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Special Article

# Developing Treatment Models for the Delivery of the Antiamyloid Therapy, Lecanemab: Considerations for Implementation of Lecanemab in Healthcare Systems

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ABSTRACT

*We describe the model developed by two separate healthcare systems to deliver the antiamyloid therapy, lecanemab, to patients with mild cognitive impairment and mild dementia. Based on current guidelines, the experience of two separate healthcare systems that developed lecanemab clinical care delivery programs is described in detail including the development of patient eligibility criteria, cooperation with specialty services, patient monitoring, and practical steps required to safely implement lecanemab programs at a systems level. Geriatric psychiatrists have a prominent role in prescribing and monitoring antiamyloid therapy in both systems and we highlight the unique role of the geriatric psychiatrist in the future delivery of antiamyloid therapies as memory care specialists.* (Am J Geriatr Psychiatry 2025; 33:601–610)

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**Highlights**

- **What is the primary question addressed by this study?**
  How do different healthcare systems develop their respective models for lecanemab implementation?.
- **What is the main finding of this study?**
  We describe the model developed by two separate healthcare systems for the delivery of lecanemab to provide guidance for other health care systems.
- **What is the meaning of the finding?**
  Implementation of lecanemab in health systems is a complex and multidisciplinary process that requires institutional investment for appropriate delivery and monitoring, however institutions can develop unique delivery models based on their infrastructure.

## OBJECTIVE

Alzheimer's Disease (AD) is the most common cause of dementia worldwide, with an estimated 6.9 million Americans over 65 living with AD.1 As increased age is the biggest risk factor for development of AD, the number of Americans with Alzheimer's disease is expected to increase to 13.8 million by the year 2060 as the number of Americans aged 65 and above increases.[1,2] The amyloid cascade hypothesis describes the pathogenesis of AD as the accumulation of amyloid beta (A$\beta$) protein into cerebral plaques. These plaques lead to downstream neurotoxic effects from the subsequent development of hyperphosphorylated tau which progresses to intraneuronal neurofibrillary tangles. This progression is thought to lead to subsequent neurodegeneration and clinical symptoms of AD.[3] Treatment of AD is limited - there are few treatments available for management of cognitive and functional decline. Recent research has focused on amyloid-beta as a potential target for disease-modifying therapy given its role in neurotoxicity.[4]

Lecanemab is the first monoclonal antibody granted traditional approval by the United States Food and Drug Administration (FDA) indicated for treatment of mild cognitive impairment (MCI) and mild dementia due to Alzheimer's disease. Lecanemab is a monoclonal antibody with affinity for soluble amyloid-beta protofibrils, a prefibrillar form of A$\beta$ formed by soluble A$\beta$ aggregates and part of treatment now known as antiamyloid therapies (AAT).[5] In studies, lecanemab has been shown to decrease the presence of A$\beta$ plaques in the brain while slowing the clinical progression of neurocognitive decline in patients with early AD.[6]

Administered via intravenous infusion at two-week intervals, current guidelines require that patients have evidence of amyloid deposition obtained through amyloid PET scan or CSF analysis prior to lecanemab infusion.[7] Recent FDA approval was informed by a Phase 2b and the Clarity AD Phase 3 trials, both randomized placebo-controlled trials which demonstrate amyloid removal and slowing of cognitive decline on the Alzheimer's Disease Assessment Scale-Cognitive subscale, version 14 (ADAS-Cog 14) and Clinical Dementia Rating Sum of Boxes (CDR-SB) in patients with MCI and mild dementia due to AD.[7,8] While results from the CLARITY- AD trial showed cognitive decline in both treatment and placebo groups, treatment with lecanemab demonstrated 27% slower cognitive decline in the treatment group compared to placebo after the 18-month trial.7

Following FDA approval in 2023, guidelines were published for the delivery and clinical monitoring of lecanemab. Given potential side effects associated with lecanemab, appropriate use guidelines were developed by Cummings et al.[9] to inform eligibility criteria and clinical monitoring of patients receiving lecanemab. A potentially serious side effect of antiamyloid therapy is amyloid-related imaging abnormalities (ARIA). There are two types of ARIA associated with lecanemab treatment including edema (ARIA-E) and hemorrhage (ARIA-H). In the CLARITY-AD trial, the overall incidence of ARIA-E was 12.6% compared to 1.7% in the treatment and placebo groups respectively. For ARIA-H, the overall incidence was 17.3% in the treatment group compared to 8.7% for placebo. ARIA-E and H can occur in isolation or in

combination. It is known that ARIA-H incidence is increased in patients with ARIA-E.[10] There was also increased risk of ARIA in patients with one or two copies of the APOE4 allele, leading to the recommendation for APOE genotype testing in clinical candidates. Hemorrhage was also seen more frequently in patients on anticoagulation, which has become a consideration for eligibility criteria. Given the increased risk of ARIA and cerebrovascular hemorrhage seen in treatment groups, current guidelines recommend regular monitoring of patients by brain MRI.[9]

