Challenges for addressing dementia

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Dementia is a syndrome, characterised by impairment of cognitive function—memory, thinking, orientation, comprehension, learning ability and judgement—and is often accompanied by neuropsychiatric symptoms including agitation, anxiety, irritability, depression, and hallucinations. More than 55 million people have dementia worldwide, representing the seventh leading cause of death globally and a major cause of disability and dependence among older people. One of the main risk factors is age, and as life expectancy improves and more of the population grow older, cases of dementia will increase as a result. In Europe, by 2050, the proportion of people aged older than 55 years is projected to reach 40·6% of the population and the prevalence of all-cause dementia is expected to double to almost 20 million cases. Dementia is therefore one of the greatest global challenges of the future, and therefore it must become a clinical, public health, and social care priority.

At present, there are three major challenges for addressing dementia: economic costs, societal awareness, and clinical setbacks. First, the total economic costs of dementia need to be acknowledged to allocate resources appropriately. Although the social welfare systems in Europe cover most of the direct costs of dementia, they do not protect families against the burden of unpaid care, known as informal care. In this issue of *The Lancet Regional Health — Europe*, Erik Meijer and colleagues found that, among 11 European countries, the total estimated annual costs of dementia ranged from €2687 to €15 468 per individual. Most importantly, informal care accounted for a large share of the total cost of dementia (48·1% in France to 88·7% in Italy). In their linked Comment, Linus Jönsson highlighted that this high reliance on informal care calls for the development of caregiver support programmes to ensure adequate financial support and to prevent caregiver exhaustion.

Second, increased awareness of dementia is needed, which can be achieved by providing accurate information to overcome the associated stereotypes, stigma, and discrimination. Stereotypes about people with dementia, such as being a family burden, being hopeless, or being unable to contribute to society, are perpetuated through the language used to refer to individuals with dementia (eg, demented or victims) and through the misconception that dementia results in an inevitable loss of personality and self. The theme of this year's World Alzheimer's Day on September 21—Know dementia, know Alzheimer's— aims to raise awareness about the disease with a focus on the need to support people with dementia and their families after diagnosis.

Third, at present, no disease-modifying effective drugs are available for the treatment of Alzheimer's disease, which contributes to between 60 and 70% of total dementia cases, and the state-of-the-art treatments include drugs that only improve symptoms temporarily. The available support for newly diagnosed patients with Alzheimer's disease consists of neurological and mental health care, home adaptations and adaptive equipment, assistive technology and symptomatic medications. However, the best post-diagnostic support for patients with Alzheimer's disease would be the provision of life-changing treatment to modify and halt the progression of the disease, which can only be possible through advances in the field of research.

Most research into the development of disease-modifying drugs for Alzheimer's disease has focused on the 'amyloid hypothesis'—although not universally accepted—which is the assumption that accumulation of the peptide amyloid-β in the brain is the main cause of Alzheimer's disease. It is believed that when amyloid-β plaques aggregate together, neurodegenerative processes are initiated that lead to the loss of memory and cognitive ability observed in Alzheimer's disease. Amyloid-β has therefore been an obvious therapeutic target. However, the continued failure of clinical trials of drugs designed to interrupt the formation of amyloid-β plaques has raised questions about the importance of the amyloid hypothesis in Alzheimer's disease. Recent complaints, have been filed with the US Food and Drug Administration (FDA), about manipulation of images and data in several research articles on the experimental drug simufilam, which was designed to ease cognitive symptoms of patients with Alzheimer's disease. The FDA refused to stop ongoing phase 3 clinical trials of the drug, however, seven articles have already been withdrawn from scientific journals and three others have received expressions of concern. Another drug, Adulhem became the subject of controversy after it was approved by the FDA in June, 2021, despite paucity of evidence that it can slow cognitive decline in addition to other safety concerns. Adulhem is now only available in the USA to people currently enrolled in clinical trials and does not have marketing authorisation by the European Medicines Agency. Furthermore, allegations of misconduct have emerged this

year regarding the results of a key study that largely shaped Alzheimer's disease research since 2006, reporting a link between an unknown subtype of amyloid-β and memory impairment in rats. These research and clinical setbacks have raised questions as to whether research has been misguided over the past 16 years regarding the causal role of amyloid-β plaques in clinical symptoms of Alzheimer's disease.

These economic, social, scientific, and clinical challenges represent substantial setbacks for the treatment and management of dementia at an individual and societal level. To prepare for the expected increase in dementia burden in the future, fast-paced research advancements will be needed to improve drug therapy, enhance economic support from governments, and increase in awareness and sensitivity about the disease.