Data from largest Phase III trial of pre-symptomatic Alzheimer's disease now shared with scientists around the world

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Data from the Anti-Amyloid Treatment in Asymptomatic Alzheimer's (A4) study, the first and largest clinical trial of pre-symptomatic Alzheimer's disease, is now widely available to researchers studying the condition. The comprehensive dataset has already yielded key insights about Alzheimer's disease, which affects nearly seven million people in the United States, and sharing the data opens avenues for further progress.

A4 researchers screened more than 7,500 people and enrolled 1,169 people with pre-symptomatic Alzheimer's disease. This stage of this

disease, when amyloid protein begins to collect in the brain, but cognitive decline is not yet evident, is seen as an optimal time to intervene and slow progression.

The researchers collected a wealth of information from each participant—including brain scans, blood samples, genetic information and cognitive tests—over a period of 4.5 years, and up to 8 years in the extension study.

"We were able to track decline and gain a much deeper understanding of this stage of the disease," said Paul Aisen, MD, co-leader of the A4 study and a professor of neurology and founding director of the Alzheimer's Therapeutic Research Institute (ATRI) at the Keck School of Medicine of USC.

"Now, we want to make sure everybody has access to this information. We consider it essential to share all that we've learned with anyone else who can study this."

The latest effort is an extension of a long-standing priority of ATRI and the Keck School of Medicine to broadly share data while simultaneously protecting participant privacy. The institute also leads the clinical arm of the Alzheimer's Disease Neuroimaging Initiative, a massive collaborative data collection and sharing effort that is celebrating its 20th anniversary this year.

"This dataset is part of a much larger and longer-term commitment to open science," said Gustavo Jimenez-Maggiora, MBA, director of informatics at ATRI.

"It demonstrates the strong commitment that ATRI, USC and our collaborators have to not just using data for our immediate purposes, but sharing it with the broader scientific community to support and

accelerate further discoveries in Alzheimer's disease research."

The Epstein Family Foundation's Research Collaboration and matching donors have made the complex work for data sharing possible.

A wealth of data

The A4 study, a public-private partnership between the National Institutes of Health's National Institute on Aging, Eli Lilly and Company, the Alzheimer's Association, GHR Foundation and several philanthropic groups, was launched in 2014.

From thousands of volunteers, researchers screened and selected 1,169 participants, ages 65 to 85, who showed signs of amyloid protein buildup on a positron emission tomography (PET) scan but had no memory impairment or other clinical signs of Alzheimer's disease.

The researchers collected extensive data from each participant, including PET scans, magnetic resonance imaging (MRI) scans, blood samples, genetic information, clinical details and neuropsychological tests—both at the time of enrollment and during monthly visits over a period of 4.5 years.

They tested the efficacy of an early anti-amyloid drug, solanezumab. The drug did not decrease amyloid from baseline levels and did not slow the progression of Alzheimer's disease when given during the pre-symptomatic stage.

A4 researchers have already gained valuable knowledge from the data they collected, including that the progressive buildup of amyloid in the brain is closely linked to corresponding declines in memory and cognition. They also found that a blood test can be used to track amyloid buildup early in the disease.

In 2024, Robert A. Rissman, Ph.D., a professor of physiology and neuroscience, the W.M. Keck Endowed Professor in Medicine and director of ATRI's Biomarker Laboratory and Biorepository, won the *Journal of Alzheimer's Disease* Alzheimer Award for his publication on the new blood test.

In addition to A4, the Longitudinal Evaluation of Amyloid Risk and Neurodegeneration (LEARN) study measured cognitive changes in approximately 500 cognitively unimpaired older adults who did not have enough amyloid to qualify for the A4 trial. Data from this group can provide a key point of comparison for future trials of pre-symptomatic Alzheimer's disease.

All the study data, de-identified so that study participants' personal information cannot be linked to their data or biosamples, is now available for broader use: A4STUDYDATA.ORG. Researchers around the world studying Alzheimer's disease can apply for access and receive everything from brain scan images to biological specimens to support their work.

The data discovery and download interface was enabled by the Global Research and Imaging Platform (GRIP), a nonprofit focused on optimizing the ability of researchers to find and use data.

"We are breaking new ground here, but we're also continuing to work on our platform—including developing new approaches to data visualization and data exploration—to make it as useful as possible to investigators at all stages of training and professional experience," Aisen said.

Getting ahead of Alzheimer's disease

Aisen and his colleagues anticipate a flood of requests for data access

after they publicize the release of the A4 dataset at the upcoming Alzheimer's Association International Conference.

They have also launched a follow-on study, known as the AHEAD3-45 Study, to test the efficacy of the drug lecanemab for people with pre-symptomatic Alzheimer's disease. Lecanemab received approval in 2023 from the U.S. Food and Drug Administration to treat patients with later stages of the disease.

"We hope that the A4 and LEARN data will inform ongoing and future prevention trials in order to accelerate the quest to prevent Alzheimer's dementia," said Reisa Sperling, MD, co-leader of the A4 study, a professor of neurology at Harvard Medical School and director of the Center for Alzheimer Research and Treatment at Brigham and Women's Hospital and Massachusetts General Hospital.

More information: Clinical trial data: www.a4studydata.org/

Provided by Keck School of Medicine of USC

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