Enrollment of Older Adults in Dementia Clinical Trials

Phases · Enrollment Challenges & Successes · Resources for Cognitive Changes

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Agenda

01 Dementia Impact

02 Why Clinical Trials Matter

03 The Reality of Time

04 The Representation Gap

05 Enrollment Challenges

06 Benefits of Trial Participation

07 Clinical Trial Basics

08 Successes and Promising Strategies

09 Resources and Support: How you can help

The Growing Impact of Dementia

Current and future concerns

What is Dementia?

DSM-5 criteria - “Major neurocognitive disorder”

Evidence from history and assessment of decline in at least one cognitive domain:

- Learning and memory
- Language
- Executive function
- Complex attention
- Visual perception
- Social cognition

Must represent a decline from previous level of function
Must interfere with ADLS/iADLS

Progressive, irreversible loss of cognition and function

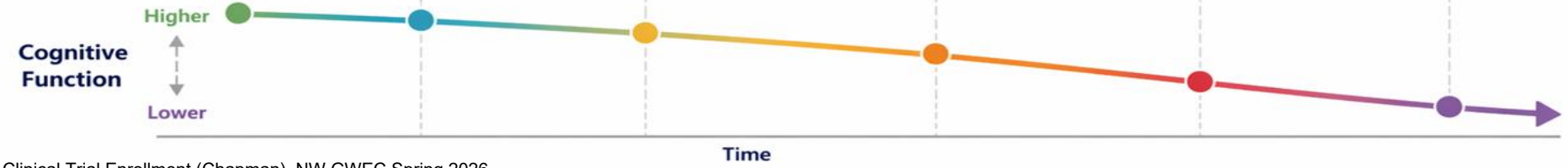
Spectrum of Cognitive Change to Dementia

A continuum from normal cognitive function to severe dementia

Increasing Cognitive Impairment and Functional Decline

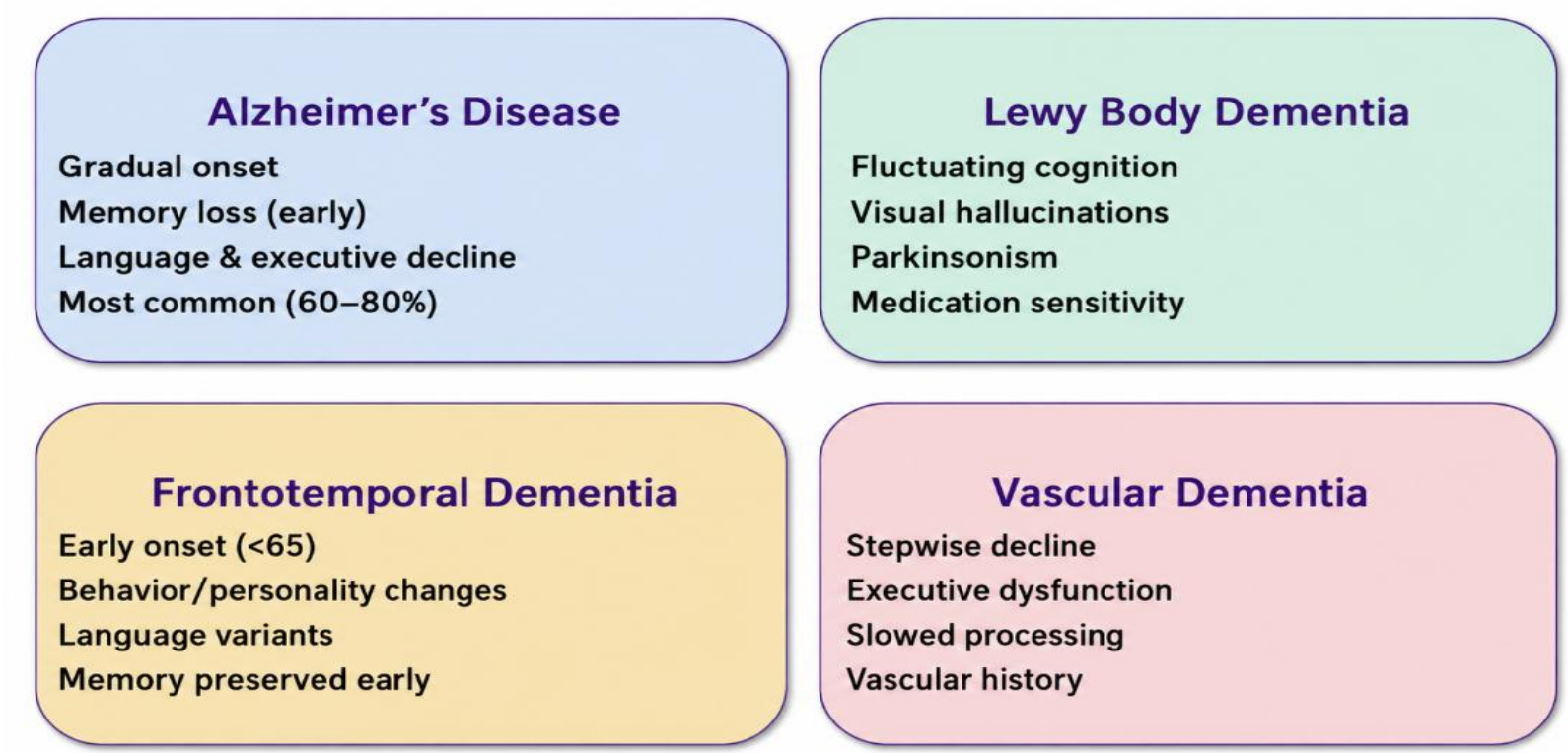
Normal Cognitive Aging	Subjective Cognitive Decline (SCD)	Mild Cognitive Impairment (MCI)	Mild Dementia	Moderate Dementia	Severe Dementia
• Cognitive changes typical for age • No impact on daily functioning • Normal performance on cognitive tests	• Noticeable decline in cognition reported by individual • Normal cognitive performance on testing • No impairment in daily function	• Measurable cognitive decline greater than expected for age • Preserved independence in daily activities • Increased risk of progression to dementia	• Cognitive decline interferes with complex daily activities • May need help with some instrumental activities (e.g., bills, medications, driving)	• Clear decline in cognition and daily functioning • Needs help with many activities of daily living (e.g., bathing, dressing, managing medications)	• Severe cognitive and physical decline • Full dependence in activities of daily living • Loss of communication skills and recognition of family/friends