Implementing a clinical delivery structure to effectively and safely deliver lecanemab to patients is a major undertaking for the memory care specialist. Current guidelines outlined by Cummings et al. advise clinicians on 1) how to identify appropriate candidates for lecanemab treatment, 2) MRI intervals for imaging assessment prior to treatment and during treatment to monitor for ARIA, 3) assessment of amyloid pathology based upon lumbar puncture or amyloid PET scans, 4) screening recommendations for APOE status to assess risk with treatment and how to provide adequate counsel of these results to patients and families, 5) need for infusion centers where patients can receive bi-weekly lecanemab infusions, and 6) ensuring trained medical staff is available to manage severe side effects of ARIA. Clinics currently use these guidelines to develop effective and safe delivery models for lecanemab implementation.[11] In addition, health systems show that lecanemab infusion is feasible and financially sustainable.[12]

Cognitive evaluation, diagnosis and treatment is a sub-specialty of geriatric psychiatry and geriatric psychiatrists receive formal fellowship training in dementia care. As patients and caregivers seek more knowledge and understanding of their disease, geriatric psychiatrists, who see primarily patients ages 65 and over, are in a strong position to manage cognitive evaluation and treatment as the primary cognitive disorder specialist and may contribute to patient and caregiver satisfaction. Geriatric psychiatrists bring unique perspectives to new onset psychiatric symptoms, especially late life depression, that many times turn out to be early signs of cognitive decline.[13] In addition, geriatric psychiatrists employ treatment approaches that focus on psychoeducation. A recent study shows psychiatrists were more likely than primary care physicians or geriatricians to discuss etiology of MCI or mild AD with patients at the time of diagnosis.[14] Geriatric psychiatrists provide cognitive care at several academic institutions nationally and have served in key leadership roles in clinical trials of antiamyloid therapies.[7] Therefore, it is appropriate for the geriatric psychiatrist, as the primary memory care specialist to oversee and manage new treatments such as antiamyloid therapy as part of the treatment plan.

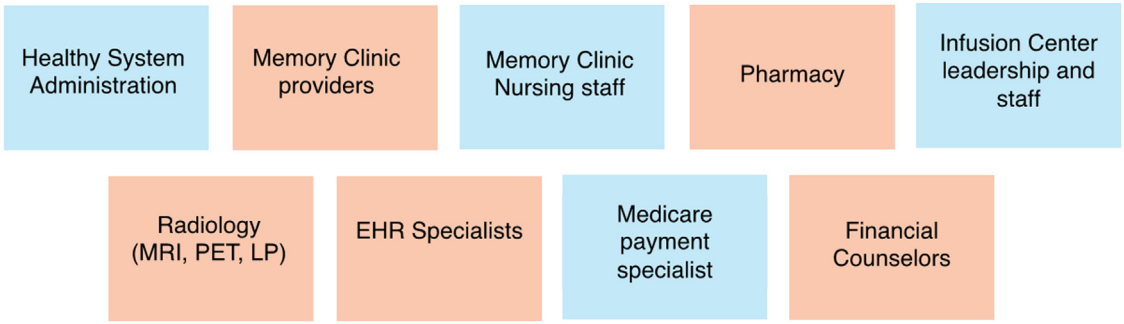
In this paper, we describe processes to safely prescribe lecanemab in two separate health systems, Duke University and the University of North Carolina (UNC) where geriatric psychiatrists, along with neurologists and geriatricians play a key role in providing cognitive care and prescribe lecanemab. We discuss how these academic medical centers developed protocols to 1) accommodate increased referrals and streamline assessment to identify appropriate treatment candidates, 2) assess eligibility for treatment, 3) develop processes for coordinating infusions and following safety monitoring protocols, 4) develop imaging protocols, efficient scheduling and coordinate serial MRI safety review practices, and 5) implement processes to reduce emergency room medication risks and optimize safety surrounding urgent evaluations. Additionally, we discuss the importance of developing a standardized way to document findings appropriately, manage health care system reimbursement, and effectively communicate with patients and across disciplines. We anticipate these models in our health systems will extend to the offering of all approved antiamyloid therapies, including donanemab, which was recently approved by the FDA in July 2024.

