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Inherited Alzheimer
Network Expanded
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Department of Neurology



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Contact the Editor

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Connections Across Borders

One of the difficult aspects of coping with a rare disease is the isolation often felt when navigating its hardships. While symptom management and future planning offer their own challenges, loneliness can compound the strain of these tasks. To help alleviate this isolation—while also sharing scientific findings and research updates—we offer an annual DIAD Family Conference. This year, we are able to host two regional conferences: one in Mexico City for families living in Latin America, and a second gathering in the Netherlands in July for families living in Europe.

This year's Latin American Regional DIAD Family Conference, held in conjunction with the Alzheimer's Association AAIC Satellite Symposium, offered family members affected by DIAD, as well as caregivers of individuals with DIAD, the opportunity to gather in Mexico City on May 20, 2023. This event hosted 125 attendees from Argentina, Brazil, Colombia, Mexico, and Puerto Rico. This year's theme, *Juntos Podemos* (Together We Can), reflected researchers' and participants' hopes for a future cure as well as the uniting spirit of community.

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Connections Across Borders (continued)

Speakers presented on topics including recent advances in Alzheimer's treatment and prevention, current knowledge about non-pharmacological prevention in AD, explanations of the genetic component of DIAD, and the importance of working together to find a cure for AD. Featured presenters and panelists included academic researchers as well as representatives from the Alzheimer's Association and Alzheimer's Disease International (ADI). After these morning presentations, family members were able to gather in smaller groups for conversation and support on topics such as genetic counseling, symptom management, caregiving, and a question-and-answer session about participation in DIAN studies. These conversations allow family members to share wisdom and strategies for dealing with Alzheimer's as well as the comfort of mutual understanding.

Clinical Research Coordinator Karina Skrbec, after spending several months tirelessly assisting conference planning, reflected on the event. "The unwavering dedication and enthusiasm of all involved was truly inspiring. This experience will undoubtedly strengthen the sense of community within researchers, family members, and coordinators and foster the continued support of DIAD research."

Footage from past family conferences can be found online at <https://dian.wustl.edu/families/family-conferences/>.



Pictured: Researchers attending the Latin American DIAD Family Conference gather for a pre-meeting to discuss new genetic counseling and testing protocols for families

Cognitive Testing with New eCDR Assessment

The global Covid-19 pandemic disrupted a majority of activities over a longer timespan than anyone expected, causing people to reconsider how they conduct business, research, or daily tasks such as shopping and leading to rapid adoption of technological solutions such as remote work, video conferencing, and increased home delivery. The DIAN studies also looked at various techniques and tools, such as MyDIAN, ARC, and others, that could be implemented in our research to engage and collect new or more frequent data from participants in different ways. One of these tools that is currently being piloted at the Washington University DIAN Observational site is the electronic Clinical Dementia Rating (CDR) web application for assessing dementia staging.

Originally developed by clinicians including Dr. John Morris at Washington University, the CDR assessment involves a semi-structured interview by trained raters and is used in both research and dementia care clinics. The electronic CDR, or eCDR, was developed by a team of researchers led by Michael Weiner at University of California, San Francisco to adapt the CDR questions into a more structured web-based questionnaire through the Brain Health Registry (BHR). Answers to these questions are analyzed to produce an overall score similar to the standard CDR. Participants in the pilot study receive a postcard with a personalized link to register for the eCDR assessment. Participants are asked to include the same study partner they use for the DIAN study in-person CDR assessments. Results from the eCDR are to be compared to the in-person CDR results.

The eCDR has already been piloted with the BHR volunteers from the general population or those with brain diseases, as well as the late onset Alzheimer's disease research center populations, but we still hope to learn more about how this tool works with DIAN participants. If results show a good comparison between the in-person CDR and the eCDR, it may be used during remote follow-up of DIAN participants in order to reduce the number and/or length of time requirements for in-person visits. It could also be used for pre-screening when enrolling participants in clinical trials or to identify when patients should follow up with dementia specialists in the healthcare settings, which could streamline diagnosis and reduce healthcare costs.

Laura Courtney, CCRP, Manager of Clinical Research



Staff Perspectives with Ellen Ziegemeier

Those who have joined the DIAN Expanded Registry, participated in a DIAN clinical trial, or even just asked questions about research participation within the past decade have almost certainly spoken to Senior Clinical Research Coordinator Ellen Ziegemeier. In early June, I sat down with Ellen to learn about her time in DIAN and her insights on more than two decades of Alzheimer's research work. (Our conversation has been lightly edited for length and clarity.)

Editor: You haven't always worked in clinical trials. What drew you to this research work?

Ellen: I was first intrigued because of the topic of Alzheimer's. Since I graduated with my master's in anthropology, I was doing interviews with Alzheimer's caregivers. I worked in a memory clinic in Honduras and came back to the United States during a low point in grant funding for qualitative studies. I wanted to get back into doing Alzheimer's research with families. When I interviewed with Dr. Bateman, he said that through research, he could help many more people than he could in clinical care. While qualitative studies help disparity research, which I liked, [the results aren't] as immediate as going to the root of the distress in these families, which is the disease.

What skills and experiences from your previous work were you able to bring to the DIAN Expanded Registry?

I did a lot of interviewing for my master's thesis ethnography, so I developed a skill set for interviews. I'm just a natural question-asker; I'm curious. In my first professional role, I was going into people's homes, mostly caregivers, and seeing their loved ones, and interacting with them. It made me want to be in that space with families. The questions that I had to ask caregivers that were really hard ... it was translatable, the way I could transition from probing questions to emotional support. And I just like people. I also did neuropsych testing, in English and Spanish, with people who were symptomatic.



