen or Jen, you can also contact either [Dr. Bateman](#) or [Dr. McDade](#).

The DIAN Steering Committee consists of a group of doctors, scientists, clinicians, staff and family members who work together to develop and continue the protocols for the DIAN studies. There are four family members who serve on the DIAN Steering Committee to provide input from the family perspective and to be a voice for you. We each have a unique personal connection to DIAN. Three of us have been involved in the DIAN Observational study and the DIAN-TU trials, and the fourth is a caregiver in a DIAN family. We are passionate about being your voice and representing you well to the DIAN Steering Committee. We would be happy to hear from you about questions, concerns or suggestions that you would like brought to their attention. The Steering Committee meets quarterly (three times by phone conference and once per year in person). If we can represent you, please reach out. -Rachel Huber, Family Member



## Steering Committee family members:

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## View From a Participant

I am sure everyone reading this or anyone who has a loved one diagnosed with Early Onset Alzheimer's has had an uncomfortable or unsettling experience with people who are not familiar with the gene. It can be upsetting, frustrating, and at times, even disheartening.

In the summer of 2020, I visited a new primary care physician. As usual, he asked about my medical history and eventually my family's, so I quickly, well as quick as this type of thing can be, explained that my mother is 39 and living with Early Onset Alzheimer's Disease, as is my 41-year-old uncle. I explained how my two siblings and I have a 50 percent chance of inheriting the same genetic fate. I had also previously mentioned that I had plans of attending medical school and becoming a physician myself, so the moment these condemning words about my family's medical history left my mouth, I was met with ignorance. Ignorance about Alzheimer's Disease, ignorance about how the specific PSEN1 gene affects people, and ignorance and disregard for my own health decisions. This doctor exclaimed that I must get tested before I go to medical school. If I have it, that would just be a waste of my time. I need to get tested as soon as possible. I am 20 years old, and I was 19 then. I was in therapy every week trying to cope with my family's experiences with Alzheimer's, alongside the weight of deciding to learn my genetic status. As many of you can imagine, this was traumatizing. This decision is scary, and I am sure many of us young people who have lost loved ones to Early Onset AD are facing very similar challenges and choices.

There is so much misinformation and mistrust that gets thrown into the journey and process of making choices like getting genetically tested, but something that has been more than reassuring to me is the guidance and support I have received from the people at the ADRC and DIAN. Since that incident almost a year ago, I have taken the time to educate myself about the new and exciting Primary Prevention Trial in the hopes of having a better foundation and platform of knowledge to move forward with. This has helped in my decisions of not only whether I want to get genetically tested and find out my status, but also whether I want to participate in the Primary Prevention Trial or not. I know this is a very relevant and interesting topic people my age in the DIAN community are wanting to learn more about, so here you go!

The Primary Prevention Trial is a new leg of DIAN's clinical trials. Researchers have found that the build-up of Amyloid Beta, which is a primary causation factor in Alzheimer's, can be seen accumulating years ahead of onset, meaning that there is this period of opportunity to implement potentially preventative treatments. DIAN plans to run this trial by targeting Amyloid Beta in individuals who are at risk of developing Alzheimer's but are far out from their family's age of onset. They hope to be able to prevent Amyloid Beta buildup in people who are at risk and eventually prevent the cascade of pathology that leads to AD.