## METHODS

### Clinic Provider Composition

The Memory Disorders Clinics at Duke and UNC are multidisciplinary in nature, housed in the Departments of Neurology with physician providers from neurology, geriatric psychiatry, and geriatric medicine. Providers from these different home disciplines participate equally in new and follow-up assessments. At Duke, the leader of the Duke Memory Disorders Division is a geriatric psychiatrist, and at UNC the leader of the Memory Disorders Clinic (the UNC Aging Brain Clinic), is a behavioral neurologist.[15] Advanced practice providers (APPs) including physician assistants and nurse practitioners at both Duke

**FIGURE 1. Stakeholders in lecanemab health system initiative.**




and UNC play important roles, performing new and return evaluations to increase clinic access.

### Lecanemab Program Implementation

The implementation of lecanemab programs at both Duke and UNC was started with weekly stakeholder meetings across different departments in the health systems. At Duke, the Vice President of Neurosciences led the meetings, and at UNC hospital leadership appointed a high-level operational project manager responsible for implementing new programs. Having an administrative leader with contacts and leverage across the hospital system was key in both health systems for achieving successful and efficient implementation. Stakeholders across the health system were present, including physician leadership at the Memory clinics, clinic nursing staff and managers, hospital and clinic central scheduling staff, neuroradiology, central pharmacy, infusion center leadership and staff, insurance authorization and payment specialists, and electronic health record (EHR) specialists. See Fig. 1. Duke and UNC both use Epic Systems for their EHR. This weekly virtual meeting platform, with about 20 people in attendance was ideal to run through issues and obtain updates from each stakeholder. Key issues were diagnostic evaluation of eligible patients, memory clinic inclusion and exclusion criteria, infusion center procedures and safety, pharmacy preparation of the drug, coordination of MRI scans and reports with neuroradiology, Epic builds for pharmacy orders and clinical notes, ensuring health system reimbursement of diagnostic services and treatment, and patient understanding of financial considerations.

### Clinic Capacity and Access Challenges

Antiamyloid therapy is most effective when initiated in early cognitive impairment, with recent data indicating that those patients on the mildest end of MCI benefit most,[16] which creates an increase in demand for memory care appointments to identify patients with early memory issues. Therefore, it is necessary to ensure access for evaluation in a timely manner when patients will benefit the most. Many clinics struggle with timely access to cognitive evaluations and long wait times. Strategies to address this problem within the Duke health system delivery structure include triaging patients with early cognitive decline and mild dementia to Department of Neurology Memory Clinic and patients with moderate to severe dementia to Geriatric Medicine clinic who focus on long term dementia care. The Neurology Memory Clinics at Duke and UNC require that referrals include a Montreal Cognitive Assessment (MOCA), Saint Louis University Mental Status (SLUMS) Exam, or Mini Mental State Exam (MMSE) score and a Functional Activities Questionnaire score (FAQ) to help triage patients with more moderate to severe impairments to Geriatric Medicine or other clinics. We do use cut off scores, which could lead to disparities of care; however we collaborate closely with Geriatric Medicine clinics to refer patients back and forth who are more suitable for a particular clinic based on further formal evaluation.

### Ensuring Timely Laboratory Workup and Assessment

Another important issue in the workup for lecanemab candidacy is timely laboratory evaluation and follow up on results. For the UNC clinics, follow-up and return appointment times were not always easy to schedule at shorter time frames, so they changed the scheduling system to a "yoked appointment model", in which patients were scheduled with 2 appointments at the same time 8 weeks apart. This allowed clinic providers to guarantee follow-up would occur in a timely fashion, and that patients could be counseled in person regarding the biomarker results and therapy if they qualified.

At Duke and UNC, laboratory work-up for lecanemab is expedited and completed prior to the follow-up appointment. All laboratory and radiology appointments are made at check-out (rather than coordinated at a later time). Amyloid testing and required baseline MRI are scheduled within a 2-6 week time frame in dedicated slots. Laboratory work up which includes APOE genotyping occurs on the same day as the initial appointment.

Clinic efficiency was further supported by building an EHR based set of preclinic questionnaires the patients and caregivers complete on-line through their patient health portal prior to appointments to assess cognitive symptoms, sleep, neuropsychiatric symptoms and functional status in the home setting. UNC evaluates cognition with a separate 1-hour mini neurocognitive battery administered by psychometrists and neurospsychologists on the same day as initial appointments. Duke obtains information about cognitive status based upon repeat testing with the MOCA, MMSE or other brief cognitive tests administered by the provider during the allotted appointment time. The laboratory ordering flow was made easier by having a dedicated order set (Epic Smart Set) for lecanemab evaluations including MRI, LP, APOE genotyping, and reversible dementia laboratory testing.

