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BJPsych Editorial

Shifting paradigms in dementia care: navigating new therapies and prevention strategies

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The year 2024 could mark a turning point in our approach to dementia treatment. For decades, the lack of disease-modifying therapies disincentivised investment in dementia diagnosis and care. This was at odds with the growing importance of dementia in the UK and worldwide as a cause of disability and mortality. At the time of writing, dementia is projected to become the costliest healthcare condition by 2040.

The controversial approval of Aducanumab by the US Food and Drug Administration (FDA) in 2021 has led to renewed interest in dementia therapeutics research. Aducanumab belongs to a class of immunotherapeutics that clear cortical amyloid-beta (Aβ) plaques by a range of mechanisms: reducing Aβ production, preventing Aβ aggregation and promoting Aβ clearance. Mechanistic data showed that Aducanumab reduces the amyloid burden. However, the two trials evaluating its clinical efficacy were marred by methodological issues.[1] Despite fast-track approval from the FDA, this controversy and uncertainty regarding its effects on cognition and progression affected its impact, leading Biogen to announce its discontinuation in 2024.

In 2023, trials for Lecanemab and Donanemab, both similar anti-amyloid drugs, demonstrated modest but consistent slowing of cognitive and functional decline in people with Alzheimer's disease with mild cognitive impairment or mild dementia. The FDA approval process was initially swift with approval given to Lecanamab in 2023. However, in March 2023 it was announced that the FDA would convene an advisory committee meeting to evaluate the evidence of Donanemab efficacy. In the UK, the Medicines and Healthcare products Regulatory Agency (MHRA) decision on Lecanemab is due in the first half of 2024, with National Institute of Health and Care Excellence (NICE) consideration to follow.

Questions about the utility of Lecanemab and Donanemab and related compounds remain. First, their impact on disease progression is modest. For example, Lecanemab is modelled to delay progression to more severe forms of dementia by about 2 years relative to placebo.[2] Second, the safety profile of these drugs is concerning. Around 1 in 10 treated patients develop cortical haemorrhages and oedema visible on magnetic resonance imaging (MRI) known as amyloid related imaging abnormalities (ARIA). While most such cases remain asymptomatic, 1% of cases treated were reported as serious, and three patient deaths were reported in Lecanemab trials.[3] Finally, the cost of implementation of these therapies is significant. A health-economic analysis showed that if they were to be given to everyone eligible in the European Union, the cost of the drug alone would equal what the European Union block currently spends on all medication.[4] Moreover, this analysis did not include the cost of infrastructure investment required to administer and monitor these therapies. Nevertheless, it is evident that the approach to dementia management is shifting towards earlier intervention and prevention.

In this issue, we explore the significant changes in Alzheimer's and broader dementia care, addressing both the challenges and promising developments this new direction presents. Laurell and colleagues sought to estimate demand for the new therapies by examining the records of two National Health Service (NHS) Trusts covering around 2.2 million people. They found that out of 82 386 people referred to Memory Clinic services, 906 annually would meet the disease severity and comorbidity criteria of the amyloid clearance therapies. Nationally, they estimated that just over 30 000 individuals would be eligible. The authors' calculations assumed weekly infusions for 3 years: in the Cambridge and Peterborough NHS Trust alone this amounts to 90 infusions per day. The authors point out that these complexities are compounded by the uncertainties involved in establishing and sustaining the infrastructure for amyloid and genetic tests, along with MRI scans for ongoing monitoring.

In a complementary paper, Kinchin and colleagues explored the perceptions of healthcare professionals and the public to the new therapies. They found that around half of the public responders were likely to accept a disease-modifying therapy for Alzheimer's disease, compared with three-quarters among the healthcare professionals. The latter placed a heavier emphasis on concerns about effectiveness and safety, while members of the public prioritised costs and logistics of arranging treatment. The survey also demonstrated higher acceptance among those of higher socioeconomic status.

The high expenses associated with new dementia treatments call for a more efficient organisation of care processes, both before and after the diagnosis. In terms of opportunities that lie upstream, up to a third of dementia cases are a result of preventable risk factors.[5] Thus, primary and secondary prevention of dementia can reduce the number of people requiring disease modification therapies. Two aligned papers in this issue explore the protective factor of cognitive reserve. Truin and colleagues investigated 4209 ageing adults in the Maastricht cohort and found that an individual's tendency to engage in and enjoy mental activities is associated with higher cognitive ability and lower levels of cerebral small vessel disease. Yang and colleagues also assessed cognitive reserve in data from 210 631 initially dementia-free older adults in the UK Biobank. They found that a cognitive reserve composite (educational and occupational attainment, frequency of cognitively loaded activities) predicted delay in the onset of dementia and mediated a 30% lower risk for dementia.

Prevention approaches to dementia can involve enhancing protective factors but also curbing detrimental ones. In this context, multimorbidity has been established as a target for

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interventions. Hamilton and colleagues demonstrated the complex relationship between multimorbidity and dementia pathology. They combined antemortem and autopsy data from 767 individuals to show that the presence of physical comorbidity weakened the link between the clinical syndrome of dementia and Alzheimer's pathology. The authors underlined the importance of factors associated with multimorbidity, such as psychiatric conditions and polypharmacy, on the clinical course of the dementia syndrome.

Dementia preventative programmes, such as the Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER) study, are difficult to scale because they rely on face-to-face interactions.[6] Digital platforms, with automated interventions, offer new opportunities to address modifiable risk factors. In the current issue, Reid and colleagues show that a dementia risk assessment app is highly acceptable to their sample of 756 UK adults. Cognitive testing delivered via the app was reliable over time. The same platform was recently used in a clinical study setting to deliver tailored behavioural modification interventions for dementia risk. These results emphasise the role that digital technologies will likely play in the future care pathways for adults at risk of dementia.

Post-diagnostic dementia care will also need to adapt to the new landscape. Dementia services frequently only provide diagnosis, after which general practitioners manage care until people begin showing behavioural symptoms. Depression and anxiety, for example, are both known prodromes of dementia and a common comorbidity in the developed syndrome. These symptoms often drive unfavourable health outcomes[7] and addressing them effectively can reduce the pressure in the post-diagnostic care space. Psychological therapies are a valuable therapeutic option and Bell and colleagues present data on the factors that mediate outcome of therapy. They analysed data from 1522 people living with dementia who received psychological therapy for affective symptoms. The authors highlight the potential gains for patients receiving psychological therapies appropriately adapted to their needs.

As Memory Clinic services adopt biomarker-informed diagnostic processes, propelled by advances in disease-modifying treatments, there is an anticipated convergence of neurological and psychiatric expert input. Binks and colleagues highlight an area where the two specialties can learn from each other. The paper discusses the consideration of autoimmune encephalitis as a differential diagnosis option in Memory Clinic settings and sets out guidance on initiating discussion with neurologists for suspected cases. Shifting to early diagnosis, as part of the broader disease process, will require differential considerations to account for the array of potential underlying causes at these incipient stages.

In summary, the emergence of new treatment options for Alzheimer's disease, the most common underlying cause of dementia, forces a reconsideration of care pathways across all stages of dementia management. We hope that this issue will provide practitioners with a useful overview of the key challenges that these therapies pose, but also the important opportunities for a long overdue step-change in brain healthcare for ageing adults.

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Data availability

Data availability is not applicable to this article as no new data were created or analysed in this study.

Author contribution

I.K. prepared the first draft of the paper; J.H., R.D., P.M. and B.S. revised the draft. All authors reviewed the final version.

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