The Federal Role in Bringing Breakthrough Treatments to Patients

Advisory Council on Alzheimer's Research, Care, and Services Meeting

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National Institutes of Health
Turning Discovery Into Health

August 3, 2026

Highlighted Progress in Dementia Research

	2012	2026
Understanding disease mechanisms	Fewer than 20 genetic variants known to influence AD risk	• 100+ genetic variants identified that influence AD risk • Stratification by population reveals some variants are more prevalent in different populations and may have different effects • Several protective genetic variants identified • Mixed pathologies are the norm, not the exception
Diagnostics	Amyloid PET agent for AD	• Amyloid and Tau PET agents for AD • Commercially available blood tests to help diagnose AD, including two cleared by the FDA. • Validated behavioral assessments
Disease-modifying treatments	None (treatments for symptom management available)	• Two disease-modifying therapies available in the U.S. (donanemab & lecanemab, including an at-home injection version of lecanemab)
Prevention/Risk Reduction	No effective strategies known	• Intensive blood pressure control, specific forms of cognitive training exercises, and multidomain lifestyle interventions (e.g., combining diet, exercise and cognitive stimulation)
Care & caregiving	Foundational work to develop and test care models	• Collaborative care models and Resources for Enhancing Alzheimer's Caregiver Health (REACH) II are interventions for care and/or caregiver support ready for broader implementation with continued evaluation

The Federal Pipeline: From Research to Coverage

Each agency operates independently but their decisions are interdependent.

Funds foundational science & translational and clinical infrastructure; derisks the field for follow-up industry-funded investigations

- Ensures the safety, efficacy, and security of human and veterinary drugs, biological products, and medical devices
- Helps to speed innovation that makes medical products more effective, safe, and affordable
- Helps the public get the accurate, science-based information they need to use medical products and foods to maintain and improve their health

Ensures our most vulnerable receive high-value care by leading all payors and supporting providers

The Role of NIH

National Institute on Aging

NIH-Funded Research Helped Usher in Disease-Modifying Alzheimer's Treatments

The increased federal investment in AD/ADRD research over the last decade has yielded discoveries that have advanced treatments, including **a new category of anti-amyloid antibodies to target the underlying disease processes of Alzheimer's**, instead of only treating the symptoms of the disease.

Lecanemab (Leqembi®)

Donanemab (Kisunla™)

NIH did not fund the specific trials that were the basis of FDA approval, but NIH funded investigations behind the discovery and validation.

NIH National Institute on Aging

NIH-Funded Research Made Recent Progress Possible

Understanding of amyloid biology

NIH-funded research revealed **how amyloid forms, accumulates, and contributes** to Alzheimer's disease, establishing the scientific foundation for today's therapeutic strategies.

Testing in model systems

NIH has funded **experimental treatments**, demonstrated proof of concept for amyloid-targeting approaches, and advanced the most promising candidates toward clinical trials.

NIH-Funded Research Made Recent Progress Possible Cont.

Clinical Trial Infrastructure

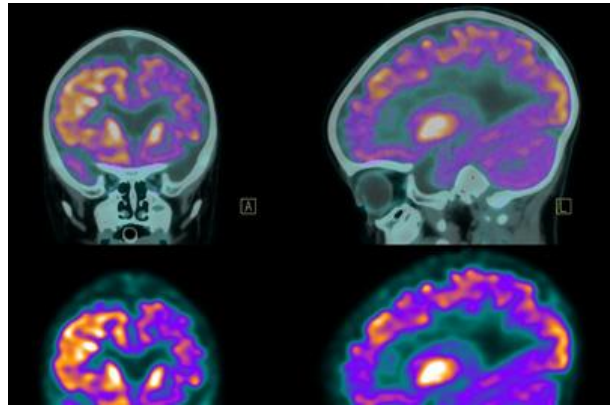
NIH funding contributed to the **development of trial procedures, cognitive and functional outcome measures, site networks, recruitment approaches, and investigator expertise** that became standard across the field.

National Institute on Aging

NIH-Funded Research Made Recent Progress Possible Cont.

Selection of Trial Participants

NIH funding led to the development of **amyloid PET imaging**, which has been used to select participants for pivotal clinical trials of lecanemab and donanemab.



Measuring treatment effects

NIH funding helped establish and validate **key cognitive assessment measures**, such as the CDR-SB scale, which are used as primary and secondary endpoints in trials.