**Clinic nuts and bolts: Screening for lecanemab candidacy, patient introductions to biomarker assessment, and lecanemab consent.**

### Inclusion/ Exclusion Checklist

Memory Disorders Clinic leadership developed an inclusion and exclusion criteria checklist based on the Cummings Appropriate Use article, the CLARITY AD Study and FDA guidelines. See Suppl S1. This requires a clinical diagnosis of mild cognitive impairment or mild dementia, confirmation of presence of amyloid as well as review of medical conditions, medications and MRI findings. The inclusion and exclusion checklists differed slightly across institutions. At Duke, the inclusion and exclusion criteria include all APOE genotypes including APOE4/4 but excludes patients on anticoagulant medications. UNC allows anticoagulation, but not patients with the APOE4/4 genotype. The inclusion and exclusion check list is stored in the Epic EHR systems and can be placed in the providers note to assist the provider.

### Choices of Biomarker Testing and Recommendations

At the initial evaluation appointment if patients meet criteria based upon cognitive testing and clinical diagnosis of mild cognitive impairment or mild dementia, testing is ordered including APOE genotype, amyloid testing and baseline MRI. Providers offer patients the choice of lumbar puncture with spinal fluid testing or amyloid PET to confirm presence of amyloid. In patients with early disease, providers at Duke and UNC prefer testing of amyloid-beta 42/40 ratio to detect amyloid as this measure is often more sensitive than clinical amyloid PET at detecting the presence of amyloid.[17] For spinal fluid testing the clinic uses Mayo labs Beta-Amyloid Ratio (1-42/1-40) Spinal Fluid (AMYR) and Alzheimer's Disease Evaluation, Spinal Fluid (ADEVL) tests. APOE genotyping is required to help stratify risks for ARIA should patients be a candidate for therapy, but is not determinant in establishing a diagnosis of Alzheimer's disease.

### Visit 1: Preparatory Counseling and Discussion

If it appears that the patient will be a potential candidate for lecanemab at the first visit, the general outline of how lecaneamb works, and its potential benefits and risks are briefly introduced. In addition at visit 1, the patients are educated about the meaning of biomarker results, since these may become available to them through their patient health portal prior to their next appointment. In particular, it is emphasized that the amyloid biomarkers do not indicate

that the patient has debilitating "dementia," but rather that they have early amyloid disease consistent with Alzheimer's disease pathology. Their clinical diagnosis will remain either mild cognitive impairment or mild dementia. It is emphasized that the goal in the clinic is to offer them therapy early in the disease to delay cognitive loss which may postpone development of functional loss in patients with MCI.

### Visit 2: Results Discussion, Risk and Benefit Handouts; Consent; Summary Documentation

At the follow-up appointment, patients discuss their eligibility and risk for adverse events in light of their APOE genotype and MRI findings. This discussion is critical to introduce the benefits and the complexity of the treatment with patients and families. We emphasize that this therapy is not a "cure" but "on average" offers benefit of about a 27% cognitive slowing with some people having more benefit, and some have no benefit at all, over an 18-month period per the CLARITY AD Trial.[7] This discussion helps manage expectations about the benefits or potential capability of the antiamyloid therapy. Potential risks are also discussed, providing a full table with data to indicate percent risk of asymptomatic and symptomatic ARIA-E, ARIA-H as per the APOE genotype status, again based upon the CLARITY AD Trial. Patients and families are provided a handout and reference explaining the mechanism of the medication, risks, and benefits to review and are also informed about the intensity of therapy and requirement for frequent infusions and follow-up MRIs. See Supplement S2. Finally, at visit 2, the provider completes an additional summary note if the patient consents to treatment. This summary note documents the consent discussion and organizes clinical items that assists with Medicare and insurance reimbursement, as well as registry and insurance submission and tracking. See Suppl S3 and S4.

### Role of the Clinic Support Nurse Coordinator: Postorder Coordination

After consent and the summary sheet is documented, an order is placed in the EPIC system for pharmacy infusions services in a therapy plan by the provider. The lecanemab coordinator then plays a critical role entering the patient into required monitoring registries including the required Centers for Medicare and Medicaid Services (CMS) registry, educating the patient and families about the process and requirements, and coordinating follow-up visits and safety MRI scans. Clinic leadership and the health systems at both institutions identified the need for this nurse or clinical coordinator position specifically dedicated to antiamyloid coordination of care.

