New global initiative to tackle Alzheimer's disease

The Davos Alzheimer's Collaborative aims to build a diverse patient cohort for study, coordinate clinical trials, and improve care. Nayanah Siva reports.

A new international initiative to collectively tackle the challenges of Alzheimer's disease has been launched by the World Economic Forum and the Global CEO Initiative on Alzheimer's Disease. Aiming to accelerate the discovery, testing, and delivery of precision interventions for Alzheimer's disease, the initiative, called the Davos Alzheimer's Collaborative (DAC), will include governments, academics, private sector leaders, and non-governmental organisations.

About 50 million people live with dementia, most commonly Alzheimer's disease. This number is projected to reach 132 million by 2050, with 71% of these new cases in low-income and middle-income countries (LMICs). It is estimated that there are 9·9 million new cases of Alzheimer's disease a year globally. The cost of the disease in 2018 was said to be US$1 trillion, which is projected to double by 2030.

"With over 100 years of research and no available disease-modifying therapy, the burden that dementia will cause our society over the next decade is unprecedented", said Tarun Dua of WHO's Mental Health and Substance Abuse Department.

Experts have said that an initiative like DAC is essential—with Alzheimer's disease being a global problem, it needs a global, collaborative solution. "As a hugely complex disease, Alzheimer's cannot be solved by working in silos", said Hilary Evans, chief executive of Alzheimer's Research UK. The problem will need a multifaceted approach with researchers, governments, industry, and charities, and resources and expertise on an international scale, explained Evans.

DAC has prioritised three main goals: first, global development of the science on Alzheimer's disease by collecting diverse population data on a global scale; second, building and coordinating an international platform for clinical trials to reduce the time taken to bring new treatments to global markets; and third, facilitating health-care system preparedness and implementation of potential new innovations, diagnosis, and care.

"Currently, we don't understand the biomarkers for the disease, the clinical

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trials network is insufficient, and, if a drug were to emerge, health systems are simply not ready", Arnaud Bernaert, head of Shaping the Future of Health and Healthcare at the World Economic Forum, told *The Lancet*.

In the foundation phase, DAC aims to create a centralised set of data to help researchers conduct longitudinal studies of a large global cohort. Currently the database is very skewed, with a stark gap in inclusion of LMICs. "I think more than 90% of the participants [in clinical trials and genome studies] are from the US and Europe, and less than 5% are of Hispanic or African origin", said Bernaert. "Not only is this unfair from an ethics and moral standpoint, but from a scientific standpoint; we may learn from some populations about certain biomarkers or certain resistance to the disease that could actually lead to drug discovery to benefit global populations, but we have not studied those populations, so we simply do not know."

Adesola Ogunniyi (Department of Neurology, University of Ibadan, Nigeria) is part of DAC, and one of his aims is to ensure that data from LMICs are represented. "The gap will continue to widen unless efforts are made to get researchers in these countries involved in DAC initiatives", Ogunniyi told *The Lancet*.

Progress is already being made as DAC has already mobilised 30 cohorts across the world, representing 21 million people over six continents. Each cohort includes 100 000–500 000 people in a biomedical database, containing a range of genetic and health information. The data will be used to develop new targets for drug development and associated biomarkers. "That's priority number one, maximising the power of cohorts", said Bernaert. DAC aims to facilitate the use of these data on a global platform for researchers to access.

The second main goal of DAC is to address clinical trials by creating a global clinical trial network. Despite decades of research, there have been over 200 failed trials in Alzheimer's disease in the past two decades. Clinical trials are inherently expensive, slow and time-consuming, and often operate independently. In the first phase of the initiative, DAC will begin to build a global clinical trial infrastructure to increase the speed, efficiency, and quality of clinical trials worldwide. In addition, DAC hopes that this network will ensure the inclusion of under-represented populations. In 2021, network goals include establishing links with Singapore, Australia, Japan, China, South America, and Africa, in addition to Europe and North America. DAC also hopes to initiate the first transatlantic therapeutic clinical trial with a minimum of 110 sites.

In a session opening the launch of the new collaboration last week, Andrea Pfeifer, chief executive officer of AC Immune, reported that there were 121 ongoing clinical trials last year, with 80% of them investigating disease-modifying drugs. She is hopeful that there is potential for change to the current treatment landscape. "Today we have biomarkers which allow us to select patients 10–20 years before their symptoms

occur, actually allowing us to think about prevention studies. So, [we are] moving from treating a disease where a lot of the brain has been damaged to actually preventing the disease."