NIH National Institute on Aging

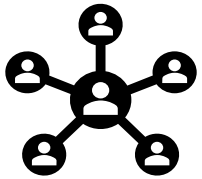
Continued Efforts in the Development Pipeline

Developing & Testing New Candidates

- Target identification studies
- Translational research programs
- Clinical trials

Drug Repurposing

- Preclinical & clinical studies
- Include drugs as well as dietary supplements



Continued Investigation of FDA Approved Therapeutics

- Research in new populations
- Evaluation across broad clinical settings
- Exploration of combination therapies
- Approaches to mitigating side effects (e.g., ARIA)

Investing in Clinical Trials to Prevent & Treat Dementia

Non-Pharmacological

148 TRIALS

Modality

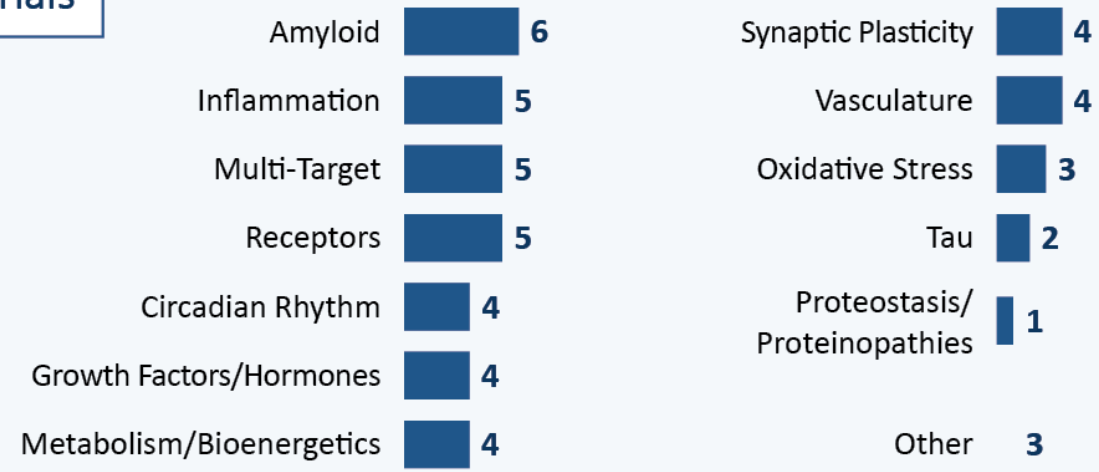
Pharmacological

63 TRIALS

Phase I & Phase II

50 trials

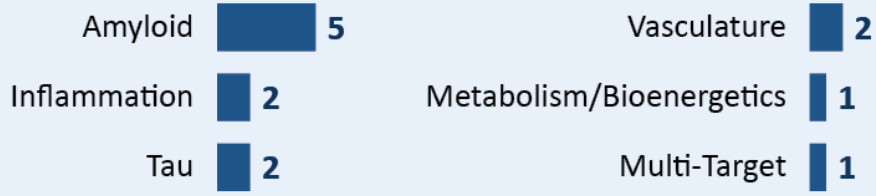
Targeted Disease Process



Phase II/III, III, and IV

13 trials

Targeted Disease Process



Active NIH-funded non-pharmacological trials as of March 2025

www.nia.nih.gov/research/ongoing-AD-trials

Agency Mission

Protects the public health by ensuring the safety, efficacy, and security of human and veterinary drugs, biological products, and medical devices

Advances the public health by helping to speed innovation that make medical products more effective, safe, and affordable and by helping the public get the accurate, science-based information they need to use medical products and foods to maintain and improve their health

Medical Product Centers at FDA

FDA


Center for Food Safety & Applied Nutrition


Center for Drug Evaluation & Research


Center for Biologics Evaluation & Research

Center for Tobacco Products


Center for Devices & Radiological Health


Center for Veterinary Medicine


National Center for Toxicological Research

CDER: small molecules, monoclonal antibodies, proteins, diagnostic imaging agents

CBER: cell and gene therapy products, tissue products, blood products, vaccines

CDRH: therapeutic devices and diagnostic devices (e.g., in vitro assays, imaging)