### Initial Nurse Coordination Steps: Registry and Counseling

Patients on lecanemab must be enrolled in a registry as per the FDA approval guideline. The dedicated coordinator is responsible for entering information into the CMS registry required for all Medicare participants. Duke and UNC also participate in the more detailed Alzheimer's Network for Treatment and Diagnostics (ALZ-NET) registry sponsored by the Alzheimer's Association and the American College of Radiology. In addition to initiating the registry process, the coordinator maintains close contact with the insurance prior authorization team. Nursing helps schedule the initial infusions, review potential adverse events including infusion reactions, and gives the patient and family a wallet/pocket card to indicate that they are receiving lecanemab infusions with potential ARIA symptoms listed and guidelines for emergency care if needed. See Suppl S5.

### Nurse Coordination After Therapy is Started: Timeline of Safety MRIs and Follow-Up Visits

The coordinator takes on the primary coordination role for scheduling safety MRI scans and follow-up provider visits. Three safety MRI scans are ordered with the initial lecanemab order and scheduled after infusions # 4, # 6, and # 13. At UNC, follow-up visits are as follows: the nurse coordinator does a phone list check-up on any possible symptoms after the 1st safety MRI at 2 months, there is an APP visit in clinic after the 2nd MRI at 3 months, and an APP visit after the 3rd MRI at 6 months. At Duke, the coordinator sends an inquiry checklist through the patient health portal after 5 weeks and 11 weeks of treatment and

the first follow up visit is after 6 months. Both clinics schedule subsequent follow up visits every 6 months. See Supplement S6. A spreadsheet is maintained that includes all patients on therapy with columns for their infusion timeline, MRI scheduling times, visit follow-up times, as well as a record of any emergent symptoms/ side effects, infusion reactions, or ARIA events.

### Radiology

Prior to launching the lecanemab program, clinic leadership met with neuroradiology scheduling staff to ensure MRI scheduling is accessible and precise to meet the required surveillance MRI schedule and for urgent situations to assess for possible ARIA. Regarding MRI protocols, clinic leadership requested all scans on 3T scanners with susceptibility weighted imaging (SWI) and T2 FLAIR sequences to adequately detect ARIA-H and ARIA-E respectively. The CLARITY trial used gradient echo (GRE) sequences to detect microhemorrhages but our clinics chose to use SWI which has an increase in sensitivity at detecting microhemorrhages.[18] Neuroradiology also devised a special MRI report template for lecanemab patients that includes quantification of microhemorrhages, measurement of white matter lesions (graded on the Fazekas scale), stroke, presence of superficial siderosis, and brain volumes. The MRI template comments on the presence of ARIA-E or H and the severity ranging from mild, moderate, severe compared to the baseline scan.

### Infusion Center Protocols

The infusion center and clinic team require a care partner to accompany the patient for the first 5 visits. After visit 5, clinic providers decide on an individual basis about whether it is safe for the patient to come on their own. Infusion center staff ensure that all scheduled MRIs are completed before designated infusions. In addition, the infusion center manages infusion reactions with a standard hypersensitivity protocol and transfer to the emergency room if needed. If a patient has a significant infusion reaction, the infusion center orders a preinfusion treatment protocol that includes acetaminophen and diphenhydramine and a possible immunosuppression agent if needed for subsequent infusions.

### Emergency Services and Urgent Assessment Protocols for Possible ARIA Symptoms

Nursing provides patients with a wallet/pocket card stating they are receiving lecanemab infusions with potential ARIA symptoms listed and guidelines for emergency care. ARIA symptoms may present similar to stroke symptoms[19] and guidelines list increased risk of death from thrombolytic medications. Patients having stroke-like symptoms are advised to seek emergency care. Therefore, it is important for patients to have a wallet/pocket card to alert emergency room providers that they are receiving lecanemab, especially for patients who present to emergency departments outside of Duke or UNC. Memory clinic providers at Duke and UNC held education sessions with emergency medicine personnel and stroke neurology at their institutions before the initiation of lecanemab therapy. At UNC, a medication warning banner pops-up on the patient's EHR to indicate the patient is receiving lecanemab including general warnings about increased risks for hemorrhage with thrombolytics. When possible, the stroke and emergency room personnel are advised to ascertain if a stroke is occurring versus ARIA by obtaining diffusion weighted MRI sequences if an initial CT angiogram is not definitive. Other urgent safety considerations include the importance of monitoring for symptoms that might indicate ARIA as an outpatient. When patients experience any symptoms, they are scheduled for same day MRI preferably at a Duke or UNC location before they can proceed with the next treatment. If ARIA is present, guidance included in the product prescribing information is followed when making decisions about whether to continue or stop infusions.