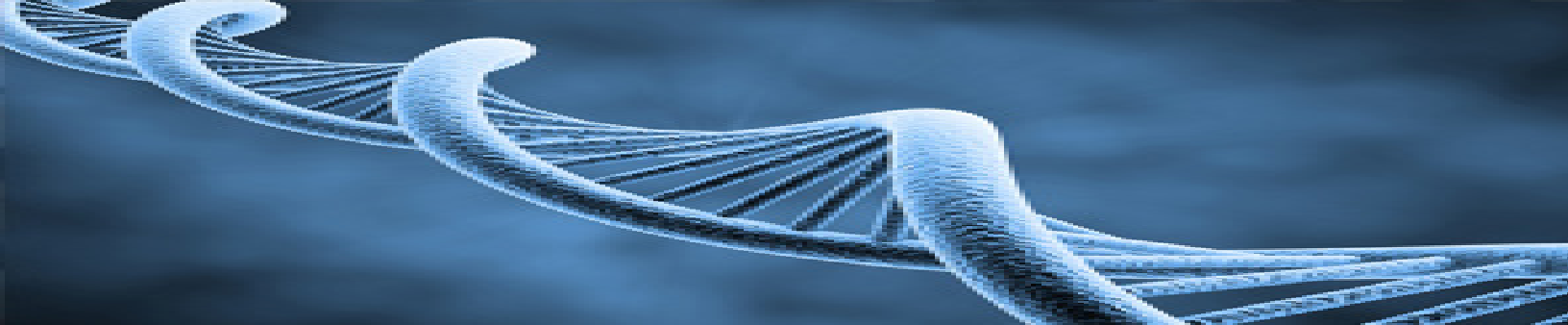
One thing that initially turned me off to this whole trial was the thought that I would have to find out my genetic status as someone who is at risk of developing Early Onset AD, and I am sure you are probably wondering the same thing right about now, but no worries! No one who participates in the Primary Prevention trial, unless they want to, will have to find out their status. This was a huge weight off of my shoulders, and I am hoping yours too.

I have spent such a large amount of my life looking up to my mom, and my uncle, and all of the people who participate in the DIAN trials, subjecting themselves to something that is unfamiliar and at times scary, all for the sake of fighting and one day curing this awful disease. So going forward, with the knowledge and information gained, I plan to do my part in ending Alzheimer's, as I hope you will begin to consider yours.

*-Hannah Richardson, Family Member*







## MyDIAN en Español

¡El portal para participantes de MyDIAN pronto estará disponible para los participantes de habla hispana! El portal se basa en una aplicación llamada Linkt y es una forma directa para que los participantes reciban artículos, anuncios y alertas sobre oportunidades de investigación. Si está registrado inscrito en el rRegistro ampliado y sies español es su lengua maternahispanohablante principal, pronto verá una invitación por correo electrónico para descargar la aplicación Linkt. Los correos electrónicos provienen de Datacubed Health, nuestro socio para a empresa asociadael de desarrollo de software quiene creó la aplicación para nosotros.

Actualmente se ofrece un estudio de encuesta llamado “Encuestas de estilo de vida DIAD” utilizando MyDIAN. Este proyecto tiene como objetivo examinar cómo los factores del estilo de vida, como el sueño y la dieta, influyen en el riesgo de enfermedad de Alzheimer. Una vez que haya instalado la aplicación Linkt en su teléfono inteligente y haya aceptado participar en el estudio de la encuesta, aparecerán cuestionarios en la aplicación de vez en cuando cada pocos meses para preguntarle sobre sus actividades y hábitos diarios. Con el tiempo, estos datos se analizarán para buscar relaciones entre los factores del estilo de vida y los otros tipos de datos que recopila la DIAN, como la edad al inicio de los síntomas, la progresión de la enfermedad, los biomarcadores y las imágenes. Las familias suelen a menudo preguntarn cómo pueden cambiar los hábitos diarios para reducir su riesgo. Esperamos que la investigación sobre los factores del estilo de vida pueda finalmente ayudarnos a dar sugerencias que estén respaldadas por evidencia científica.

Si tiene preguntas sobre las invitaciones, las encuestas o la solución de problemas de MyDIAN, comuníquese con nosotros en cualquier momento ([dianexr@wustl.edu](mailto:dianexr@wustl.edu) o 1-844-342-6397) y estaremos

## MyDIAN in Spanish

The MyDIAN participant portal will soon be available to Spanish speaking participants! The portal is based on an app called Linkt and is a direct way for participants to receive articles, announcements, and alerts for research opportunities. If you are registered with the Expanded Registry and a primary Spanish-speaker, you may soon see an email invitation to download the Linkt app. The emails come from Datacubed Health, our software development partner company who built the app for us.