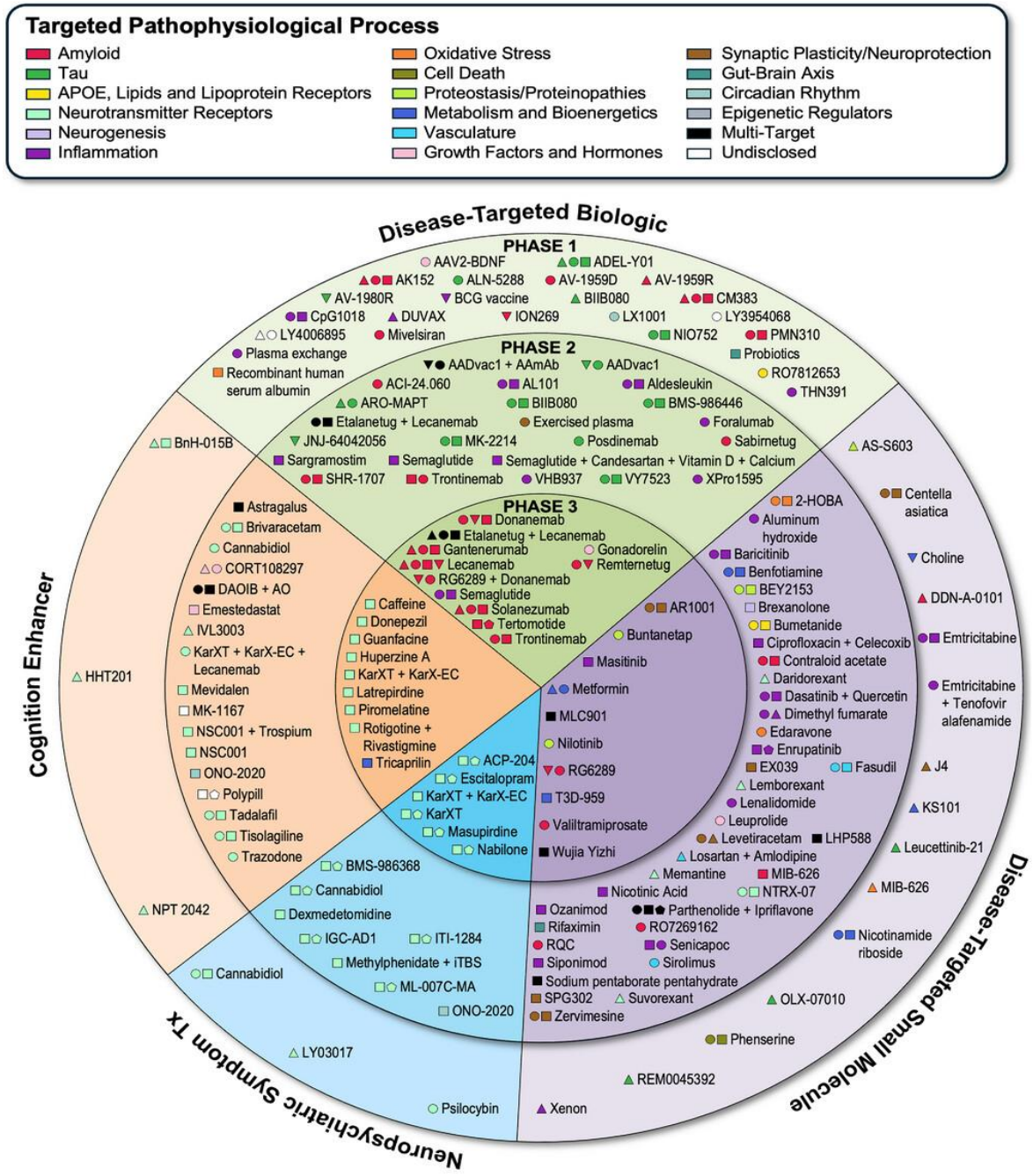
FDA-Approved Medical Products for AD

- Drugs
  - Amyloid-directed monoclonal antibodies (lecanemab, donanemab)
  - Acetylcholinesterase inhibitors (donepezil, galantamine, benzgalantamine, rivastigmine)
  - NMDA-antagonist (memantine)
  - Therapies for behavioral symptoms (brexipiprazole, dextromethorphan-bupropion)
  - Suvorexant for insomnia- labeling describes use in patients with AD
- Diagnostics
  - Blood-based biomarkers
  - CSF-based biomarkers
  - PET Imaging agents
  - Digital Cognitive Assessment Devices