## DISCUSSION

The development of lecanemab delivery models in healthcare systems is a robust multispecialty process that requires significant investment. Current treatment guidelines offer direction for patient eligibility criteria and the healthcare frameworks needed to deliver lecanemab safely. While these guidelines are essential for safe delivery and monitoring of lecanemab, current healthcare systems vary in their delivery models. As outlined above, there is a collaborative

effort between Duke and UNC on developing their delivery pathways, but each institution has different criteria for patient eligibility. While there are patient factors that both institutions deem necessary for lecanemab infusion such as AD pathology confirmed by biomarkers,[20,21] access to multiple MRI scans,[22] and stage of clinical disease,[21] they differ in other patient eligibility factors. Given the risk of hemorrhage associated with patients on anticoagulants, Duke determined that they would not infuse patients currently taking anticoagulant medications. However, Duke does infuse patients with APOE4/4 genotype who are well informed of their risks of adverse events and choose to have the treatment. After reviewing current guidelines, UNC chose different eligibility criteria for their patients, determining that APOE4/4 would be a contraindication for patients while opting to infuse patients on anticoagulants following appropriate informed consent discussion. Healthcare systems developing their own delivery models will need to determine their patient eligibility criteria based on current evidence, administrative leadership and clinician comfort, and informed consent procedure with patients. The difference in pathways developed by both Duke and UNC highlight room for separate guidelines, even in neighboring, collaborating institutions.

It will be important to develop a workforce of skilled clinicians and staff who can clinically diagnose MCI and mild AD, complete appropriate biomarker workup, assess patient eligibility for lecanemab treatment, and engage in informed consent discussions.[23,24] As part of the workup for patient eligibility, there must be access to APOE genetic testing and discussion of APOE4 carrier status with patients and their families.[25] Additionally, health systems will require skilled radiologists to interpret diagnostic imaging such as amyloid PET and identify potentially serious adverse events of ARIA on MRI.[26] At Duke and UNC, partnerships with radiology are necessary to standardize MRI interpretations. Health systems also need to establish protocols for management of ARIA in outpatient and emergency settings when it is identified and have available access to emergency and inpatient services including ICU settings.

Since lecanemab is administered intravenously, health systems must plan to accommodate infusion services. Considerations include capacity of existing infusion services and expansion of infusion services if needed to meet demand. Possible long-term duration of lecanemab treatment with the need for continuous infusions and the future approval of additional antiamyloid therapies, will require healthcare systems to develop new infusion delivery models, possibly with home infusion services.[27]

As antiamyloid therapies become more widely available, increased access to clinical evaluations at early stages of cognitive decline is a requirement. The collaboration between neurology, especially behavioral neurology, psychiatry and geriatric medicine as primary cognitive specialists is vital to increasing cognitive evaluation and treatment access. In fact, current opinion is that multidisciplinary teams including psychiatrists, neurologists and other specialists such as geriatricians are required to ensure early diagnosis and treatment.[28] Geriatric psychiatry in particular may play an essential role in the development of antiamyloid therapy delivery programs and should be aware of health system processes and challenges.

Future considerations for antiamyloid therapy delivery must include disparities in treatment availability and patient resources, which presents a current significant challenge and may limit delivery of the drug to certain patient populations. Treatment disparities will not only be important as health systems implement therapy, but also as delivery is scaled to meet patient needs. A major limitation to care is the resources and coordination in a health system required to provide antiamyloid therapy. Large private and academic health centers in urban areas may have more ability to offer treatments; whereas smaller centers in more rural areas or economically disadvantaged areas may lack necessary resources including infrastructure and specialized clinicians and staff. Lack of resources, whether due to geographic location or to socioeconomic variables, leads to other considerations including patient access to clinical specialists, ability to schedule diagnostic procedures including lumbar puncture or amyloid PET and access to 3T MRIs for surveillance and urgent concerns.[22] Patients also require reliable transportation to infusion services, MRIs and follow up appointments with clinicians. Limited access to transportation may impact a patient's ability to start or continue treatment especially for the cognitively impaired and for people in rural areas who require travel to larger health systems. In addition to transportation services, in this initial phase of treatment, Duke requires that patients

have access to reliable support system such a friends or family to accompany them to infusion appointments for the first five treatments. Limited access to this support system may impede a patient's eligibility for treatment. Cognitively impaired patients will continue to require support for travel to treatment centers and clinical appointments. An important disparity to consider is that underrepresented populations often present at later stages in the disease, when they may be past the stage of qualifying for antiamyloid therapy.[29] Outreach and education programs in these communities may encourage patients and caregivers to seek earlier detection. Finally, disparities in ability to pay for treatment must be considered for health systems to meet the needs of the entire patient population. Fortunately, the Centers for Medicare and Medicaid Services (CMS) has expanded coverage for diagnosis and antiamyloid treatment including coverage of amyloid PET and 80% coverage of drug and infusion treatment costs.[30] However, the additional 20% cost may be a barrier for patients with traditional Medicare plans and no additional coverage.