Progression may vary across individuals



This spectrum is a general representation and not intended for diagnostic use.

Clinical Characteristics of Common Dementias



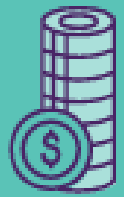
2026 ALZHEIMER'S DISEASE FACTS AND FIGURES

OVER
7 MILLION
Americans are living with Alzheimer's

NEARLY
13 MILLION
Americans provide unpaid care for people with Alzheimer's or other dementias

In 2026, Alzheimer's and other dementias will cost the nation
$409 BILLION

By 2050, these costs could rise to nearly
$1 TRILLION



1 in 3
older adults dies with Alzheimer's or another dementia

It kills more than breast cancer and prostate cancer
COMBINED

Why Clinical Trials Matter

The foundation of evidence-based medicine

Why Clinical Trials Matter

- 80-90% of medical treatments today were developed through validated clinical trials
- Major medical breakthroughs have been made possible through clinical trials
- Clinical trials are required before FDA approval to ensure safety and efficacy
- Improve standards of care
- Support personalized medicine, precision therapeutics, earlier disease detection

The Reality of Time

When innovation moves slower than disease

Why Clinical Trials Matter

400,000+

Active clinical trials globally

ClinicalTrials.gov 2024

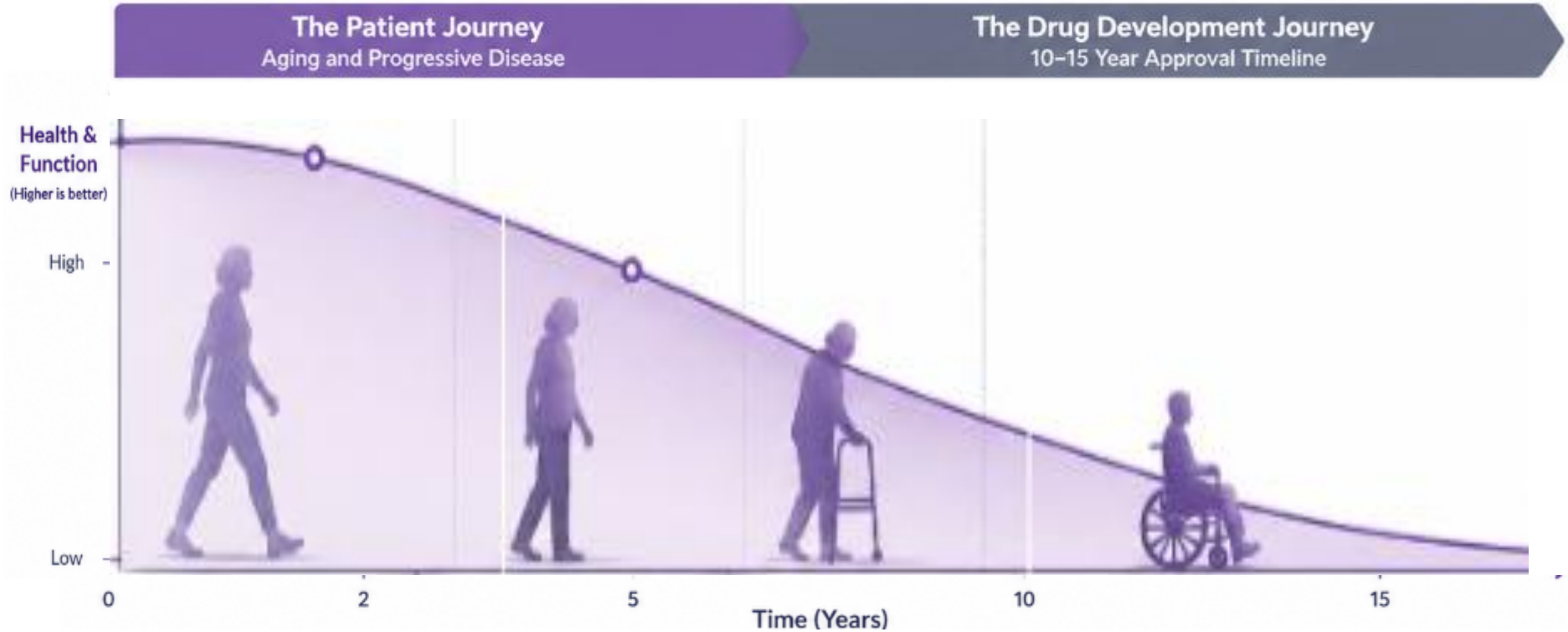
<5% of eligible enroll

NCI Enrollment Data

10-15 years for FDA approval

FDA Drug Development

Timeline Reality



The Representation Gap

Enrollment gaps

Older Adults in Clinical Trials

65+

Age group most likely to use medications

CDC Medication Use Data

<25%

Clinical trial participants who are 65+

JAMA Internal Medicine

50%

Trials that exclude adults with comorbidities

FDA Demographic Analysis

Key Differences in Dementia Enrollment and Retention

Metric	Dementia / Alzheimer's trials	Many non-dementia trials
Screen → enroll conversion	**~10–20% (often lower in practice)**	**~25–60% (varies widely)**
Eligible → randomized	Often **~10–15% effective yield**	Often **~30–70%**
Participants lost due to eligibility	High (~70–90% of screened excluded or declined)	Moderate (~30–60%)
Driver of loss	Cognitive impairment, caregiver burden, strict criteria	Mostly medical eligibility or preference

Enrollment Challenges

Structural, systemic, and individual barriers

Barriers to Enrollment

Structural Barriers

- Restrictive eligibility criteria (age cut-offs, comorbidity exclusions)
- Trial locations that require frequent travel
- Lack of transportation assistance
- No caregiver accommodation policies
- Complex procedures
- Technology barriers for remote participation

Individual & Social Barriers

- Fear of receiving a placebo or experimental treatment
