Few UK people likely to be suitable for new Alzheimer's drugs when they become available

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Few people in the UK with early stage Alzheimer's disease are likely to be suitable for the latest drugs that aim to halt progress of the condition, yet many are nevertheless likely to be referred for these treatments, finds research published online in the *Journal of Neurology Neurosurgery & Psychiatry.*

The disease-modifying drugs, lecanemab and donanemab, slow cognitive decline in people with early stage Alzheimer's disease. They have been granted "breakthrough therapy" status in the UK because of their ability to remove beta amyloid protein in the brain, the buildup of which is thought to have a key role in the development of the disease.

Already licensed for the treatment of Alzheimer's disease in the US in 2023, regulatory approval of these drugs for use in the UK is expected shortly. But to maximize their effectiveness, a raft of clinical staff and diagnostic and monitoring tests and scans will be required, point out the researchers.

To gauge the potential level of health care demand, the researchers retrospectively evaluated patients attending five community memory services across North and East London and a national specialist cognitive disorders service between January and June in 2022.

The team wanted to determine the proportion of patients who would likely be referred for treatment from the memory services for these new drugs as well as those from the specialist service who would potentially be suitable for treatment with them.

In all, the anonymized case files of 1,017 patients were included, 517 of whom were seen in community memory services and 500 in specialist clinics.

Just over 40% of the memory service patients were men; their average

age was 79, with just 14% (72) under the age of 70. After exclusions due to incomplete data and factors, such as symptom severity, frailty, and other coexisting conditions, nearly 1 in 3 (163; 31.5%) were potentially eligible for treatment with the new drugs.

Of these,161 had undergone neuroimaging; but fluid biomarker tests were carried out in only two patients. This is equivalent to less than 1% of the memory clinic patients included in the study, "making this an urgent area of need for service development to enable identification of suitable patients," emphasize the researchers.

Based on these figures, they suggest: "With an average memory clinic caseload of 815 and 80 nationally accredited memory clinics in England and Northern Ireland, potentially over 20,000 people per year will need access to such confirmatory investigations."

More of the specialist clinic patients were men (53%) and they tended to be younger. Their average age was 66, but well over half (58%; 290) were under the age of 70. Alzheimer's disease was the most common diagnosis (177; 35.5%), followed by frontotemporal dementia (72; 14.5%).

Most of them (492) had been given diagnostic scans: computed tomography or magnetic resonance imaging. And fluid biomarker tests were performed in nearly two thirds (62%; 109/177) of those with Alzheimer's disease.

But after exclusions due to frailty and contraindications for treatment, etc., only 40% (70) of the Alzheimer's disease patients were potentially eligible for treatment with the new drugs, equivalent to just 14% of all the cases reviewed at the specialist cognitive clinics.

"Systems need to be set up to deal with this potential large mismatch

between referral and ultimate eligibility in order to avoid overwhelming services," highlight the researchers.

They add, "A significant issue is that due to the lack of biomarker testing in community memory clinics, the clinical suspicion of [Alzheimer's disease] is likely to be incorrect in at least 30% of cases."

Accurate diagnosis would reduce the number of patients ultimately eligible for the new therapies. But that would only be possible with confirmatory fluid biomarkers or brain (PET) scans, which aren't usually available to memory services in the UK, they point out.

"While there are limitations on the accuracy of our estimates, given current barriers to early clinical presentations and referral, our study provides predicted numbers based on real-world community cohorts," they write.

Demand for diagnostic services among those with early cognitive concerns is only likely to grow once the new drugs have been licensed and formally appraised by the National Institute for Health and Care Excellence, "placing further demands on already overstretched services," they warn.

"While a sizable proportion of patients attending memory clinics may be referred for triaging for [disease modifying drugs for Alzheimer's disease], only a minority are likely to be suitable for these, as demonstrated in patients seen in specialist cognitive services. This will need to be considered when designing pathways for delivery [of these drugs]," they conclude.

In a linked editorial, Dr. Benjamin Underwood, of Fulbourn Hospital, Cambridge, highlights the study limitations. "It is retrospective and several 'unknowns' remain, including how many people would choose to

have treatment if eligible, how many would meet criteria for 'amyloid positivity,' and whether the advent of treatment might encourage more people to present," he writes.

"Nevertheless, if these treatments are approved for use, the work presented here will help plan services. It also provides a reminder that only a minority of people will be appropriate to receive these treatments. It is essential that services retain focus on the majority of people who will need other forms of treatment and care," he concludes.

More information: Eligibility for anti amyloid treatment: preparing for disease-modifying therapies for Alzheimer's disease, *Journal of Neurology Neurosurgery & Psychiatry* (2024). DOI: 10.1136/jnnp-2024-333468

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