Cochrane Systematic Review (16 April 2026)

Amyloid-beta-targeting monoclonal antibodies for people with mild cognitive impairment or mild dementia due to Alzheimer's disease

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Key Messages

In people with mild memory and thinking problems (mild cognitive impairment, MCI) or mild dementia due to Alzheimer's disease, laboratory-produced medicines (anti-amyloid monoclonal antibodies) that target and remove potentially damaging build-ups of amyloid proteins in the brain, **probably result in little to no difference** in the decline in memory functioning and thinking ability, or in how severe dementia symptoms are, compared with placebo (sham treatment) 18 months after the start of treatment.

Anti-amyloid monoclonal antibodies **probably cause more brain swelling and tiny (micro) bleeds** than placebo. They do not increase other serious unwanted effects or deaths compared with placebo.

Successful removal of amyloid proteins from the brain does not seem to be associated with clinically meaningful improvements in people with MCI or mild dementia due to Alzheimer's disease. Future research on disease-modifying treatments for Alzheimer's disease should focus on other treatments.

Background: What is Alzheimer's disease?

In Alzheimer's disease, brain cells die following the build-up of proteins (called amyloid plaques). Alzheimer's disease affects people's memory and thinking abilities. Symptoms are usually mild to begin with and do not interfere with everyday life. This is called "mild cognitive impairment" (MCI). Over time, it can progress to mild dementia, where memory and thinking difficulties are serious enough to interfere with everyday activities. About 15% of people with MCI will develop dementia due to Alzheimer's disease within two years. It is the most common form of dementia among older people.

What are anti-amyloid monoclonal antibodies?

Antibodies are made by the body as a defence against disease. They can also be produced in a laboratory for use as a medical treatment. Anti-amyloid antibodies are designed to target the amyloid proteins that cause plaques due to Alzheimer's disease, and remove them from the brain. They are "monoclonal" because they only target amyloid proteins. Removing amyloid proteins from the brain may slow the progression of Alzheimer's disease.

What did the authors want to find out?

The authors wanted to know if anti-amyloid monoclonal antibodies are an effective medicine for people with MCI or mild dementia due to Alzheimer's disease. They evaluated whether they slowed down:

- the decline in memory and thinking;
- the decline in ability to manage everyday activities; and
- the worsening of dementia symptoms.

They also wanted to know if they caused any unwanted effects.

Methodology

The authors searched for studies that investigated one or more anti-amyloid monoclonal antibodies to treat people with MCI or mild dementia due to Alzheimer's disease, compared with placebo (sham treatment that does not contain any medicine but looks identical to the medicine being tested and is delivered in the same way). They summarised the results of the studies, and rated their confidence in the evidence, considering aspects such as study sizes and methods.

Search strategy: CENTRAL, MEDLINE (PubMed), Embase, and two clinical trials registries (Clinicaltrials.gov and WHO International Clinical Trials Registry Platform), plus reference checking and citation research. Most recent search date: 7 August 2025.

Drugs assessed: Aducanumab, bapineuzumab, crenezumab, donanemab, gantenerumab, lecanemab, ponezumab, remternetug, and solanezumab.

What did they find?

They found **17 studies** that were carried out in different countries and involved **20,342 people**. The average age across studies was from 70 to 74 years. **All studies were funded by companies that produced the anti-amyloid monoclonal antibodies.**

Main Results

After 18 months of treatment, anti-amyloid monoclonal antibodies:

1. **May make little to no difference** to how bad people's dementia symptoms are (9 studies, 8,053 people);
2. **Probably make little to no difference** in the decline in memory and thinking ability (13 studies, 9,895 people) or the ability to manage everyday activities (3 studies, 3,478 people);

3. May result in a small improvement in more complex everyday tasks, such as shopping, managing finances, taking medication, and using transportation (1 study, 1,252 people);

4. **Probably result in a small increase in the occurrence of brain swelling.** For every 1,000 people using monoclonal antibodies, **119 developed brain swelling** compared with only **12 of 1,000 people using placebo** (11 studies, 13,595 people);

5. May result in a small increase in **microbleeds in the brain** (3 studies, 4,308 people);

6. Do not increase other serious unwanted effects as defined by the study authors (9 studies, 11,904 people); and

7. Do not increase deaths from any cause (7 studies, 9,733 people).

Authors' Conclusions

> *"The effect of amyloid-beta-targeting monoclonal antibodies on cognitive function and dementia severity at 18 months in people with mild cognitive impairment or mild dementia due to Alzheimer's disease is **trivial**, while on functional ability, it is **small at best**. Amyloid-beta-targeting monoclonal antibodies increase the risk of amyloid-related imaging abnormalities (ARIA). Both desirable outcomes and adverse events were inconsistently reported in the studies included in the review."*
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> *"Successful removal of amyloid from the brain does not seem to be associated with clinically meaningful effects in people with mild cognitive impairment or mild dementia due to Alzheimer's disease. **Future research on disease-modifying treatments for Alzheimer's disease should focus on other mechanisms of action.**"*

Expert Quotes

Lead author Francesco Nonino, neurologist and epidemiologist at the IRCCS Institute of Neurological Sciences of Bologna, Italy:

> *"Unfortunately, the evidence suggests that these drugs make no meaningful difference to patients. There is now a convincing body of evidence converging on the conclusion that there is no clinically meaningful effect. While early trials showed results that were statistically significant, it is important to distinguish between this and clinical relevance. It is common for trials to find statistically significant results that do not translate into a meaningful clinical difference for patients."*

Senior author Edo Richard, Professor of Neurology at Radboud University Medical Centre:

> *"I see Alzheimer's patients in my clinic every week and I wish I had an effective treatment to offer them. Existing approved drugs offer some benefit for some patients, but there remains a high unmet need for more effective treatments. Sadly, anti-amyloid drugs do not offer this and bring additional risks. Given the absence of correlation between amyloid removal and clinical benefit, we need to explore other pathways to help address this devastating disease."*

Limitations of the Evidence

The confidence in the evidence is limited for two reasons. Firstly, people who received monoclonal antibodies had more brain swelling and microbleeds than people receiving placebo. However, most studies did not separate people with symptoms of brain swelling and microbleeds from those in whom these effects were only visible with a scan. This reporting gap leaves patients without the information they need to understand the seriousness of potential unwanted effects. Secondly, the results came from studies that did not last very long. These are important limitations in the evidence for people with Alzheimer's disease, who need to know the longer-term benefits and unwanted effects of medicines.

Six ongoing studies were found. The review's conclusions may change as new results become available.

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Registration

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This document compiles the publicly available plain language summary, abstract, authors’ conclusions, and press release materials from the Cochrane Collaboration. The full review with complete data tables, forest plots, and risk of bias assessments is available at: https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD016297