- Concerns about side effects and existing health conditions
- Distrust of medical institutions (especially in communities of color)
- Low trial awareness among patients and providers
- Fixed incomes and inability to take time off work / caregiving

Additional Barriers for Caregivers

Caregiver burden is often overlooked in study design

- Participation often depends on a caregiver to attend visits, manage schedules, monitor symptoms
- Caregivers may already be overwhelmed
- Time off work, stress, and logistics can discourage involvement

Ethical Considerations

Decisional Capacity and Consent:

- Need for a legally authorized representative (LAR), DPOA, or study partner may limit eligibility

Autonomy vs Protection

- Support inclusion while minimizing risk and weighing risk-benefit

Equity and Justice

- Ethical trial design requires equitable access, research populations should reflect patients most affected by disease

Key Principle: protecting vulnerable populations should not mean excluding them from scientific progress

Benefits of Participation

Quality of Life and Outcomes

Benefits to Study Participation

🩺 Care Quality & Monitoring

- Participants receive **2–4x more clinical assessments per year** than standard care
- May get something that helps them
- Trials may include regular lab testing, physical assessments, medication review
- Earlier detection of complications or comorbidities improves clinical management in up to **25% of cases**

😊 Quality of Life

- **~80% of participants** report a sense of purpose or meaning from participation
- Quality of life scores improve by **~20–25%** in some supportive-care trials

Benefits to Study Participation

👩‍⚕️ Caregiver Outcomes

- **64% of caregivers** report improved understanding of the disease through trial participation
- **30–40% reduction in caregiver burden** after 6–12 months (in structured-support trials)
- Access to education, training, and support services improves caregiver confidence by **~40%**

Perspectives

Participant perspectives:

- “I wanted to do something that might help others in the future, even if it doesn’t help me.”
- “It gives me a sense that something is being done instead of just waiting.”
- “Being in the study makes me feel like I’m still contributing.”
- “They treat me like a person, not just a diagnosis.”
- “Even if the medicine doesn’t work, the attention and monitoring are worth it.”
- “I like having somewhere to go where people understand what I’m going through.”

Caregiver perspectives:

- “It connects us to experts who understand the disease.”
- “We feel less alone managing this.”
- “It helps us plan for what’s coming.”
- “Even small slowing of decline matters to our family.”