## CONCLUSION

Lecanemab is a novel antiamyloid therapy which presents new challenges for health system implementation and delivery. Given the multiple stakeholders involved and workup required for patient eligibility and clinical monitoring, there is significant investment necessary from a health system for implementation. While Duke and UNC have both collaborated on the development of their treatment pathways, each has approached lecanamab implementation in unique ways given available infrastructure and protocols. To increase access to lecanemab, health systems will need to approach implementation from a multisystem perspective given the multiple stakeholders and specialists required for appropriate delivery and monitoring. The models developed by Duke and UNC may provide guidance to other health systems who are beginning the process of implementing this novel therapy. However, disparities must be considered as delivery methods evolve. Geriatric psychiatrists are in a pivotal position to provide cognitive evaluations for patients with early cognitive symptoms and to implement these new treatment delivery models with adequate health system support.

## AUTHOR CONTRIBUTIONS

*Michael Weber drafted the objectives, discussion, and conclusion portions of the article. He also contributed to the preparation and formatting of the article to AJGP guidelines. Heidi L Roth drafted the procedure developed by UNC for the implementation and delivery of lecanemab. Amy Abramowitz provided edits to a majority of the paper in preparation for review. Kim G. Johnson drafted the procedure developed by Duke for the implementation and delivery of lecanemab, directed and oversaw the manuscript preparation. All authors extensively edited the manuscript.*

## DATA STATEMENT

*Previous Presentations: American Association of Geriatric Psychiatry Annual Conference. Atlanta, GA. March 2024.*

*American Psychiatric Association Annual Meeting. New York, NY. May 2024.*

## DISCLOSURES

*Michael Weber, reports no conflicts with any product mentioned or concept discussed in this article. Amy Abramowitz reports no conflicts with any product mentioned or concept discussed in this article. Heidi Roth is the primary investigator of ALZ-NET at UNC. Kim Johnson is the primary investigator of Eisai Inc. AHEAD clinical trial on lecanemab therapy for cognitively normal participants, the primary investigator of ALZ-NET at Duke, the primary investigator of LEXEO Therapeutics gene therapy trial, a speaker for Eisai at the 2024 Alzheimer's Association International (AAIC) annual meeting, a consultant with University of Southern California and a Lilly Preclinical Diagnosis Advisory Board member.*

## SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.jagp.2025.02.007.

## References


1. Rajan KB, Weuve J, Barnes LL, et al: Population estimate of people with clinical AD and mild cognitive impairment in the United States (2020-2060). Alzheimers Dement 2021; 17 (12):1966–1975
2. Alzheimer's Association: Alzheimer's Disease Facts and Figures. Chicago: [Ebook], 2024. Retrieved from: https://www.alz.org/media/Documents/alzheimers-facts-and-figures.pdf
3. Yadollahikhales G, Rojas JC: Anti-amyloid immunotherapies for Alzheimer's Disease: a 2023 clinical update. Neurotherapeutics 2023; 20(4):914–931
4. Lord A, Gumucio A, Englund H, et al: An amyloid-$\beta$ protofibril-selective antibody prevents amyloid formation in a mouse model of Alzheimer's disease. Neurobio. Dis. 2009; 36(3):425–434
5. Ono K, Tsuji M: Protofibrils of amyloid-$\beta$ are important targets of a disease-modifying approach for Alzheimer's disease. Int J Mol Sci 2020; 21(3):952
6. Chowdhury S: Monoclonal antibody treatments for Alzheimer's disease: aducanumab and Lecanemab. Discoveries 2023; 11(3):e173
7. van Dyck CH, Swanson CJ, Aisen P, et al: Lecanemab in early Alzheimer's disease. N Engl J Med 2023; 388(1):9–21
8. Swanson CJ, Zhang Y, Dhadda S, et al: A randomized, double-blind, phase 2b proof-of-concept clinical trial in early Alzheimer's disease with lecanemab, an anti-a$\beta$ protofibril antibody. Alzheimers Res Ther 2021; 13(1):80;doi:10.1186/s13195-021-00813-8
9. Cummings J, Apostolova L, Rabinovici GD, et al: Lecanemab: appropriate use recommendations. J Prev Alzheimer's Dis 2023; 10(3):362–377
10. Salloway S, Chalkias S, Barkhof F, et al: Amyloid-related imaging abnormalities in 2 phase 3 studies evaluating Aducanumab in patients with early Alzheimer disease. JAMA Neurol 2022; 79 (1):13–21
11. Shane R, Kreman S, Tan ZS, et al: Lecanemab planning: blueprint for safe and effective management of complex therapies. Neurol Clin Pract 2024; 14:e200361
12. Rosenbloom MH, O'Donohue T, Zhou-Clark D, et al: A framework for the administration of anti-amyloid monoclonal antibody treatments in early-stage Alzheimer's disease. CNS Drugs 2024; 38(7):493–505
13. Szymkowicz SM, Gerlach AR, Homiack D, et al: Biological factors influencing depression in later life: role of aging processes and treatment implications. Transl Psychiatr 2023; 13(1):160
14. Gopalakrishna G, Brunton S, Pruzin J, et al: Understanding the role of psychiatrists in the diagnosis and management of mild cognitive impairment and mild Alzheimer's disease dementia: a cross-sectional survey. BMC Psychiatr 2023; 23(1):716
15. Abramowitz A, Johnson K, Weber M, et al: Managing mild cognitive impairment in the age of anti-amyloid therapies. Am J Geriatr Psychiatr 2024; 32(4):S12–S13
16. Sims JR, Zimmer JA, Evans CD, et al: Donanemab in early symptomatic Alzheimer disease: the TRAILBLAZER-ALZ 2 randomized clinical trial. JAMA 2023; 330(6):512–527
17. Hansson O, Lehmann S, Otto M, et al: Advantages and disadvantages of the use of the CSF amyloid $\beta$ (A$\beta$) 42/40 ratio in the diagnosis of Alzheimer's disease. Alzheimers Res Ther 2019; 11(1):34
18. Raji CA, Benzinger TLS: The value of neuroimaging in dementia diagnosis. Continuum (Minneap Minn) 2022; 28(3):800–821
19. Kmeid M, Blanden AR, Kaur N, et al: Abstract number - 224: stroke Mimic—Patient with symptomatic amyloid-related imaging abnormalities presenting with stroke-like symptoms. Stroke-Vasc Interv N 2023; 3:S1
20. Lissa JL, Seleri Assunção S, Cummings J, et al: Practical recommendations for timely, accurate diagnosis of symptomatic Alzheimer's disease (MCI and dementia) in primary care: a review and synthesis. J Intern Med 2021; 290(2):310–334
21. Jack C.R. Jr, Andrews JS, Beach TG, et al: Revised criteria for diagnosis and staging of Alzheimer's disease: alzheimer's Association Workgroup. Alzheimers Dement 2024; 10(8):5143–5169
22. Hampel H, Elhage A, Cho M, et al: Amyloid-related imaging abnormalities (ARIA): radiological, biological and clinical characteristics. Brain 2023; 146(11):4414–4424
23. Anderson M, Sathe N, Polacek C, et al: Site readiness framework to improve health system preparedness for a potential new Alzheimer's disease treatment paradigm. J Prev Alzheimers Dis 2022; 3(9):542–549
24. Hlavka JP, Mattke S, Liu JL: Assessing the preparedness of the health care system infrastructure in six European countries for an Alzheimer's treatment. Rand Health Q 2019; 8(3):2
25. Langlois CM, Bradbury A, Wood EM, et al: Alzheimer's Prevention Initiative Generation Program: development of an APOE genetic counseling and disclosure process in the context of clinical trials. Alzheimers Dement (NY) 2019; 5:705–716
26. Cogswell PM, Barakos JA, Barkhof F, et al: Amyloid-related imaging abnormalities with emerging Alzheimer Disease therapeutics: detection and reporting recommendations for clinical practice. Am J Neuroradiol 2022; 43(9):E19–E35
27. Liu JL, Hlavka JP, Hillestad R, et al: Assessing the Preparedness of the U.S. Health Care System Infrastructure for an Alzheimer's Treatment. Santa Monica, California: RAND Corporation, 2017 RR-2272-BIOG
28. Galvin JE, Aisen P, Langbaum JB, et al: Early Stages of Alzheimer's Disease: evolving the care team for optimal patient management. Front Neurol 2021; 11:592302
29. Lin PJ, Daly AT, Olchanski N, et al: Dementia diagnosis disparities by race and ethnicity. Med Care 2021; 59(8):679–686
30. Accessed October 14, 2024. https://www.alz.org/alzheimers-dementia/treatments/cms-medicare-coverage