A survey study called “DIAD Lifestyle Surveys” is currently offered using MyDIAN. This project aims to examine how lifestyle factors such as sleep and diet impact risk of Alzheimer’s disease. Once you have installed the Linkt app on your smartphone and agreed to participate in the survey study, questionnaires will pop up in the app every few months to ask you about your daily activities and habits. This data will eventually be analyzed to look for relationships between lifestyle factors and the other types of data DIAN collects, like age at symptom onset, disease progression, biomarkers and imaging. Families often ask about how they can change daily habits to reduce their risk. We hope that research on lifestyle factors can ultimately help us give suggestions that are supported by scientific evidence.

If you have questions about MyDIAN invites, surveys, or troubleshooting, please contact us at any time ([dianexr@wustl.edu](mailto:dianexr@wustl.edu) or 1-844-342-6397) and we would be happy to help you. We are excited to grow this new facet of DIAN and hope it provides a valuable research connection to you, the participant!

*-Sarah Adams, DIAN EXR*



## Brain Donation

Individuals who join The Dominantly Inherited Alzheimer Network Expanded Registry (DIAN EXR) may choose to become a Participant in either the DIAN Observational study or a clinical trial as part of the DIAN Trials Unit. DIAN Participants (and in some instances their first degree relatives) are eligible for the DIAN brain donation program.

Participation in the DIAN brain donation program is an extraordinarily important part of these studies. Neuropathological assessment is the only definitive method to understand the many changes that occur in the brain from dominantly-inherited Alzheimer disease (DIAD) and to determine whether investigational study drugs reduce or slow Alzheimer disease neuropathological changes or introduce any treatment-associated neuropathological complications. Even though there is an approved drug for the treatment of Alzheimer disease, much more research is needed to find treatments that may be more effective. Evaluating brain tissue is a critical component of this research. Although all individuals with DIAD share common features of Alzheimer disease, the disease affects every brain somewhat differently – even within a single family. To understand the effects of treatments and the disease itself, it is critically important to study as many DIAD brain donations as possible. Every single brain donation is unique and precious. And, because the DIAD population participating in DIAN studies is limited, it is important for all participants to consider this opportunity. Only a collective effort from many participants will maximize the potential of research studies to make new discoveries and find new, effective treatments.

Importantly, this ultimate gift of brain donation also multiplies the value of the data that the participant graciously contributed during life. In addition to neuropathological assessments, the DIAN Neuropathology Core also provides DIAN brain tissue samples to approved qualified investigators around the world, in accordance with DIAN data and sample sharing policies. All these data derived from direct examination and study of the brain can be evaluated for associations with clinical, genetic, neuropsychological, and neuroimaging data obtained during life at participating DIAN investigative sites. Such cross-discipline studies have already yielded ground-breaking new insights into the biology of DIAD, and will most certainly do the same for our understanding of the effects of DIAN-TU treatments.

Upon enrollment, DIAN participants will be approached by the study staff to discuss brain donation. Once consent is given, brain donation arrangements are made well ahead of the participant's passing to simplify the process for the participant's family members. The procedure is carried out at little to no expense to the participant's family and should be completed within hours of the participant's passing. There are no changes to an individual's appearance, so no alteration of funeral proceedings are required. If the participant wishes, their family will receive a neuropathology research report describing the findings of the assessment completed by our board-certified neuropathologists. The study staff is available to help interpret these findings for the family.

Although members of the Neuropathology Core do not regularly have the pleasure of interacting with the participants and their families, we hold them in the highest regard and are very grateful to them for their donations and devotion to DIAN and DIAN-TU. Together, we will find truly effective treatments for Alzheimer disease!

*-Erin Franklin, Senior Clinical Research Coordinator*





## Family Voices on Brain Donation



It's not the nicest thing to think about so I wanted to share my experience of donating my mum's brain and choosing to register to donate my brain when the time comes.

Mum lived with Alzheimer's for a long time, and when we knew that the end was near I knew that if she could do something that would help people in the future she would want to do it. I contacted Queen Square Brain Bank which works closely with the Dementia Research Centre in London, and the lovely coordinator with the calmest of voices listened to me as I cried a lot and asked loads of questions. From that point onwards, they organised everything - they told us to contact our preferred funeral directors and get them to call the brain bank.