Clinical Trial Basics

Safety → Efficacy → Confirmation → Surveillance

Defining Clinical Trials

- A research study conducted with human volunteers to answer specific health questions
- Test safety and efficacy
- Follow strict scientific standards overseen by regulatory agencies (FDA, IRB, Ethics Committees)

- Types of clinical trials include:
  - Treatment
  - Prevention
  - Screening
  - Diagnostic
  - Behavioral
  - Quality of Life

PHASES OF A CLINICAL TRIAL

0 — PRE-CLINICAL

Lab – based research to tell if a treatment is useful and safe

1 — SAFETY

10 – 80 participants to assess effect of treatment in humans

2 — SAFETY & DOSING

100 - 300 participants to evaluate safety & effective dose of treatment

3 — SAFETY & EFFICACY

300 - 3000 participants to confirm benefit and safety of the treatment

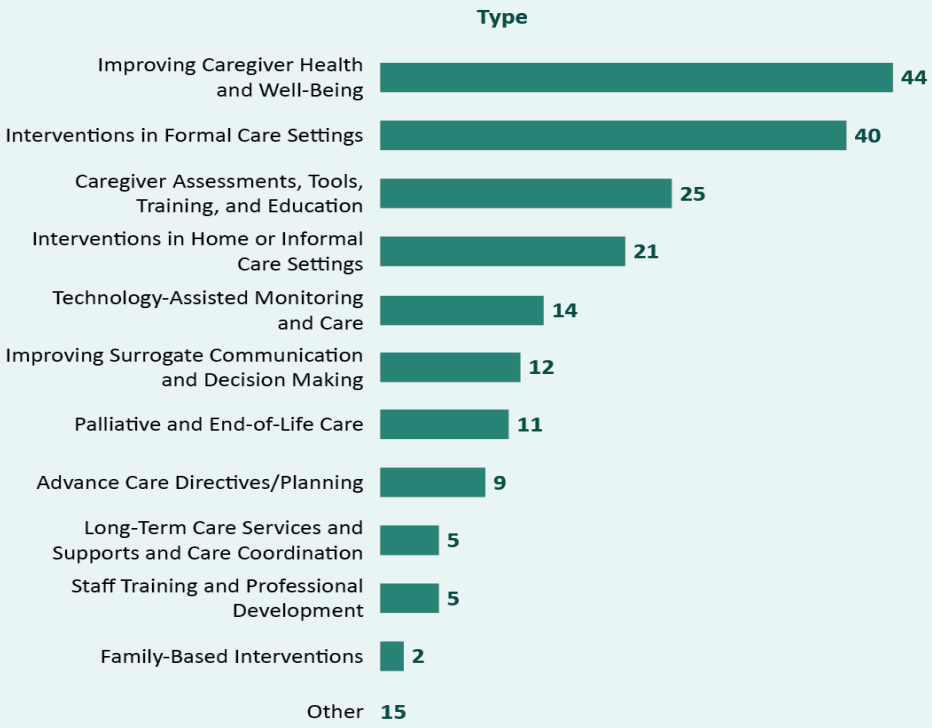
4 — POST-APPROVAL

Post-approval surveillance to evaluate long - term effects of treament

Active NIA AD/ADRD Clinical Trials

Dementia Care and Caregiving

203 TRIALS



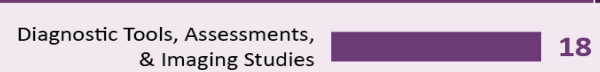
Clinical Trial Enrollment (Chapman), NW GWEC Spring 2026

Understanding Disease Processes

32 TRIALS

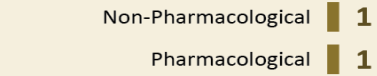
Diagnostic Tools, Assessments, & Imaging Studies

18 TRIALS



Treatments for Neuropsychiatric Symptoms

2 TRIALS



Total Number of Trials

466

For more information please visit
www.nia.nih.gov/research/ongoing-AD-trials

NIH National Institute on Aging

Data last updated: March 2025

Active NIA AD/ADRD Clinical Trials

Pharmacological — 63 TRIALS

50 trials

Phase I & Phase II

Targeted Disease Process

Amyloid	6	Synaptic Plasticity	4
Inflammation	5	Vasculature	4
Multi-Target	5	Oxidative Stress	3
Receptors	5	Tau	2
Circadian Rhythm	4	Proteostasis/ Proteinopathies	1
Growth Factors/Hormones	4		
Metabolism/Bioenergetics	4	Other	3

13 trials

Phase II/III, III, and IV

Targeted Disease Process

Amyloid	5	Vasculature	2
Inflammation	2	Metabolism/Bioenergetics	1
Tau	2	Multi-Target	1

