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[Down syndrome families' fight for access to Alzheimer's trials, treatments | Reuters](#)

Down syndrome families' fight for access to Alzheimer's trials, treatments

By [Julie Steenhuysen](#)

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CHICAGO, Oct 10 (Reuters) - When Lianor da Cunha Hillerstrom of Lexington, Massachusetts, learned her now 9-year-old son Oskar had Down syndrome, she was concerned but not panicked.

As a child, Lianor lived for a time in Santo Amaro de Oeiras, Portugal, near her aunt Teresa who had Down syndrome, which causes intellectual disability. Had Lianor, who is 47, stayed in Portugal, she would have witnessed her aunt decline and then die at age 60 of Alzheimer's - the most common cause of death for people with Down syndrome.

Now, Lianor's husband and Oskar's father, former biotech executive Hampus Hillerstrom, 46, is leading an effort to gain parity with neurotypical adults for his son and others with Down syndrome.

That means being able to get them promising new drugs like Eisai ([4523.T](#)) and Biogen's ([BIIB.O](#)) recently approved Leqembi and Eli Lilly's ([LLY.N](#)) experimental donanemab, as well as inclusion of people with Down syndrome in clinical trials of treatments for Alzheimer's.

"The goal is to make sure we get access," he said. "Ideally, we needed to be part of these trials from the beginning."

Reuters interviewed five top neurologists who recommend against immediate use because the drugs are untested in this population, whose unique predisposition to Alzheimer's could pose extra safety risks. This puts Hillerstrom, chief executive of the Down syndrome research organization LuMind IDSC, and other advocacy groups in the unusual position of being odds with prominent experts in the field.

Reuters has learned that advocacy groups have taken their message directly to the U.S. government Medicare health program, seeking changes to written policies they believe could disqualify people with Down syndrome from reimbursement for the treatments.

Down syndrome affects 400,000 people in the United States and more than 6 million globally. People with the condition inherit a third copy of chromosome 21, giving them an extra helping of a gene that causes them to overproduce a protein called beta amyloid.

By age 30, most individuals with Down syndrome have abnormal clumps of amyloid in their brain, and many show signs of dementia in their 40s and 50s.

Clinical trials of Leqembi and donanemab, which is expected to win U.S. approval later this year, have shown that removing beta amyloid can slow cognitive decline in people with early-stage Alzheimer's. Patient advocates and three neurologists interviewed by Reuters believe the same may be true of people with Down syndrome.

However, the drugs can cause brain swelling and bleeding, a risk that is especially high among people with a condition called cerebral amyloid angiopathy (CAA) which affects nearly half of Alzheimer's patients. In an extended portion of Eisai's main Leqembi trial, CAA was associated with one death.

People with Down syndrome, who were not included in either Eisai or Lilly's late-stage trials, have higher-than-average rates of CAA, and neurologists are concerned that removing amyloid with a drug like Leqembi could weaken artery walls, leading to bleeding in the brain.

'THE DIGNITY OF RISK'

Hillerstrom said the groups are "very strongly" lobbying Eisai and Lilly to conduct the safety trials in Down syndrome, and said he has been meeting with the companies to push them to design such trials. Because of the unique risks, LuMind and others advise families to wait for the data.

With such trials only in planning stages, it could be three or four years before they yield answers, so advocates and others on the front lines also want barriers to FDA-approved drugs removed.

Emily Largent, a bioethicist and health policy expert at the University of Pennsylvania Perelman School of Medicine, said when faced with a fatal disease, people with Down syndrome should be allowed to weigh the risks and benefits of treatment, which she referred to as "the dignity of risk."

Part of that entails convincing Medicare to change language in its national coverage policy, advocates including Hillerstrom say. That would involve including validated cognitive assessment scales to detect memory changes in people with Down syndrome, three expert sources told Reuters.

LuMind and a coalition of six other advocacy groups made their case in a July 25 meeting with Medicare. They stressed that all other treatments approved by the U.S. Food and Drug Administration are available to people with Down syndrome, even when they had not been tested in people with the condition, sources who attended the meeting told Reuters.

A Medicare spokesperson said current coverage policy does not prohibit people with Down syndrome from accessing Leqembi, but did not respond when asked if the agency is considering changes to the Alzheimer's registry requirements.

Already, doctors are fielding requests for the drug. Dr. Beau Ances, a neurologist at Washington University in St. Louis, said he will not offer the treatment until it is shown to be safe and is [following published guidance](#) from leading neurologists.

But he is frustrated by the wait. "I've lost a number of patients this year alone," Ances said. "I'm tired of giving hugs. I really want to give a therapy."

Instead, Ances asks patients to join a clinical trial sponsored by the National Institute on Aging that has been screening potential patients using cognitive tests

designed to measure changes in memory, language and attention specifically in people with Down syndrome.

They also undergo genetic testing, brain scans and other tests necessary to take part in a treatment trial, and provide informed consent themselves or through a legally authorized representative.

So far, 19 specialty clinics including Washington University have enrolled 180 volunteers. Dr. Michael Rafii, a University of Southern California neurologist who is leading the trial, said he is negotiating with drugmakers about testing one or more anti-amyloid treatments in a placebo-controlled safety and efficacy trial starting next year.

Lilly declined to comment on whether it is considering either a safety trial or taking part in that study. An Eisai spokeswoman said the company "has no immediate plans" to conduct clinical trials of Leqembi in people with Down syndrome.

'LIVING LONGER'

Alzheimer's is a relatively recent worry for people with Down syndrome. Advances in care have resulted in a more than doubling of life expectancy, from an average age of 25 in 1983 to 60 currently. That longer lifespan has brought with it the near-certainty of developing Alzheimer's.

Dr. William Mobley, a neurologist at UC San Diego School of Medicine, said people with Down syndrome have come far since the 1950s, when standard medical advice was to send infants to an institution.

"They're living longer, but almost all of them are dying of Alzheimer's disease when they get beyond age 60," he said.

Mobley and many other neurologists and patient advocates agree on the importance of safety trials, and the inclusion of people with Down syndrome in trial designs for future drugs, rather than waiting years until they are approved.

"Clinicians want to see that kind of safety information before they can prescribe in our population," Hampus Hillerstrom said.

Dawn Brooks, Lilly's global development leader for donanemab, said in a statement that the company did not explicitly exclude people with Down

syndrome. Because Alzheimer's typically occurs in people with Down syndrome by their mid-50s, it was challenging to find people who could take part in the main donanemab study, which enrolled people starting at age 60.

The company is collaborating with LuMind in a study gathering data on how Alzheimer's manifests in people with Down syndrome.

Margot Rhondeau of the National Down Syndrome Society, whose daughter, Hannah, 5, has the condition, said that for some families whose adult children are showing signs of dementia, safety data is too far off.

"At the end of the day," she said, "our belief is that a physician and a family should have the right to decide what is best for them."

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