When mum died, there were certain things that needed to be done in certain time frames, and we received regular updates from the coordinator every step of the way; we always knew what was happening and when.

Although mum didn't participate in research while she was alive, I love knowing that her brain will benefit Alzheimer's research for decades to come.

We received a beautiful letter thanking us for donating mum's brain and telling us how much will be learned from it and we also received a detailed report of what they found initially. We were also invited to meet with a consultant to discuss the genetics and had the mutation in our family confirmed which at that point we didn't have.

I registered myself with Queen Square Brain Bank years ago as have most of my family and I kind of love that one day my brain will be hanging out with my families brains and some of my friends brains too - our participation in research won't end. I'm also thankful that I've been able to share with my loved ones why I want to donate my brain, how important it is to me and they know who to contact and what to do when that time comes.

I'm awaiting more news of how the DIAN Brain Bank will work for people in the UK but one way or another I know that researchers will continue to learn more about Dominantly Inherited Alzheimer's Disease and sporadic Alzheimer's and a long time after I've died I will still be a part of that!

*-Sophie Leggett, Family Member*

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My younger brother, Dave, passed away December 28, 2019. He died at home after declining from Dominantly Inherited Alzheimer's Disease. He was 49 years old and left behind a wife, 3 sons, 3 brothers and 2 sisters, 3 sister-in-laws, 1 brother-in-law and 11 nieces and nephews.

Long ago even before Dave was symptomatic and without knowing his genetic status, he agreed to donate his brain to the Memory and Aging Project at Washington University in St. Louis. He knew the importance of this research in finding a treatment and cure for this disease that had affected his family and so many others.

As Dave's disease progressed and we knew the end of his life was nearing, with his wife's permission, I contacted our study nurse at Washington University, to get help making sure things were ready for the brain donation at the time of Dave's death. Peggy assisted me by making calls and putting me in contact with the appropriate people both at Washington University and in our home community to coordinate the arrangements. This allowed us to only have to make one phone call after Dave died and the rest was taken care of. As I went through this process, I did feel that anything I needed was respected and taken care of with minimal stress for a difficult task.

Overall the process was efficient and easy to coordinate.

*-Rachel Huber, Family Member*

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For more information on how to sign up for brain donation, please contact your site coordinator or the [DIAN EXR](#).



## Alzheimer's Disease in the News

Investigational Alzheimer's drug improves biomarkers of the disease

<https://medicine.wustl.edu/news/investigational-alzheimers-drug-improves-biomarkers-of-the-disease/>

Protein linked to heart health, disease a potential therapeutic target for dementia

<https://medicine.wustl.edu/news/protein-linked-to-heart-health-disease-idd-as-potential-therapeutic-target-for-dementia/>

WashU, Pitt awarded \$10.7 million for Alzheimer's disease research

<https://medicine.wustl.edu/news/washu-pitt-awarded-10-7-million-for-alzheimers-disease-research/>

Draining brain's debris enhances Alzheimer's therapies in mice

<https://medicine.wustl.edu/news/draining-brains-debris-enhances-alzheimers-therapies-in-mice/>

Can changes in driving habits predict cognitive decline in older adults?

<https://medicine.wustl.edu/news/can-changes-in-driving-habits-predict-cognitive-decline-in-older-adults/>

International Alzheimer's clinical trial to test tau drugs

<https://medicine.wustl.edu/news/international-alzheimers-clinical-trial-to-test-tau-drugs/>

Holtzman, Karch honored for research into neurodegenerative diseases

<https://medicine.wustl.edu/news/holtzman-karch-honored-for-research-into-neurodegenerative-diseases/>

## Recent DIAN Publications

A trial of gantenerumab or solanezumab in dominantly inherited Alzheimer's disease

<https://www.nature.com/articles/s41591-021-01369-8>

GPS driving: a digital biomarker for preclinical Alzheimer disease

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8204509/>

Resting-State Functional Connectivity Disruption as a Pathological Biomarker in Autosomal Dominant Alzheimer Disease