“There are currently 158 drugs in 192 AD trials”

Cummings JL, Zhou Y, Yang Y, et al. Alzheimer's disease drug development pipeline: 2026. Alzheimer's Dement. 2026;12:e70251. https://doi.org/10.1002/trc2.70251

Likely an underestimate because Phase 1 trials are not required to be reported in clinicaltrials.gov



Medical Product Development Cycle

IND: Investigational New Drug Application
IDE: Investigational Device Exemption

Medical Product Development for Alzheimer's Disease and Related Disorders (AD/ADRD)

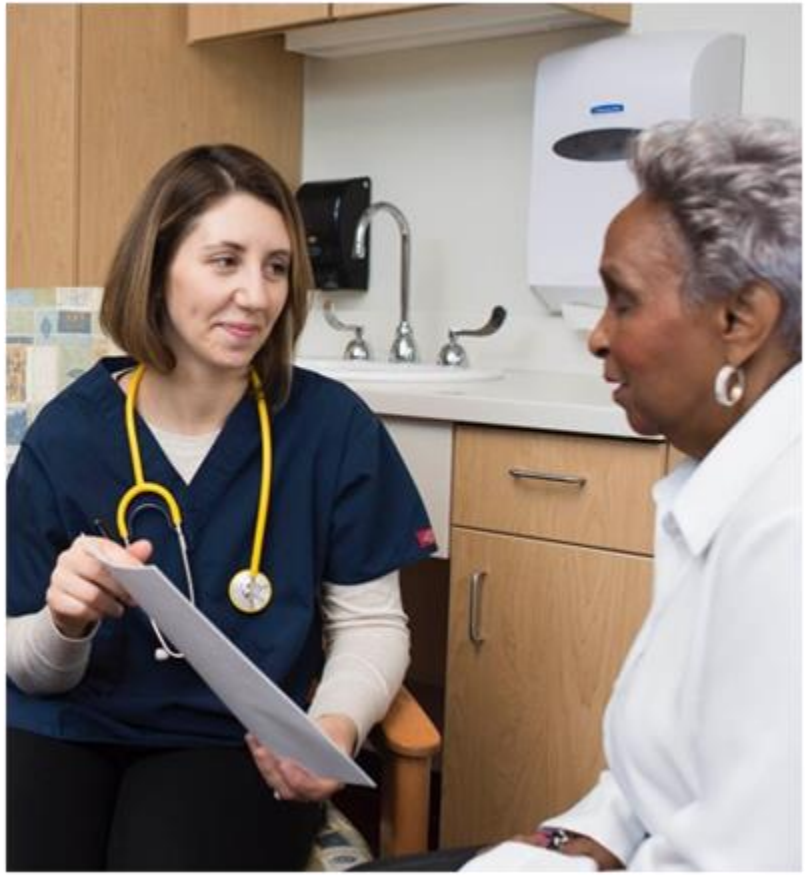
- Key review activities of FDA medical product centers
  - Provide advice to sponsors of drug or device applications during product development on the data needed to support initiation of clinical trials or support a future marketing application
  - Monitor ongoing clinical trials for safety
  - Conduct regulatory assessment of efficacy and safety of medical products for marketing applications
  - Continued surveillance of safety in the post-marketing setting
- Many active product development programs for ADRD in CDER/CBER/CDRH
  - Therapies may target symptoms, underlying disease pathophysiology, or causal genetic variants

Medical Product Development

- Pre-competitive and regulatory science efforts to address areas of opportunity to support current and future development
  - Draft Guidance for Industry: Early Alzheimer's Disease: Developing Drugs for Treatment (2024)
  - Biologic staging of disease to guide early intervention strategies
  - Regulatory research
  - Public-private partnerships (Critical Path for Alzheimer's Disease, Accelerating Medicines Partnership for Alzheimer's Disease)
  - Engagement with ADRD stakeholders, patient community, industry, academia and other federal agencies