Non-Pharmacological — 148 TRIALS

Modality

For more information please visit
www.nia.nih.gov/research/ongoing-AD-trials

NIH National Institute on Aging

Data last updated: March 2025


Targeted Pathophysiological Process
Amyloid
Tau
APOE, Lipids and Lipoprotein Receptors
Neurotransmitter Receptors
Neurogenesis
Inflammation
Oxidative Stress
Cell Death
Proteostasis/Proteinopathies
Metabolism and Bioenergetics
Vasculature
Growth Factors and Hormones
Synaptic Plasticity/Neuroprotection
Gut-Brain Axis
Circadian Rhythm
Epigenetic Regulators
Multi-Target
Undisclosed
Disease-Targeted Biologic
PHASE 1
AAV2-BDNF
ADEL-Y01
AK152
ALN-5288
AV-1959D
AV-1959R
AV-1980R
BCG vaccine
BIIB080
CM383
CpG1018
DUVAX
ION269
LX1001
LY3954068
LY4006895
Mivelsiran
NIO752
PMN310
Plasma exchange
Probiotics
Recombinant human serum albumin
RO7812653
THN391
PHASE 2
AADvac1 + AAmAb
AADvac1
ACI-24.060
AL101
Aldesleukin
ARO-MAPT
BIIB080
BMS-986446
Etalanetug + Lecanemab
Exercised plasma
Foralumab
JNJ-64042056
MK-2214
Posdinemab
Sabirnetug
Sargramostim
Semaglutide
Semaglutide + Candesartan + Vitamin D + Calcium
SHR-1707
Trontinemab
VHB937
VY7523
XPro1595
PHASE 3
Donanemab
Etalanetug + Lecanemab
Gantenerumab
Gonadorelin
Lecanemab
Remternetug
RG6289 + Donanemab
Semaglutide
Solanezumab
Tertomotide
Trontinemab
BnH-015B
Astragalus
Brivaracetam
Cannabidiol
CORT108297
DAOIB + AO
Emestedastat
IVL3003
KarXT + KarX-EC + Lecanemab
Mevidalen
MK-1167
NSC001 + Trospium
NSC001
ONO-2020
Polypill
Tadalafil
Tisolagiline
Trazodone
HHT201
NPT 2042
Caffeine
Donepezil
Guanfacine
Huperzine A
KarXT + KarX-EC
Latrepridine
Piromelatine
Rotigotine + Rivastigmine
Tricaprilin
ACP-204
Escitalopram
KarXT + KarX-EC
KarXT
Masupirdine
Nabilone
BMS-986368
Cannabidiol
Dexmedetomidine
IGC-AD1
ITI-1284
Methylphenidate + iTBS
ML-007C-MA
ONO-2020
Cannabidiol
LY03017
Psilocybin
AR1001
Buntanetap
Masitinib
Metformin
MLC901
Nilotinib
RG6289
T3D-959
Valiltramiprosate
Wujia Yizhi
Ozanimod
Parthenolide + Ipriflavone
Rifaximin
RO7269162
RQC
Senicapoc
Siponimod
Sirolimus
Sodium pentaborate pentahydrate
SPG302
Suvorexant
Zervimesine
AS-S603
2-HOBA
Aluminum hydroxide
Baricitinib
Benfotiamine
BEY2153
Brexanolone
Bumetanide
Ciprofloxacin + Celecoxib
Contraloid acetate
Daridorexant
Dasatinib + Quercetin
Dimethyl fumarate
Edaravone
Enrupatinib
EX039
Fasudil
Lemborexant
Lenalidomide
Leuprolide
Levetiracetam
LHP588
Losartan + Amlodipine
Memantine
MIB-626
Nicotinic Acid
NTRX-07
OLX-07010
Phenserine
REM0045392
Xenon
Centella asiatica
Choline
DDN-A-0101
Emtricitabine
Emtricitabine + Tenofovir alafenamide
J4
KS101
Leucettinib-21
MIB-626
Nicotinamide riboside
Cognition Enhancer
Neuropsychiatric Symptom Tx
Disease-Targeted Small Molecule
Trial Population
Healthy Volunteers
Prodromal
MCI (Prodromal) and MCI-Mild AD Dementia
Mild-Moderate AD Dementia
Severe AD Dementia

The Progress and Future of Dementia Trials

Past and future

The Evolution of Alzheimer's Diagnosis and Treatment

Diagnostic Progress

- Advances in brain imaging – CT and MRI, PET scans for amyloid and Tau tracers
- CSF biomarkers: amyloid-β, tau proteins
- Emerging plasma biomarkers (p-tau217)
- Genetic Insights: APOE-ε4 allele as a major risk factor, dominantly inherited genes: APP, PSEN1, PSEN2

Early Symptomatic Treatments

- Cholinesterase inhibitors: donepezil, rivastigmine, galantamine
- NMDA receptor antagonist: memantine

Shift Toward Disease-Modifying Therapies

- Immunotherapies targeting amyloid, recent approvals: lecanemab, donanemab

Successes & Promising Strategies

What is working — and what we can build on

Evidence-Based Enrollment Strategies

Build Trust

- Partner with community organizations, senior centers, faith groups
- Use trusted messengers (primary care, community leaders)
- Train clinicians to introduce trials as part of standard of care
- Maintain ongoing presence of support
- Be transparent about benefits and risks
- Engage study partners early in the process
- Regular updates and return of results

Evidence-Based Enrollment Strategies

Reduce Burden

- Simplify visit schedules and reduce frequency/duration
- Flexible scheduling
- Utilize home-based visits, hybrid models
- Leverage technology thoughtfully
- Provide transportation or reimburse travel costs
- Minimize invasive procedures when possible
- Include caregiver support