[https://www.liebertpub.com/doi/10.1089/brain.2020.0808?url\\_ver=Z39.88-2003&rfr\\_id=ori%3Arid%3Acrossref.org&rfr\\_dat=cr\\_pub++0pubmed&](https://www.liebertpub.com/doi/10.1089/brain.2020.0808?url_ver=Z39.88-2003&rfr_id=ori%3Arid%3Acrossref.org&rfr_dat=cr_pub++0pubmed&)

Plasma Amyloid-Beta Levels in a Pre-Symptomatic Dutch-Type Hereditary Cerebral Amyloid Angiopathy Pedigree: A Cross-Sectional and Longitudinal Investigation

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8000178/>

Spatially constrained kinetic modeling with dual reference tissues improves 18 F-flortaucipir PET in studies of Alzheimer disease

<https://link.springer.com/article/10.1007%2Fs00259-020-05134-w>

Longitudinal Accumulation of Cerebral Microhemorrhages in Dominantly Inherited Alzheimer Disease

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8032370/>

Modeling autosomal dominant Alzheimer's disease with machine learning

<https://alz-journals.onlinelibrary.wiley.com/doi/10.1002/alz.12259>

Flortaucipir (tau) PET in LGI1 antibody encephalitis

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7886030/>

Dominantly inherited Alzheimer's disease in Latin America: Genetic heterogeneity and clinical phenotypes

<https://alz-journals.onlinelibrary.wiley.com/doi/10.1002/alz.12227>

Biphasic cortical macro- and microstructural changes in autosomal dominant Alzheimer's disease

<https://alz-journals.onlinelibrary.wiley.com/doi/10.1002/alz.12224>

Pattern and degree of individual brain atrophy predicts dementia onset in dominantly inherited Alzheimer's disease

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8256623/>

The informed road map to prevention of Alzheimer Disease: A call to arms

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8293489/>

Comparison of CSF biomarkers in Down syndrome and autosomal dominant Alzheimer's disease: a cross-sectional study

<https://www.sciencedirect.com/science/article/abs/pii/S1474442221001393?via%3Dihub>

Spatially constrained kinetic modeling with dual reference tissues improves 18F-flortaucipir PET in studies of Alzheimer disease

<https://link.springer.com/article/10.1007%2Fs00259-020-05134-w>

Comparing amyloid- $\beta$  plaque burden with antemortem PiB PET in autosomal dominant and late-onset Alzheimer disease

<https://link.springer.com/article/10.1007%2Fs00401-021-02342-y>

*The DIAN data are increasingly published in scientific reports to enable investigators worldwide to learn of our progress and to advance scientific understanding of Alzheimer's disease. Because of this, there is a small but possible risk that a DIAN participant reading or hearing of these scientific reports might guess, correctly or incorrectly, information about themselves. This includes guessing one's own or a family member's mutation status. We at DIAN take every step to minimize this risk, including ensuring that all DIAN data in journal articles, scientific meetings, press coverages, etc., lack identifying information for any participant, but it is possible that even such de-identified data may reveal a pattern of symptoms or a relationship with other medical disorders that could suggest that a particular person is mutation positive. You can avoid reading these scholarly articles or listening to presentations related to the DIAN study to decrease this risk.*



The DIAN website is a great place to learn more about our research and find additional information. Please visit the "News" page at <https://dian.wustl.edu/news/> for articles related to DIAN and Alzheimer's disease. Family members share their stories on the "Family Voices" page at <https://dian.wustl.edu/for-families/family-voices/>. If you are interested in research opportunities, please contact the DIAN Expanded Registry at [dianexr@wustl.edu](mailto:dianexr@wustl.edu). If you are not part of the registry and would like to be, please visit [dian.wustl.edu](https://dian.wustl.edu) to register.

**SAVE THE DATE**

The DIAN-TU will share important information about the next tau drug arm and Primary Prevention study at our upcoming DIAD Family Webinar on **Saturday, November 20, from 4:00 - 6:00 PM CST**. Please watch your inboxes in October for an invitation to the webinar. Registration is required.