Centers for Medicare & Medicaid Services (CMS) Mission

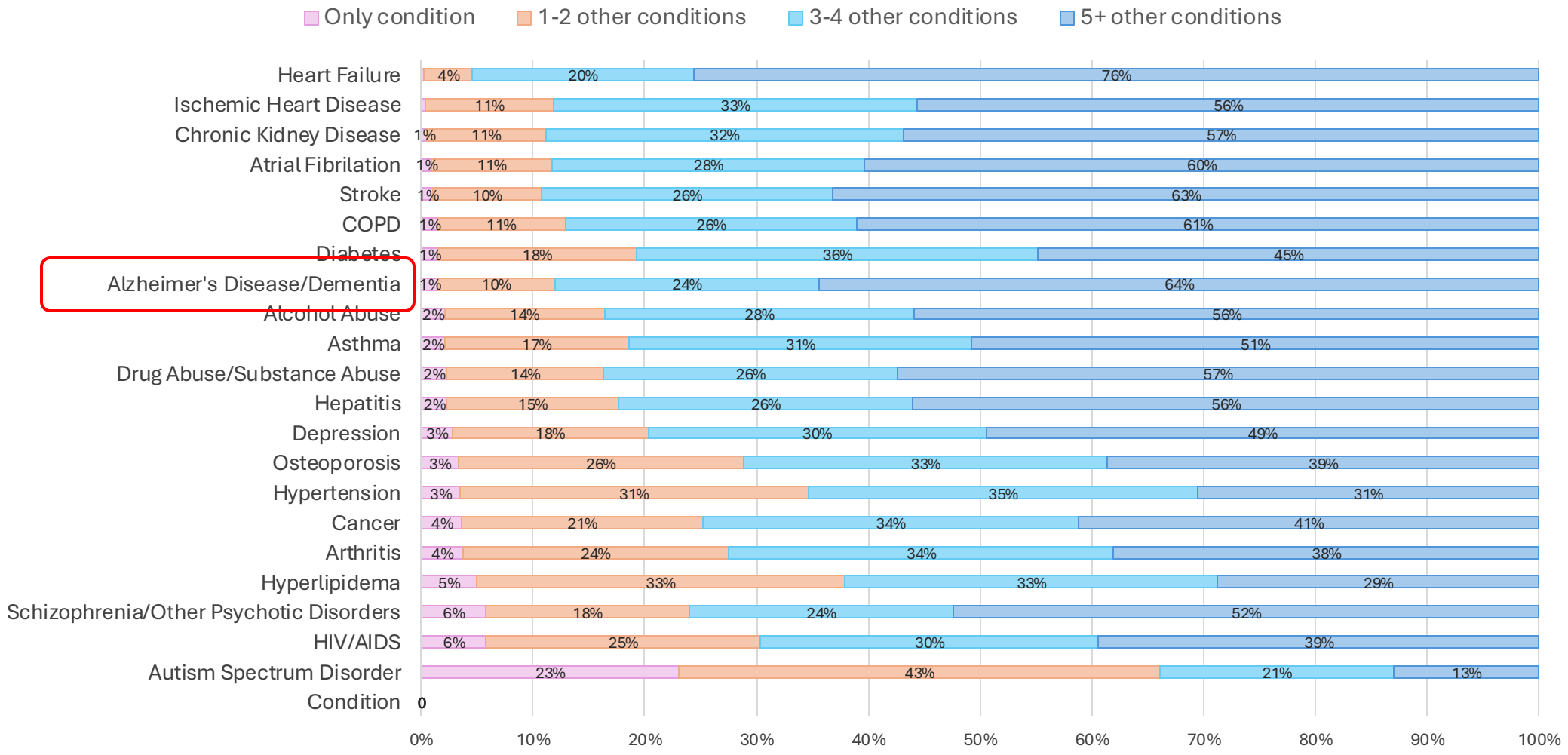
is to ensure our most vulnerable receive high-value care by leading all payors and supporting providers



CMS: Scope

- As the largest single purchaser of health care dollars, Medicare plays a key role in transitioning our health care system away from fee-for-service and towards value-based care.
- CMS is the largest purchaser of health care in the world
- CMS programs provide health care coverage to over 170M people, or 1 of every 2 Americans (Medicare, Medicaid, CHIP, Marketplace)
- In 2024, more than 67M people were enrolled in Medicare, with more than 82M enrolled in Medicaid and CHIP
- More than 12 million people are enrolled in both programs, and these individuals have very high rates of chronic illness; most with multiple chronic conditions
- Most Medicare beneficiaries - over 80% - are over age 65
- Some people come into Medicare first, typically through age, and others become beneficiaries because of disability or other health status (e.g. renal disease)

Percentage of Medicare FFS Beneficiaries with 21 Selected Chronic Conditions: 2024



