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Dementia research needs a global approach

The international community needs to prioritize research on interventions and preventative measures for dementia that are likely to produce the greatest global impact.

Dementia is the seventh leading cause of death worldwide, and the number of people living with this disorder is expected to triple by 2050. The burden of dementia is not equal across all countries, with around two thirds of people with dementia living in low- and middle-income countries (LMICs), where increases are predicted to occur more rapidly than in higher-income countries (HICs). Women are disproportionately affected by dementia, with greater prevalence rates than men in all age groups and a higher proportion of deaths. Women are also responsible for providing roughly 70% of informal care hours globally, with the highest proportions being in LMICs.

Although progress has been made, research into dementia remains fragmented and siloed to areas unlikely to generate the greatest global impact. Even the recent approval of lecanemab by the US Food and Drug Administration is tempered by the fact that the cost and infrastructure requirements of this treatment are likely to be prohibitive for LMICs — where most people with dementia reside. The World Health Organization (WHO) global status report on the public health response to dementia in 2017–2025 highlights the need for increased efforts globally to reach the dementia targets set for 2025 by Member States. The report's bottom line is unequivocal: it is time for the international community to prioritize research on interventions and preventative measures that are likely to benefit all people at risk of dementia.

On 4 October 2022, the WHO released a dementia research blueprint to support implementation of the Global action plan on the public health response to dementia in 2017–2025, representing a first-of-its-kind publication in the context of non-infectious diseases. Leveraging key lessons learned from previous WHO efforts to prioritize and coordinate research into infectious diseases, the blueprint emphasizes key objectives across the entire dementia research spectrum that will have the greatest impact on the global burden of this devastating disorder. For example, a better understanding of the prevalence and incidence of dementia, the costs of illness and the prevalence and impact of risk factors is needed in LMICs and other ethnic and regional groups. Research into the mechanisms of dementia, such as biomarkers and genetic and epigenetic markers, should include and account for differences in these groups. This may require improved engagement and collaboration with communities that may be less willing or unable to participate in these types of studies.

Studies in HICs have reported a decrease in the prevalence of dementia, linked to modifiable dementia risk factors. These exciting findings suggest that modification of risk factors could slow cognitive decline and delay the onset of dementia, or prevent it altogether. Given the costs of dementia care, primary prevention is likely to be the cheapest and easiest way to reduce the projected global impact of dementia. Yet there are little data available on modifiable risk factors in LMICs or in culturally, ethnically and sexually diverse sub-populations in both HICs and LMICs. Furthermore, the data used to calculate these risk factors are from HICs, despite studies showing that some risk factors are more prevalent than others in LMICs and account for more cases of dementia there than in the rest of the world. Differing environmental and social exposures also influence dementia risk. This includes exposure to air pollution and pesticides, which is associated with an increased dementia risk, whereas proximity to green spaces is linked to positive cognitive outcomes.

There are also few robust studies on sex-specific risk factors such as early menopause and complications during pregnancy and on the differential effect of risk factors in men and women, as recently shown for cardiovascular events. It is now generally accepted that longevity alone is not responsible for sex differences seen in dementia, and studies are increasingly highlighting a biological component. Men and women with Alzheimer's disease (AD) exhibit different cognitive and psychiatric symptoms, and women show faster cognitive decline after a diagnosis of mild cognitive impairment or AD dementia. Epidemiological studies demonstrate that the allele encoding apolipoprotein E confers different AD risk profiles on the basis of sex, with women who have the allele encoding apolipoprotein E-ε4 being at greater risk for developing AD than age-matched men are. Despite these findings, little to no data are available on sex differences in the efficacy and safety of drugs used in recently completed phase 3 clinical trials for mild to moderate AD. Furthermore, women remain under-represented in clinical trials for AD. Systematic studying and reporting of sex differences in disease symptomatology, biomarkers, progression, risk factors and treatment responses will be crucial for efforts to reduce the global impact of dementia.

Funding is obviously the key driver of research. Data for 2019 indicate that although funding for dementia has increased, it is directed mainly toward research in HICs. Of the 50 organizations and institutions that received the most grants for dementia research in 2019, 41 were in the United States, 6 were in the United Kingdom and 3 were in Canada. Furthermore, the vast majority of funding is directed toward research into AD, despite the fact that dementia is caused by several diseases. Although increased funding for dementia research is a step in the right direction, this needs to happen in a more structured and equitable fashion.

Dementia is highly complex, and the challenge of tackling the global burden of this disorder cannot be overcome by people working in silos. Considerable research gaps exist in the understanding of this disorder, particularly in areas in which its burden is greatest. Closing these gaps requires implementation of a harmonized global research plan with equitable inclusion and research capacity-building in under-resourced settings. Only such a level of global research prioritization can ensure that ongoing research efforts deliver the greatest impact possible.

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