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Staff Perspectives (continued)

What is the most rewarding aspect of working in Alzheimer's research?

It definitely has to be the families, and the relationships that I now have, some for almost ten years. Sometimes the weight of this disease will fracture a family. On the other hand, this disease unites some families, and the resilience is amazing. I take inspiration from the families. The best part is to interact with families, to get to know them and fight on their behalf. On a long day, knowing that the person who's waiting for a call needs it—if that makes this journey a little less hard, that helps me to do that.

You touched on this a bit, but what's most challenging about the work you do?

The losses—now that it's ten years, I've gotten to know some people who have passed away. I say to every family, I wish we were in time for their loved one. We're in a war, and the front line is people who are sick now, and some of them will fall. Some of [those I've met] may be helped by the drugs we have now. It's not the long hours that are hard: it's the human loss that goes with this.

Yes. *(We pause to take a deep breath.)* Outside of work—when things get tough, what helps you cope? Where do you find hope?

I'm a part of a choir at my church—making music is soothing and uplifting. I garden in the summer—it's fulfilling, being able to eat something you grew. I have two cats, which are delightful. I have a safe place with my cats, birds, my garden, my partner, and a good, solid family. I bike and go to the gym. Another thing that fuels me is working on the board of an immigration rights nonprofit.

[DIAN has] an amazing group of people who really care and work hard. That motivates me. It's a great opportunity to be a part of [this research]; the hardest things are balanced with these great positives.

What else would you want people to know about you and the work that you do?

This is a symbiotic relationship with families—they are our true partners. I've heard from so many people that [trial participation] is providing some hope for them, that they can do something about [this disease] in their family. Families' investment in this project is amazing and is worth lauding. The information we get from these trials will hopefully find answers not just for these genetic mutations, but also for sporadic AD. Our research families are heroes.

Thank you so much for sharing your thoughts with me.

Thank you. It's been an interesting, challenging, and fulfilling ten years.

DIAN Observational Study Symposium

The DIAN Observational Study hosted the DIAN Target Validation Symposium in Washington, DC on May 24-26, 2023 following the Alzheimer's Association Research Roundtable. The Symposium was a scientific gathering for academic, research, medical, and industry professionals that allowed physician investigators, researchers, and drug developers to review the scientific discoveries that inform about targets and target validation based on data from DIAD. The meeting helped to facilitate sharing of the most recent findings, discussing ideas, and networking on potential future drug development for both DIAD and sporadic Alzheimer's disease.

To learn more about the symposium and view video presentations, visit <https://dian.wustl.edu/our-research/dian-target-validation-symposium/>.



Pictured: Scientific Director of DIAN Celeste Karch and DIAN Biomarker Core Leader Laura Ibanez field questions on potential omics target validators (left); the DIAN Observational Study Administrative Core Team gathers at the conclusion of the symposium's first day of presentations (below)



Recent DIAN Publications

First presentation with neuropsychiatric symptoms in autosomal dominant Alzheimer's disease: the Dominantly Inherited Alzheimer's Network Study

<http://dx.doi.org/10.1136/jnnp-2022-329843>

Sex difference in evolution of cognitive decline: studies on mouse model and the Dominantly Inherited Alzheimer Network cohort

<https://doi.org/10.1038/s41398-023-02411-8>

Longitudinal head-to-head comparison of 11C-PiB and 18F-florbetapir PET in a Phase 2/3 clinical trial of anti-amyloid- β monoclonal antibodies in dominantly inherited Alzheimer's disease

<https://doi.org/10.1007/s00259-023-06209-0>

Genetic associations with age at dementia onset in the PSEN1 E280A Colombian kindred

<https://doi.org/10.1002/alz.13021>

Single-nucleus RNA-sequencing of autosomal dominant Alzheimer disease and risk variant carriers

<https://doi.org/10.1038/s41467-023-37437-5>

Metabolomic and lipidomic signatures in autosomal dominant and late-onset Alzheimer's disease brains

<https://doi.org/10.1002/alz.12800>

Location of pathogenic variants in PSEN1 impacts progression of cognitive, clinical, and neurodegenerative measures in autosomal-dominant Alzheimer's disease

<https://doi.org/10.1111/accel.13871>

Conquering Alzheimer's: a look at the therapies of the future

<https://doi.org/10.1038/d41586-023-00954-w>

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 coverage, 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.

Alzheimer's in the News

Study: Sleeping aid may be effective in slowing Alzheimer's

https://www.upi.com/Health_News/2023/04/20/sleeping-aids-Alzheimers-disease/2961682008414/

Stress increases Alzheimer's risk in female mice but not males

<https://medicine.wustl.edu/news/stress-increases-alzheimers-risk-in-female-mice-but-not-males/>

Lilly drug slows Alzheimer's by 35%, bolstering treatment approach

<https://www.reuters.com/business/healthcare-pharmaceuticals/lilly-drug-slows-alzheimers-progression-by-35-trial-2023-05-03/>

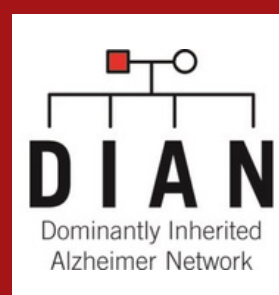
When Gut Bacteria May Be an Early Sign of Alzheimer's Disease

<https://time.com/6287229/gut-alzheimers-connection-microbiome-bacteria/>

Ten Ways to Increase Latino Participation in Alzheimer's Research from Leaders in Health Equity Science

<https://www.alz.org/news/2023/increase-latino-participation-alzheimers-research>

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



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