Evidence-Based Enrollment Strategies

Protocol Design

- Broaden inclusion criteria (allow comorbidities, polypharmacy)
- Plain-language, shorter consent forms, use of LAR
- Reconsent periodically as cognition changes
- Incorporate visual aids, teach-back methods
- Cultural and linguistic adaptation of materials
- Trained staff on trial team

Summary of Visit Activities

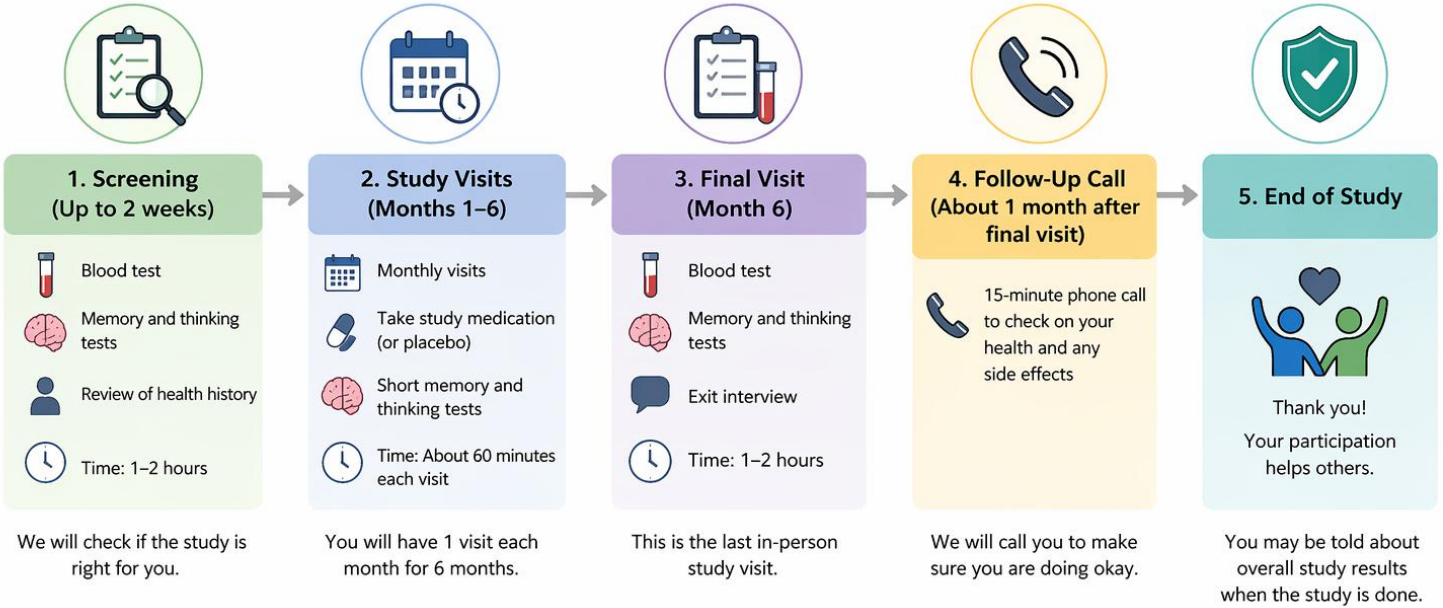
The following chart summarizes the activities that will occur during the study. Study staff will work with you to schedule your visits. Visit activities can be scheduled across multiple days.

Visit Number	6	8	10	12	18	24	30	36	42	48	54	57	60	63	66	69	72	75	78	81	84		85
Week Elapsed Since 1st Dose	0	4	8	12	24	36	48	60	72	84	96	108	120	132	144	156	168	180	192	204	216	ET	228
Study drug infusion	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		
Medication History	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Adverse events collection	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Vital signs	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Physical and neurological exam	X			X	X	X	X		X		X		X		X		X		X		X	X	X
ECG	X			X	X	X	X		X		X		X		X		X		X		X	X	X
Assessment of Well Being	X			X	X	X	X	X		X	X	X		X	X	X	X	X	X	X	X	X	
Memory & Thinking Skills Tests	X			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Answer Questionnaires				X			X				X			X			X				X	X	
MRI			X	X	X	X	X		X		X		X		X		X		X		X	X	
Amyloid PET Scan											X										X	X	
Tau PET Scan											X										X	X	
LP* (if participating in the CSF sub-study)											X										X	X	
Urine pregnancy test (for females of childbearing potential)	X				X		X		X		X		X		X		X		X		X	X	
Blood and urine collected	X	X		X	X	X	X	X	X	X	X		X		X		X		X		X	X	X
Blood Volume Approx. Totals (mLs)	60	50		50	50	25	50	25	25	25	80 *		40		30		40		30		70*	30	30

*Fasted, when possible; ET = early termination visit

What will happen if I take part in this study?

The study lasts about 6 months. Here is what you can expect:



Time Commitment
About 6 study visits over 6 months.

Travel Support
We will reimburse your travel or provide rides if needed.

Your Choice
Taking part is your choice. You may stop at any time for any reason.