DAC is hoping for a strong relationship with the pharmaceutical industry, as many companies have already come on board with the strategy. "There is limited coordination and efficiency across global clinical trial sites for Alzheimer's disease. There is an opportunity here to build a global clinical trial infrastructure that includes a standing, trial-ready support platform, and IT backbone to actually reduce trial variability and expedite recruitment and enrolment", said Bernaert.

With the third goal in mind, Bernaert explains the importance of health-care readiness, and thinks a barrier to this is diagnosis. "If drugs are to be discovered, we want to make sure they are available for everyone, but for that you need to find the patients. For the time being, diagnostic solutions are either crude or very expensive, and in most cases are not even reimbursed", said Bernaert.

DAC aims to initiate pilot programmes that will focus on early diagnosis, with particular focus on screening and early detection. In a second phase, projects will concentrate on early diagnosis of mild cognitive impairment and dementia, in the hopes of understanding who is at risk of Alzheimer's disease in earlier stages.

Craig Ritchie (The Psychiatry of Ageing Centre for Clinical Brain Sciences, University of Edinburgh) is also involved in DAC, having had experience in the past with clinical trial delivery centres. He thinks one main obstacle in Alzheimer's disease research has been that a lot of clinical trials study patients at a very late stage of disease. "That is, people with dementia, early dementia, or so-called mild cognitive impairment. And the reason the trials take place in those populations is that they are the ones coming into clinical services. Now, if we had clinical services which are identifying people at a much earlier stage of disease, that gives the

opportunity to do drug trials in the population where there's most likely to be an effect."

DAC has already collated 12 governments with equal representation across high-income, low-income, and middle-income countries who have committed to this goal of working towards better screening and detection.

In a third phase of the goal of health-care preparedness, DAC is aiming to initiate projects in optimising care planning in 2023. Providing high-quality care to patients includes translating breakthrough research into "on-the-ground reality", said Elina Suzuki, health policy analyst at the Organisation for Economic Co-operation and Development (OECD). "In most OECD countries, our analysis suggests that more than half of people living with some form of dementia do not receive a diagnosis. Even for those who do receive one, post-diagnostic support is often poor, and people living with dementia—and their families—are too often left to fend for themselves, without a clear idea of what services might be available to them."

Further complicating the matter is the current pandemic. "This was already an urgent challenge before the COVID-19 pandemic struck. People with Alzheimer's have been among the hardest hit by COVID-19", said Evans.

About 26% of people who died with COVID-19 in the UK had dementia. In some regions of Italy, this figure is 20%, with similar numbers being reported in Spain, Canada, and Australia, explained Paola Barbarino, chief executive officer of Alzheimer's Disease International. "We are hearing reports from neurologists worldwide that the rate of people seeking diagnosis has declined sharply during COVID-19", said Barbarino.

The disease is not only affecting patients—Evans also points to the threat to research efforts as projects are delayed and funding opportunities are reduced. "The DAC is launching at an important time when critical progress in research needs to be protected", said Evans.

DAC is hoping to learn from the COVID-19 pandemic, which has shown the importance and success of international multifaceted efforts. The initiative also hopes to follow models of the Coalition for Epidemic Preparedness Innovations and Gavi, the Vaccine Alliance. Both organisations have been instrumental in bringing progress to the most challenging global public health issues.

In addition to the collaboration of various sectors in tackling Alzheimer's disease, experts think there is another important aspect to the challenge: changing the current narrative of Alzheimer's disease. "In 2019 our [Alzheimer's Disease International's] survey of attitude polled 70 000 people in over 120 countries, and one of its troubling statistics was that 62% of health-care practitioners, doctors, and nurses globally still think that dementia is caused by old age", said Barbarino.

"I think the most important thing is to try and change the narrative around degenerative diseases. They have long been considered diseases of late life, which affects people who develop dementia. Whereas all the evidence is now pointing very firmly to the fact these degenerative diseases like Alzheimer's start at least in mid-life", said Ritchie.

Experts are hopeful about DAC. Margaret Chan, former director-general of WHO, described the issue of Alzheimer's disease as a pandemic but thinks prevention is still on the horizon. "I think Alzheimer's and dementia is one such disease where prevention is possible", said Chan in a DAC symposium last week.

DAC "has a lot of responsibility to get it right", says Ritchie. "We have already spent a lot of time on this. I think the field really needs disruption and I think initiatives like this with global reach have to be very bold. Otherwise we're going to end up having this conversation again in another 20 years."

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