Final National Coverage Determination (NCD) Memorandum for Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease

- On April 7, 2022 CMS released a final NCD decision memorandum regarding a National Coverage Determination to cover FDA-approved monoclonal antibodies that target amyloid for the treatment of Alzheimer's disease through our process called "coverage with evidence development" (CED); FDA-approved drugs in this class would be covered for people with Medicare only if they are enrolled in qualifying clinical trials

- CMS-approved studies of anti-amyloid mAbs approved by FDA for the treatment of AD based upon evidence of efficacy from a direct measure of clinical benefit must address all of the questions below:

  a) Does the antiamyloid mAb meaningfully improve health outcomes (i.e., slowing in the decline of cognition and function) in broad community practice?

  b) Do benefits and harms such as brain hemorrhage and edema, associated with use of the antiamyloid mAb, depend on characteristics of patients, treating clinicians, and settings?

  c) How do the benefits and harms change over time?

  The final NCD CED decision memorandum is here: https://www.cms.gov/medicare-coverage-database/view/ncacal-decision-memo.aspx?proposed=N&ncaid=305

CMS Coverage Determination Process: https://www.cms.gov/Medicare/Coverage/DeterminationProcess

More on Medicare Coverage of Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease

- On July 6, 2023, FDA approved Leqembi™ (lecanemab) for treatment of Alzheimer's disease based on a clinical endpoint. On the same day, CMS launched the Anti-Aβ mAb CED Study (CMS National Patient Registry)
- For monoclonal antibodies approved by FDA for the treatment of AD based upon evidence of efficacy from a direct measure of clinical benefit, Medicare coverage may be provided in CMS-approved prospective comparative studies; study data may be collected in a registry

Information at: Broader Medicare Coverage of Leqembi (Lecanemab) Available Following FDA Traditional Approval

Four Approved Studies

- **Alzheimer's National Registry for Treatment and Diagnostics**
  Sponsor: Alzheimer's Disease and Related Disorders Association, Inc
  Clinicaltrials.gov number: NCT06170268
  CMS Approval Date: 1/29/2024
- **Georgia Memory Net Anti-Amyloid Monoclonal Antibody Registry**
  Sponsor: Emory University
  Clinicaltrials.gov number: NCT05999084
  CMS Approval Date: 11/14/2023
- **A Prospective Comparative Study Of Monoclonal Antibodies For The Treatment Of Alzheimer's Disease**
  Sponsor: Beth Israel Deaconess Medical Center
  Clinicaltrials.gov number: NCT05925621
  CMS Approval Date: 07/11/23
- **Prospective Study on Anti-Amyloid-β Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease Coverage of Evidence Development (The Anti-Aβ mAb CED Study)**
- Clinicaltrials.gov number: NCT06058234

Coverage with Evidence Development

- CED requirements may be satisfied by several different study types, for example:
  - pragmatic clinical trials
  - single-arm registry-based studies
  - studies making secondary use of real-world data (RWD)
- In August 2024, CMS published an updated CED guidance document that provides increased policy predictability, transparency, and flexibility for manufacturers to address evidence gaps and states CED should be time-limited.
- The update CED guidance allows greater use of fit-for-purpose studies for coverage:
  - Conventional studies often require ideal conditions, smaller sample sizes, shorter follow-up duration, and narrow inclusion
  - Real-world data studies reflect real-world conditions; they often allow larger sample sizes, longer follow-up duration, and more diverse inclusion

Other Clinical Studies Under Medicare

Investigational Device Exemption (IDE) Studies

- IDE status is approved by the FDA as either category A or category B, allowing devices not yet FDA-market authorized to be used in clinical studies
- CMS approval of a Category A (Experimental) IDE study will allow coverage of routine care items and services furnished in the study, but not of the Category A device. (42 CFR § 405 Subpart B).
- CMS approval of a Category B (Nonexperimental/investigational) IDE study will allow coverage of the Category B device and the routine care items and services in the trial. (42 CFR § 405 Subpart B).
- CMS follows a centralized study approval/tracking process implemented January 1, 2015.
- Challenges: Continued Access Studies, Use of clear health outcomes

Clinical Trial Policy (NCD 310.1)

- Covers routine costs of a clinical trial (though not the investigational item or service itself unless otherwise covered outside of the clinical trial) funded by certain federal agencies (i.e., NIH, CDC, AHRQ, CMS, DOD, and VA).