Caregiver Involvement
A family member or friend can join you for visits and calls, if you wish.

Please ask questions. We want to make sure you understand everything.

Regulatory & Policy Progress

- FDA Guidance on Geriatric Studies (updated 2019): mandates age reporting in drug applications
- NIH Policy on Inclusion Across the Lifespan (2017): requires plans to include older adults or justify exclusion
- FDA's Project Equity: initiative to increase diversity and older adult inclusion in clinical trials
- NIA's Recruitment Innovation Center (RIC): provides trial sites with outreach and retention tools
- Acceptance of LAR and revisions to the Common Rule

What You Can Do

Tools, organizations, and next steps

Supporting Enrollment

- Routinely screen for cognitive impairment
- Refer to specialty medicine when appropriate
- Maintain awareness of local and national resources
- Start conversations early — before significant decline — about research values and preferences
- Understand the LAR role, appointed DPOA, involve caregivers
- Advance directives can include preferences about research participation
- Normalize clinical trials as a standard care option
- Proactively refer patients; most never self-identify as trial candidates

National Resources for Trial Participation

ClinicalTrials.gov

National database of all U.S. clinical trials. Search by condition, location, age.

NIA Alzheimer's Trial Resources

NIA resources & trial matching for older adults. **www.alzheimers.gov/clinical-trials/find-clinical-trials**

Alzheimer's Association

TrialMatch® — free service matching individuals with cognitive changes to trials. **www.alz/org**

Brain Health Registry

UCSF registry connecting adults 18+ with cognitive change research. **www.brainhealthregistry.org**

Alzheimer's Disease Research Centers (ADRCs)

NIH-funded centers at major universities/hospitals

https://depts.washington.edu/mbwc/adrc

Alzheimer's Clinical Trials Consortium (ACTC)

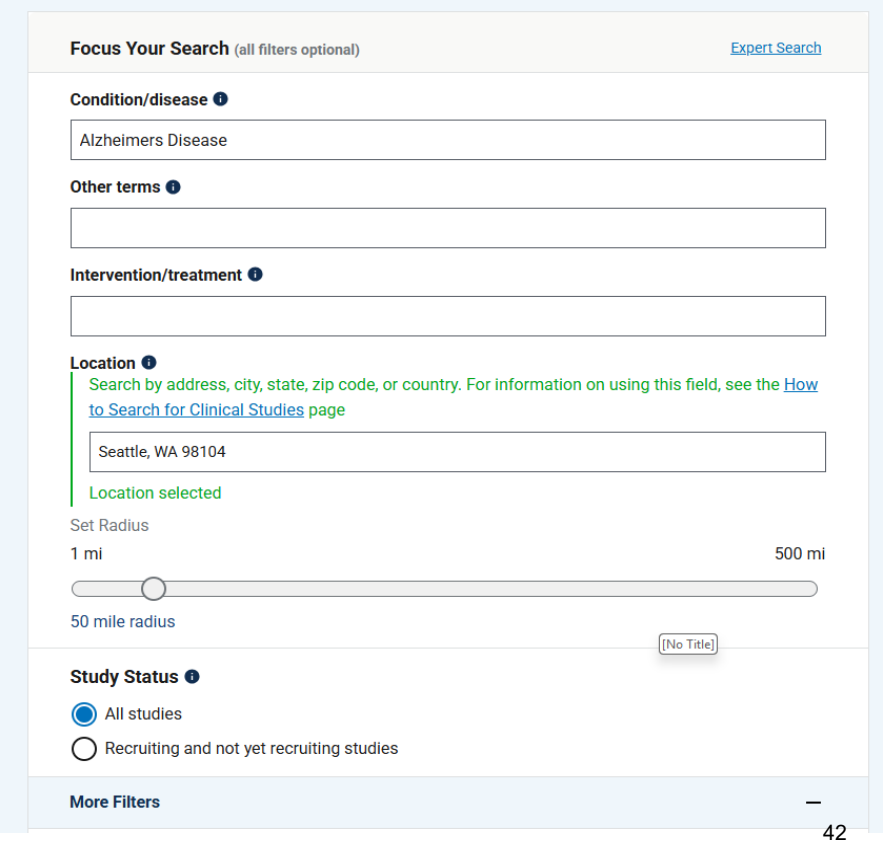
A coordinated national trial network.

https://www.actcinfo.org

Navigating ClinicalTrials.gov

- Go to: ClinicalTrials.gov and click 'Find a Study'
- Search and filter tips for older adults:
  - Enter condition (e.g., 'Alzheimer's disease', 'mild cognitive impairment')
  - Filter by 'Age Group': Older Adult (65+)
  - Enter your ZIP code and select distance radius (50–100 miles)
- Look for studies labeled 'Observational' if concerned about intervention risks
- Check 'Eligibility' section carefully — call the study coordinator with questions

- https://clinicaltrials.gov/



A Study of the Safety and Efficacy of Memantine in Moderate to Severe Alzheimer's Disease

ClinicalTrials.gov ID NCT00322153

Sponsor Forest Laboratories

Information provided by Forest Laboratories

Last Update Posted 2010-09-16

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Study Details | Researcher View | Results Posted | Record History

On this page

- Study Overview
- Contacts and Locations
- Participation Criteria
- Study Plan
- Collaborators and Investigators
- Publications
- Study Record Dates
- More Information

Study Overview

Brief Summary

The objective of this study is to evaluate the safety, tolerability, and efficacy of memantine compared to placebo in outpatients diagnosed with moderate-to-severe dementia of the Alzheimer's type on a concurrent acetylcholinesterase inhibitor (AChEI).

