

No new drugs for Alzheimer's disease in 15 years

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Credit: AI-generated image ([disclaimer](#))

How often to you read headlines proclaiming the arrival of a new, ground-breaking treatment for Alzheimer's?

The answer is probably, quite often. However, the harsh reality for patients today who are suffering from the [disease](#), and their families, is

that no new medications have been approved by the European Medicines Agency, or have entered the global market since 2003.

However, there is also some good news to share.

There are currently more than 400 [clinical trials](#) taking place around the world and the likelihood that new medications will soon reach patients in the near future, is high.

Here is a summary of the types of clinical [trials](#) that are under way and when we might expect to see new treatments for this debilitating condition.

Clinical trials testing pharmaceuticals for Alzheimer's patients

Over the years, more than 190 compounds have been tested for Alzheimer's disease. Out of these, just five have been approved and marketed globally (donepezil, galantamine, memantine, rivastigmine and a combination of memantine and donepezil).

However, none of these compounds are able to stop the progression of the disease, they can only counter the rate of disease progression for a limited period.

For that reason, numerous drugs are currently being tested to find new ways to treat the disease.

Active trials around the world

We do this by clinical trials, which are controlled studies performed on human participants to test new treatments. Of the 400 trials that I

mentioned earlier, many of them are currently testing new pharmaceuticals (medicinal drugs) and the rest are testing non-pharmaceutical treatments, which do not involve medicinal drugs, such as physical exercise and acupuncture.

Clinical trials are arranged in three phases (1, 2, and 3. See the Fact Box below for more details), which test for both the safety of the [drug](#) and its effectiveness.

There is also an earlier phase, phase 0, which is performed on animals only and a later phase, phase 4, to study sales and assess the patients' risks and benefits.

At the time of writing, there are currently 105 compounds being tested in clinical trials around the world, all of which are at various stages of development. