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ORIGINAL ARTICLE

Is Australia ready for the rollout of amyloid-targeting therapies for Alzheimer disease? Results from a national survey characterising current infrastructure capability, workforce and training needs of memory and cognition clinics

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Key words
Alzheimer disease, disease-modifying therapy, amyloid-targeting therapy, monoclonal antibody therapy, health system preparedness.

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Abstract

Background: New amyloid-targeting monoclonal antibody (mAb) therapies for Alzheimer disease (AD) are currently under review by the Therapeutic Goods Administration for use in Australia.
Aims: To determine the infrastructure, workforce and training needs of Australian memory and cognition clinics in order to characterise health system preparedness for these therapies.
Methods: A national, cross-sectional online survey of medical specialists.
Results: Thirty medical specialists (geriatricians, $n = 23$; psychiatrists, $n = 4$; neurologists, $n = 3$) from 30 different clinics participated (public, 76.7%; private, 23.3%), including from metropolitan (73.3%), regional (20.0%) and rural (6.7%) areas. On average, clinics reported assessing 5.4 (SD = 3.2) new patients per week, of which 2.4 (range: 0–5) were considered to have mild cognitive impairment (MCI). Only 40% of clinics use biomarkers to assess whether patients with MCI have AD, and 45% have intravenous infusion capability. While the majority of clinicians were confident in their knowledge of mAbs, only 33% felt confident in using these. Identified impediments to clinical implementation included (i) lack of real-world experience, (ii) lack of current Models of Care and appropriate use guidelines, (iii) current clinic set-up and (iv) information about safety.
Conclusions: Australia's health system preparedness for amyloid-targeting mAb therapies will require further investment in infrastructure, equity of access, clinician training and support. Long wait times already impact access to clinics, and with the forecast rise in MCI and dementia cases, services will need to be expanded, and appropriate Models of Care and clear and efficient inter-sector health pathways will be needed to prepare for the use of mAbs.

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Conflict of interest: J. C. Michaelian: Eisai Australia – speaker honorarium; investigator-initiated research grant via the Australian Dementia Network to undertake this work. C. C. Rowe: Enigma/Cerveau Technologies – Research grant to institution, Scientific Advisory Board; Biogen – Research grant to institution and Medical Education Working Group; Prothena – Scientific advisory board; Merck – Scientific input consultant; Janssen – Research grant to institution; Eisai Australia – Medical Advisory Board; Lilly Australia – Medical Advisory Board; Roche – speaker honorarium. S. E. Kurrle: Roche – Speaker honorarium. M. Woodward: Roche – Research grant to institution, Scientific Advisory Board; Biogen – Research grant to institution and Medical Education Working Group; Merck/MSD – Scientific advisory board; Actinogen – Scientific input consultant; Janssen – Research grant to institution; Eisai Australia – Medical Advisory Board; GSK – speaker honorarium. S. L. Naismith: Eisai Australia – Medical Advisory Board & Research grant via the Australian Dementia Network to undertake this work; Roche – speaker honorarium; Nutrica – speaker honorarium.

Introduction

Until recently, approved therapies for Alzheimer disease (AD) have been limited to symptomatic treatments that do not alter the underlying mechanisms of disease.[1] However, a new era of amyloid-targeting therapies for mild cognitive impairment (MCI) due to AD and early AD is unfolding, spurred by breakthrough developments in the use of monoclonal antibodies (mAb).[2] These therapies stimulate the body's own immune system to remove neurotoxic forms of amyloid-beta (Aβ). In the past 2 years, clinical trials of two agents, lecanemab and donanemab, have shown that these drugs demonstrate a statistically significant slowing of cognitive decline, with concomitant benefits on disease biomarkers.[3,4]

In Australia, these agents are currently before the Therapeutic Goods Administration (TGA) for regulatory approval. While the TGA recently decided not to register lecanemab for use in Australia, a request has been made to reconsider this decision, and donanemab is currently under review. Internationally, however, lecanemab has already received approval in China, Hong Kong, Israel, Japan, South Korea, the United Arab Emirates (UAE), the United States of America (USA) and the United Kingdom (UK). These countries have therefore already started their preparedness and clinical implementation,[5–7] and initial reports on early experiences and lessons learned are available from the US sites.[8]

There is now a need to consider Australia's health system readiness for such therapies. Notably, several investigations will be required to confirm a prospective patient's eligibility, including Aβ-PET imaging, which is a crucial tool for the diagnosis of AD and the current gold-standard investigation for the detection and quantification of Aβ plaques *premortem*,[9] in addition to regular infusions and the close safety monitoring of the patient for amyloid-related imaging abnormalities (ARIA). This is particularly important when considered in the context of Australia's universal public health insurance, Medicare, which provides coverage for a wide range of healthcare services. However, it does not currently cover repeat MRI scans or Aβ-PET imaging for routine diagnostic and management purposes in AD.

In this study, we therefore aimed to conduct a national survey of medical specialists involved in the assessment of dementia and cognitive decline in order to determine:

1 The infrastructure capability and additional needs to support amyloid-targeting mAb therapies for AD;
2 The clinical workforce capability needed to deliver an amyloid-targeting mAb therapy; and
3 Training needs/knowledge including skills gaps to adequately deliver treatment of an amyloid-targeting mAb therapy.

Methods

Sample and setting

The sampling frame for the survey included geriatricians, neurologists or old-age psychiatrists employed in a specialist assessment clinic for dementia and cognitive decline (i.e. the clinic did not have to identify as a memory clinic, memory and cognition clinic or a Victorian Cognitive Dementia and Memory Service (CDAMS)). Several recruitment strategies were employed. First, a single email invitation to participate in the survey was sent to the official contacts of a subsample of multidisciplinary clinics ($n = 90$) listed on the Australian Dementia Network (ADNeT) *Memory Clinic or Cognition Decline Assessment Service Online Finder Tool*.[10] Three reminder emails were sent. In addition, the survey was advertised via social media, such as the ADNeT LinkedIn account, and within professional networks and organisations (i.e. Australian & New Zealand Society for Geriatric Medicine). The survey was open from 7 September 2023 7 February 2024.

Survey development and procedure

The survey, titled 'Characterising Australian Memory and Cognition Clinics: Capability, Workforce, and Training Needs to Support the Clinical Implementation of Disease-Modifying Therapies for Dementia', received support from EISAI Australia through an investigator-initiated research grant via ADNeT. The survey was initially developed by JCM, SLN and CCR, with subsequent input from EISAI Australia representatives to ensure that the questions accurately captured the inherent requirements of clinics needed to implement an amyloid-targeting mAb therapy for AD, from a manufacturer's perspective. At the time of survey development, only the clinical trial results for lecanemab had been published. While some questions may have referenced lecanemab, we are confident that questions were applicable to amyloid-targeting mAb therapies generally, as both lecanemab and donanemab are amyloid-targeting mAb therapies requiring similar administration and management practices. Once finalised, the survey was delivered in Qualtrics.[11] Participants were given the option to complete the survey online or via phone call with the study coordinator. The conduct of this study was approved by the University of Sydney's Human Research Ethics Committee (Approval Number: 2023/480). All potential respondents provided informed consent, electronically or verbally via phone call with the study coordinator. All study methods were conducted in compliance with the

Helsinki Declaration. A copy of the full survey can be acquired from the corresponding author upon request.

The survey comprised five sections: (i) current clinical landscape of diagnosis, (ii) current treatment journey/workforce, (iii) treatment, (iv) logistics/capacity and (v) knowledge. A mix of structured (e.g. 'agree/disagree', 'yes/no') including multiple-choice 'checkbox' or single-choice 'radio buttons', answer options were employed, in addition to unstructured (e.g. free-text box) answer options.

Data analysis

All survey responses were recorded and initially saved in Qualtrics.[11] Statistical analysis was conducted in SPSS version 27 (SPSS Inc., IBM Corp. in Armonk, NY, USA). Descriptive analyses (i.e. frequencies and percentages) were performed for outcome measures. Missing or 'unable to comment' responses were recorded, and the total number of 'valid responses' became the denominator for that item. Free-text responses were reviewed in their entirety, and repeated instances of similar responses were grouped together to form broad captions, summarising each category. Quotes for free-text responses presented here in were edited for typographical and/or grammatical errors, and, where applicable, identifying information was redacted.

Results

Respondents

As shown in Table 1, responses were received from 30 medical specialists (geriatricians, $n = 23$; psychiatrists, $n = 4$; neurologists, $n = 3$) across 30 different clinics, including 23 publicly funded clinics (76.7%) and seven private clinics (23.3%), of which two were clinics embedded within universities. From the 90 clinics that were individually invited to participate in the survey, responses were received from 21 (23.3%). Most respondents completed the survey online ($n = 27$), with only three clinicians choosing to complete the survey via phone call. The majority were in metropolitan areas ($n = 22$, 73.3%), followed by regional ($n = 6$, 20.0%) and rural ($n = 2$, 6.7%) areas. While there was representation from all Australian states/territories except for the Australian Capital Territory (ACT), New South Wales ($n = 10$, 33.3%) and Victoria ($n = 10$, 33.3%) accounted for two-thirds of the respondents in proportion to population and workforce (Figure. 1). Approximately two-thirds of clinics ($n = 19$, 63.3%) offered telehealth and 16.7% ($n = 5$) offered a roving/mobile service.

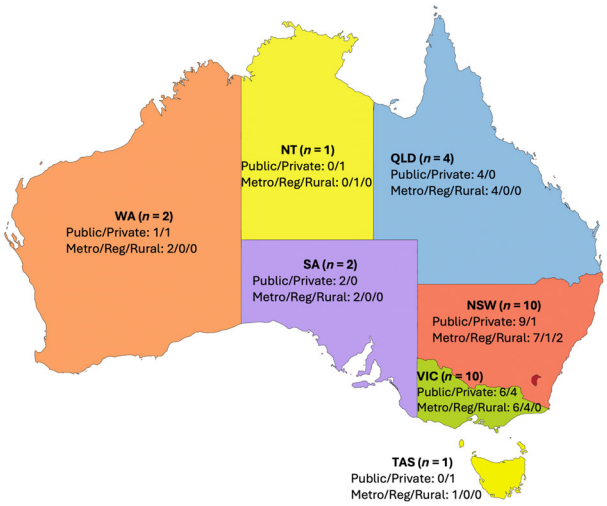

Figure 1 Survey representation across Australian states and territories for public and private clinics located in metropolitan, regional and rural regions. NSW, New South Wales; NT, Northern Territory; QLD, Queensland; SA, South Australia; TAS, Tasmania; VIC, Victoria; WA, Western Australia.

Table 1 Characteristics of survey respondents

		Clinic setting		Locality		
	Overall	Public	Private	Metropolitan	Regional	Rural
Respondents, *n* (%)	30 (100.0)	23 (76.7)	7† (23.3)	22 (73.3)	6 (20.0)	2 (6.7)
Profession, *n* (%)						
Geriatrician	23 (76.7)	17 (73.9)	6 (85.7)	16 (72.8)	6 (100.0)	1 (50.0)
Psychiatrist	4 (13.3)	4 (17.4)	0 (0)	3 (13.6)	0 (0)	1 (50.0)
Neurologist	3 (10.0)	2 (8.7)	1 (14.3)	3 (13.6)	0 (0)	0 (0)
Clinic setting: public/private (public %)	23/7 (76.7)	—	—	16/6 (72.7)	5/1 (83.3)	2/0 (100.0)
Locality: metropolitan/regional/rural (metropolitan %)	22/6/2 (73.3)	16/5/2 (69.6)	6/1/0 (85.7)	—	—	—
Telehealth availability: yes/no (yes %)	19/11 (63.3)	14/9 (60.9)	5/2 (71.4)	13/9 (59.1)	5/1 (83.3)	1/1 (50.0)
Roving/mobile service availability: yes/no (yes %)	5/25 (16.7)	4/19 (17.4)	1/6 (14.3)	1/21 (4.5)	3/3 (50.0)	1/1 (50.0)

†Includes hybrid clinics ($n = 2$).

Current clinical landscape of diagnosis

Referral pathways and number of patients assessed

The largest proportion of patient referrals was from a general practitioner (GP) (78.3%), followed by a medical specialist (15.9%). Less than 10% of clinics received referrals from allied health professionals, aged care assessment teams (ACAT) and self-referrals. On average, clinics reported seeing 5.4 (SD = 3.2, range = 1–15) new patients per week, as well as 9.4 follow-up patients per week (SD = 6.7). Approximately, 60% and 31% of patients travelled between 5 and 20 km or 20 and 40 km for their assessment respectively.

Clinical assessment of MCI and MCI due to AD

Almost all clinics ($n = 29$, 96.7%) assessed people for having MCI and estimated an average of 2.4 patients per week would meet MCI clinical criteria (range: 0–5). However, only 40% ($n = 12$) of clinics reported using imaging *biomarkers* (e.g. FDG-, Aβ- and/or tau-PET) in their diagnostic work-up. A minority ($n = 8$, 26.7%) reported that, if needed, they could refer patients for confirmatory Aβ- and/or tau-PET imaging, but only one clinic performed this routinely (>70% of patients). Indeed, 60% ($n = 18$) of clinics reported that cerebrospinal fluid (CSF) sampling to determine a patient's Aβ status was never/not available for testing, and a further 30% ($n = 9$) rarely referred their patients for testing. Similarly, more than 60% ($n = 19$) of clinics reported that apolipoprotein E (*APOE*) genotyping was never/not available for testing.

When clinicians were asked to describe current challenges and barriers towards the implementation of an early diagnosis of MCI due to AD, as detailed in Table S1 ($n = 29$), comments received suggested 'access', 'capacity' and 'availability' constraints as well as the 'out of pocket expense to patients' likely to be incurred for confirmatory biomarker investigations (i.e. Aβ- and/or tau-PET imaging). For example:

- "Access to amyloid PET, blood biomarkers, CSF clinic capacity to see new referrals – current demand is greater than clinic spots available; patients may progress while on the waiting list".
- "Availability of cheap, easy to access biomarkers. I wouldn't routinely be recommending lumbar puncture (LP) for my patients".
- "Out of pocket expense to the clients. Occasionally, after informed consent, clients are happy to do it if they can afford it".

Clinicians also noted that if they were to make a referral for imaging biomarker investigation, the 'wait times' inhibited receiving results to assist in the diagnostic work-up. For example, cited as barriers were:

- "Wait time from referral to receiving PET scan".

Moreover, certain clinicians described that their patients were not presenting 'early' in the trajectory of their illness (i.e. in later dementia stages). For example:

- "Patients being referred early enough".
- "Seeing the patient early enough in the trajectory of their illness".
- "Having the capacity to see new patients in a timely manner to capture people at the stage of MCI. Relying on GPs to perform early referrals at the MCI stage given historical waiting times to see geriatricians in our area. Usually dementia is referred more so. Difficulty in accessing and performing biomarker testing – tau/amyloid. Lack of geriatrics staff".

MRI and PET imaging investigations

The majority of clinicians ($n = 26$, 86.7%) indicated that patients with MCI or clinical AD would be referred for a brain MRI scan if appropriate and on average estimated that 59.0% (SD = 33.8) of new patients would be referred for an MRI, a result which remained consistent between public ($n = 19$, 58.3%) and private clinics ($n = 7$, 60.9%). Only a minority of clinicians ($n = 8$) refer those with MCI or suspected AD dementia for confirmatory Aβ-and/or tau-PET imaging. Approximately a quarter of new patients seen within a clinic are referred for a brain PET scan ($n = 7$, 26.6%), including referral for FDG-PET. Table 2 reports the wait times (in days) for brain MRI and PET scans. Almost two-thirds ($n = 19$, 63.3%) of clinics estimated that their service had on-site capacity to conduct brain MRI scans for diagnosis and monitoring, and the majority reported that it was likely ($n = 16$, 61.5%) to extremely likely ($n = 7$, 26.9%) that the same scanner could be used for multiple scans (i.e. for ARIA safety monitoring).

Current treatment journey/workforce

The majority of clinics ($n = 21$, 70%) employed multidisciplinary teams for diagnosis, and 66.7% ($n = 20$) provided some form of follow-up for MCI and AD, largely comprising one feedback session ($n = 14$, 70%), referral to Dementia Australia ($n = 17$, 85%) and dementia support websites ($n = 16$, 85%). For patients with MCI due to AD, 66.7% ($n = 20$) of clinicians did not prescribe pharmacological treatments,

and 33.3% ($n = 10$) were prescribing an off-label treatment, of which acetyl-cholinesterase inhibitors were the most common ($n = 9$). Only 36.7% ($n = 11$) of clinicians currently provide training to local GPs on the topic of MCI and/or dementia assessment and management.

Treatment

When clinicians were asked to indicate appropriate targets for treatment for AD, the majority indicated that addressing vascular risk factors ($n = 26$, 86.7%) and Aβ ($n = 25$, 83.3%) should be targeted, and half ($n = 15$) reported that phosphorylated-tau (i.e. neurofibrillary tangles) should be a treatment target. In addition, management of other/modifiable risk factors were identified as key targets ($n = 25$, 83.3%), with exercise/physical inactivity, inflammation and sleep commonly mentioned. Regarding the impact of treatments, as illustrated in Figure 2, all clinicians reported that it was 'very important' ($n = 14$, 48.3%) to 'important' ($n = 13$, 44.8%) that any treatment for AD has a statistically significant impact on activities of daily living (ADL). Moreover, as to be expected for any treatment, real-world evidence of safety ($n = 26$, 86.7%) alongside real-world-evidence of clinical efficacy was considered to be 'very important' ($n = 23$, 76.7%). More than 96% of clinicians also considered cognitive abilities, functional ability and independence, behavioural and neuropsychiatric symptoms as well as patient quality of life to be important markers to gauge the efficacy of any new treatment for AD.

As detailed in Table S2 ($n = 28$), comments received by clinicians highlighted that for any treatment for AD, a clinically meaningful 6- to 12-month outcome would result in an 'improvement', 'maintaining/maintenance', 'slowing' or 'stabling', for example:

- "Improvement in activities of daily living (ADLs), improvement of behavioural and psychological symptoms of dementia (BPSD), decreased carer burden".
- "Improvement in cognitive abilities, stability or improvement in functional abilities, improved quality of life".
- "Maintenance of or improvement in activities of daily living (ADLs)/ instrumental activities of daily living (IADLs)".
- "Slow down progression in cognitive decline and functional disability".
- "Slower or halted progression or improvement with minimal side effects".
- "Stability of cognition and function".

Logistics/capacity

Logistically, two-thirds of clinics ($n = 20$, 66.7%) reported that a drug-specific refrigerator (2–8°C) was available for storage. Of those clinics that had refrigeration capacity, 61% ($n = 11$) could accommodate increased demand for an amyloid-targeting mAb therapy requiring cold storage. More than half of responding clinics ($n = 16$, 55.2%) reported that their service did not currently have the required resources to facilitate intravenous (IV) administration on site using an infusion chair for mAb therapies requiring regular administration (i.e. fortnightly). Of this number, close to half ($n = 7$, 43.8%) would utilise a home infusion service to facilitate IV administration.

More than half of clinics ($n = 17$, 56.7%) reported current on-site nursing and administrative support for follow-up/coordination of patient appointments and infusions. In terms of clinician confidence in prescribing and administering an amyloid-targeting mAb therapy requiring IV administration, only 33% of clinicians were 'very confident' ($n = 6$) or 'confident' ($n = 4$) in IV administration, with the latter needing refresher training and support. A further 13.3% ($n = 4$) were 'somewhat confident' but noted they would need training, while 53.3% endorsed items indicating they were 'not at all confident' and were *not* interested ($n = 7$) or required support if they were interested ($n = 9$). For the latter, clinician support would include an appropriate nursing workforce ($n = 9$, 100%), training ($n = 9$, 100%) and

Table 2 Reported approximate wait-times for a brain MRI or PET scan across clinics surveyed

	Overall	Public	Private	Metropolitan	Regional	Rural
Clinics responded, number	26	19	7	19	5	2
MRI scan wait time, days (approximate)	26.6 ± 25.3	30.7 ± 28.3	15.3 ± 8.0	25.6 ± 27.9	28.8 ± 21.2	30.5 ± 13.4
Clinics responded, number	7†	4	3	6	1	0
PET scan wait time, days (approximate)	36.0 ± 27.6	22.3 ± 15.7	54.3 ± 32.0	34.5 ± 29.9	45.0	—

†One clinic responded 'yes' to referring new and follow-up patients with MCI or AD clinically for confirmatory Aβ- and/or tau-PET imaging; however, it was unable to estimate the current wait time (in days) for their patients.

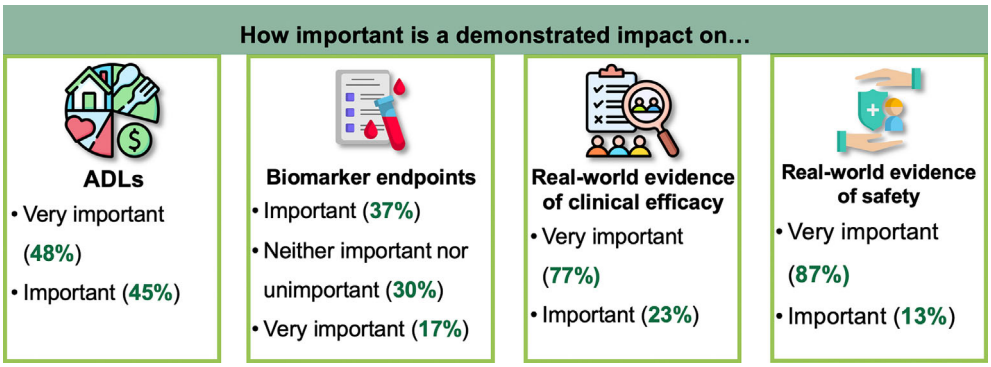

Figure 2 Importance of demonstrated impact for any new treatment for Alzheimer disease.

infrastructure ($n = 8$, 100%). When clinicians were asked 'would you prefer the patient's GP to review the patient receiving an anti-amyloid disease-modifying therapy?', the vast majority ($n = 26$, 86.7%) reported that they would prefer (over their patient's GP) to review their patient receiving a mAb therapy, on a monthly ($n = 10$, 43.5%) to quarterly ($n = 11$, 47.8%) basis. Lastly, when clinicians were asked to share any comments around IV administration, comments ($n = 21$) centred around 'staffing needs', 'location', 'resources/infrastructure needs' as well as 'capacity' (Table S3). For example:

- "To provide IV administration you would need to have the set-up of a treatment room and staffing thereof".
- "Staffing will be a big challenge (including nursing and admin to execute it). As will be the space to have an infusion clinic and post-IV observations, etc".
- "Inadequate staffing, space and resources to do this at this hospital. Likely to require the patient to go to another hospital; no on-site IV chemotherapy (oncology); very difficult to arrange IV iron therapy".
- "I run the service remotely and the nurse does not have time to administer IV medication".
- "No capacity to provide and monitor treatment effects. No capacity in private regional system to provide this without major funding change".

Knowledge

Despite the majority of clinicians reporting that they have not been involved in a recent clinical trial of an amyloid-targeting therapy ($n = 21$, 72.4%), the majority (80%) reported *confidence* around their knowledge on the mechanisms of action of a mAb against Aβ: 'somewhat' ($n = 12$, 40%), 'quite' ($n = 9$, 30%) and 'extremely' ($n = 3$, 10%) confident. Only three clinicians reported being 'not at all confident' (10%). Indeed, the majority of clinicians (80%) also reported *confidence* around their knowledge on the clinical trial outcomes of an amyloid-targeting therapy: 'somewhat' ($n = 12$, 40%), 'quite' ($n = 7$, 23.3%) and 'extremely' ($n = 5$, 16.7%) confident.

On the whole, clinicians reported a desire to receive information about patient support programmes ($n = 27$, 93.1%), reimbursement/insurance coverage ($n = 25$, 86.2%) and around the detection/management of ARIA ($n = 18$, 62.1%) if/when amyloid-targeting therapies become available. In terms of receiving training around amyloid-targeting mAb therapies for AD, a clinician's most preferred method was webinars/online demonstration ($n = 16$, 57.1%) followed by on-site hands-on demonstration ($n = 9$, 32.1%) and external seminars/workshops ($n = 3$, 10.7%).

Lastly, clinicians were asked to comment on what they perceived to be the greatest knowledge gaps in connection with the implementation of an amyloid-targeting therapy in their service. As detailed in Table S4, comments ($n = 23$) broadly covered:

- Lack of real-world experience – suggesting that there is a need to understand how treatment of a patient living with AD can be translated from the clinical trial environment to a real-world clinical setting in Australia:
  - "No real-world experience".
  - "Uncertainty about evidence in making a real-world difference…".
- Lack of current Models of Care, appropriate use criteria and protocols around infusion and therapy monitoring:
  - "The development of the Model of Care".
  - "Models of Care…Would be good to have pro-forma business cases…".
  - "Infusion and monitoring protocol".

- Current clinic set-up, such that clinics are not set up to administer an amyloid-targeting therapy on site with an infusion chair:
  - "It's more about the practicality for the implementation of a therapy. Clinic is not set up to administer therapies onsite".
- Information about safety – identifying and managing ARIA as well as overall safety monitoring:
  - "Experience in identifying and managing severe amyloid-related imaging abnormalities (ARIA)".
  - "Exclusion criteria and safety monitoring".
  - "Need to develop the processes for safety".

Additional gaps identified by clinicians not summarised above are included in Table S4.

Discussion

This study overall shows that if amyloid-targeting mAb therapies were to become available in Australia, improvement of current infrastructure capability, workforce and training will be required. Findings affirm that while clinicians were confident in their knowledge of the mechanisms of action of amyloid-targeting mAbs, further data on real-world use as well as cognition and that pertaining to functioning/ADL outcomes were desired. The survey also revealed that medical specialists perceived other/modifiable risk factors to be important targets for treatment, including exercise/physical inactivity, inflammation and sleep. To support this, other forms of post-diagnostic support around cognitive interventions, carer support programmes and care navigators will be vital.[12] Indeed, comprehensive management options will be especially important in light of international figures showing that only a small proportion (lecanemab, 8%; aducanumab, 5%) of patients presenting to a memory and cognition clinic would be eligible for an amyloid-targeting mAb therapy if the criteria used in clinical trials were applied to routine clinical practice[13].

In terms of the health service preparedness, importantly, this study shows that Australian memory and cognition clinics are limited to assessing around 5.4 patients per week, of which approximately two cases may have MCI. This estimate is concordant with our prior national surveys[14,15] that also estimates an average full-time equivalent per clinic of 2.4 (range: 0.1–14.0),[13] and with ADNeT Clinical Quality Registry data which show that ~32% of new memory and cognition clinic cases meet *clinical* criteria for MCI (i.e. not necessarily MCI due to AD).[16] Of concern, however, most multidisciplinary memory and cognition clinics only operate 1–2 days per week and may only be able to service around 5% of MCI/dementia cases, demonstrating substantial unmet need.[17] Indeed, based on limited available data of clinic numbers, frequency and capacity, it has been estimated that 12 000 patients per year may attend a public memory and cognition clinic across Australian states and territories.[17] Extrapolating from these figures and assuming clinics had the relevant infrastructure, capability and workforce needs in place, approximately 1000 patients across Australia attending a public clinic could be eligible to receive lecanemab (i.e. 8% of 12 000 patients eligible)[13] when running at current capacity, with prescriptions also likely dependent on Pharmaceutical Benefits Advisory Committee (PBAC) and Medical Services Advisory Committee (MSAC) approvals in addition to TGA approval. However, given there will be approximately 250 000 new MCI and dementia cases per year in those aged over 65 years,[17] up to 20 000 Australians could be suitable for lecanemab (8% of 250 000), though co-existing chronic diseases and neuroimaging findings are most likely to render a patient ineligible.[13] These figures, while only an approximation, suggest that public services could meet the demands for only 5% (i.e. 1000/20 000) of suitable cases. Thus, if lecanemab and donanemab were to be available and receive government subsidy in Australia, there would need to be substantial investment in expansion of public sector memory and cognition clinics, as well as key considerations and support of private sector models. Notably, there would also need to be increased access and funding for Aβ-PET imaging or lumbar puncture for CSF biomarker assays, infusion capabilities, nursing workforce and administration support, as well as frequent neuroradiological reviews. In the future, with the introduction of new blood (plasma) biomarkers for AD,[18] screening could become more effective and better integrated with primary care. Trials are under way to test the use of these plasma biomarkers in Australian memory and cognition clinics (e.g. ACTRN12622000515796), and work has begun to scope how these could best be utilised in primary care settings.

This study also highlights that workforce training and support would be required. Specifically, clinicians would require support and training in IV mAb administration, there would need to be support for patients, as well as reimbursement/insurance coverage and training around ARIA detection/management and acute infusion reactions. These findings are in agreement with initial reports on early experiences and lessons learned from treating the first wave of memory and cognition clinic patients to receive lecanemab in the USA,[8] highlighting that a 'nurse navigator' plays a crucial role in overseeing details of the treatment protocol, in being available to answer phone calls from patients and/or their significant others and in monitoring patients who may miss scheduled lecanemab infusions.

One of the major findings of the survey to emerge was the need for clear and comprehensive Models of Care and appropriate use guidelines. This is important as clinicians noted a lack of real-world experience in the use of an amyloid-targeting mAb therapy, particularly within the context of the Australian healthcare system. Such guidelines will be critical in understanding the frequency of MRI monitoring to detect ARIA, especially as ARIA cases with cerebral oedema (ARIA-E) and microhaemorrhage/hemosiderosis (ARIA-H) are common for both lecanemab (ARIA-E 12.6%; ARIA-H 17.3%) and donanemab (ARIA-E 24.0%; ARIA-H 31.4%).[3,4] Given that use of the same MRI scanner across multiple timepoints is recommended to attenuate artefacts due to different scanning protocols and/or magnet strength,[19] it was a positive finding that the vast majority of clinics indicated that it was 'likely' to 'extremely likely' that the same MRI scanner could be used across multiple scans. Nevertheless, for GPs and emergency specialists who may be involved in the routine or inadvertent management and care of a patient receiving an amyloid-targeting mAb therapy, education and training will be required for them to discern between mAb therapy-related ARIA and ischaemic stroke. Monitoring of real-world outcomes would also be important and may occur alongside the Australian Dementia Network Clinical Quality Registry for participating clinicians.[16] Given that two-thirds of medical specialists surveyed are not currently providing MCI/dementia training to GPs, there will also be a need to provide critical education and support to GPs and practice nurses who will be fielding enquiries, seeking specialist input and advice and managing potential questions and side effects that may arise during the course of treatment.

Limitations

This study has limitations. While there was broad national representation (except for the ACT), not all memory and cognition clinics previously identified by ADNeT participated in the survey. Moreover, as 70% of responses came from a subsample of multidisciplinary clinics individually invited to participate ($n = 90$), potential response bias is acknowledged, as these clinics may have greater interest or resources for amyloid-targeting therapies for AD, in turn limiting the generalisability of our findings to less-resourced or single-discipline settings. In addition, the nominated medical specialist completing the survey may have also interpreted and responded to questions specific to their clinical knowledge and practice, which may not be representative of other clinicians within that practice. It is also acknowledged that as the sampling frame for the survey included geriatricians, neurologists and old-age psychiatrists employed in a specialist assessment clinic for dementia and cognitive decline, the responses of GPs were therefore not captured. Given that GPs make up a critical part of Australia's healthcare system and are best placed to triage patients with cognitive concerns or MCI for referral to a memory and cognition clinic, future studies should seek to understand their current knowledge and training needs, including skills gaps, to adequately support the management of an individual receiving an amyloid-targeting mAb therapy.

Furthermore, we acknowledge that with the recent inclusion of MBS item 61560, which supports an FDG-PET study of the brain for the diagnosis of AD, our results reporting the use of *any* imaging biomarkers (e.g. FDG-, Aβ- and/or tau-PET) in the diagnostic work-up of patients among clinics may be inflated. Nevertheless, given that 60% of clinics reported that imaging biomarkers were not currently used in the diagnostic work-up, this gap may give support for increased access and funding for more sensitive and specific imaging biomarkers (e.g. Aβ-PET).

Lastly, it is acknowledged that our study focused on current practice, which may not fully capture preparedness for change or clinical implementation of a new amyloid-targeting mAb therapy for AD. Therefore, while the survey aimed to reflect existing guidelines and clinical practices, the lack of explicit questions seeking to elucidate readiness for change may have hindered a holistic understanding of the potential future rollout of such therapies.

Conclusion

Overall, the successful clinical implementation of amyloid-targeting mAb therapies for AD will rely on expanding memory and cognition clinic capacity, improving infrastructure capability and addressing workforce and training needs. There will also be a need to implement appropriate use guidelines and support primary care in training and support, in addition to Models of Care and health pathways, particularly for those patients that are not eligible – which is estimated to be around 92% of MCI and early AD patients. It is expected that the real-world rollout of such therapies may occur slowly, within key metropolitan centres, due to the infrastructure and workforce limitations in regional and rural areas. However, eventually, with service expansion and developments in screening (e.g. plasma biomarkers for AD) and optimised methods of drug delivery (e.g. subcutaneous administration), equitable access for all Australians seeking treatment would be expected.

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Supporting Information

Additional supporting information may be found in the online version of this article at the publisher's web-site:

Table S1. Individual respondent responses ($n = 29$) to the question 'In the space below, please comment as to what you see as the greatest challenge/barrier to implementation of early diagnosis of MCI due to AD in your service?'
Table S2. Individual respondent responses ($n = 28$) to the question 'With disease-modifying therapies, what would you consider to be a clinically meaningful outcome over a 6–12 month period?'
Table S3. Individual respondent responses ($n = 21$) to the question 'Do you have any comments that you would like to share about IV administration?'
Table S4. Individual respondent responses ($n = 23$) to the question 'What do you see as the greatest knowledge gap on the implementation of anti-amyloid disease-modifying therapies in your service?'