Detailed Description

Memantine is a therapeutic agent that represents a unique class of Alzheimer's disease (AD) treatment options. A once daily (QD) dosing regimen in an AD population would simplify administration for the caregiver. The purpose of this study is to evaluate the safety and efficacy of modified release memantine taken once daily in outpatients with moderate-to-severe AD on a concurrent AChEI.

Official Title

A Randomized, Double-Blind, Placebo-Controlled Evaluation of the Safety and Efficacy of Memantine in Patients With Moderate-to-Severe **Dementia of the Alzheimer's Type**

Conditions

Dementia of the Alzheimer's Type

Study Start
2005-06

Primary Completion (Actual)
2007-10

Study Completion (Actual)
2008-01

Enrollment (Actual)
677

Study Type
Interventional

Phase
Phase 3

Navigating TrialMatch (Alzheimer's Association)

trialmatch®
ALZHEIMER'S ASSOCIATION®
on Carebox Connect

The Alzheimer's Association has partnered with Carebox to provide access to TrialMatch®, a free, easy-to-use research studies matching service that connects individuals living with cognitive impairment, Alzheimer's disease or another dementia, caregivers and healthy participants with current research studies. Advancing Alzheimer's and dementia research starts with you. Help shape the next breakthrough with TrialMatch.

Start Here

[No Title]

If you have a specific trial or therapy in mind, you can browse and filter all trials directly.

Condition or trial ID
Alzheimer's Disease

Location
Seattle, WA 98104, USA

Browse Trials

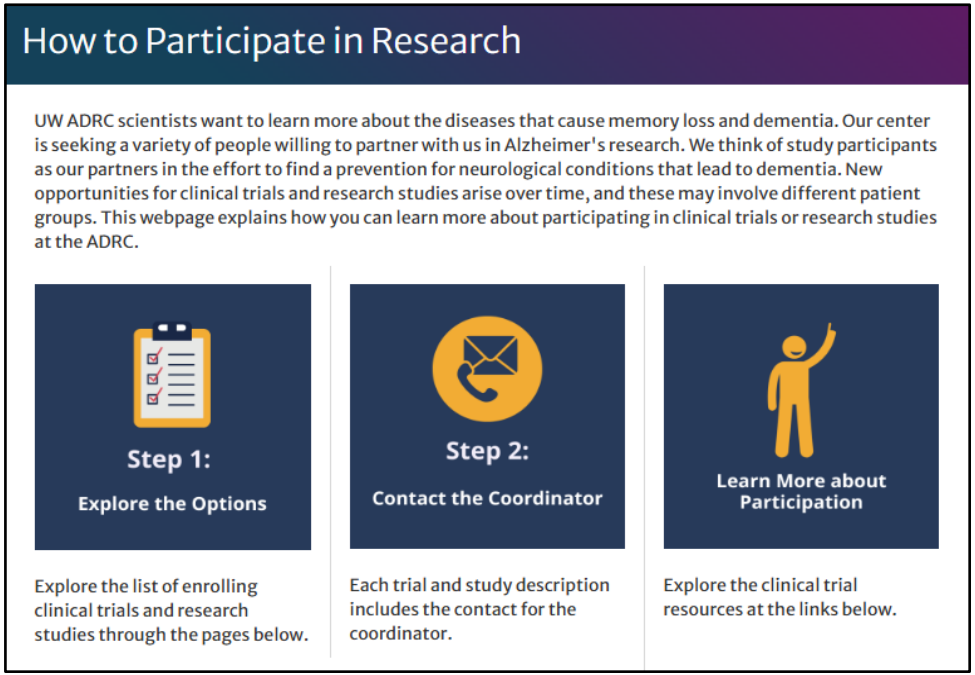
[TrialMatch: Participate in Clinical Research for Alzheimer's and Other Dementia]

Local Resources for Trial Participation

ADRC
Alzheimer's Disease Research Center

Contact: uwadrc@uw.edu
Phone: 206-616-3973

UNIVERSITY of WASHINGTON



Alzheimer's Disease Research Center

Key Takeaways

- Dementia impact
- Clinical trials are the foundation of evidence-based medicine
- Time delays and the representation gap in research
- Challenges to enrollment in trials
- Benefits of trial participation
- Success and promising strategies for inclusion of older adults into trials
- Resources and support for helping older adults and individuals with dementia to get involved

Health care providers are the single most influential referral source — your recommendation matters!!

Every Participant Counts
Thank You

Questions & Comments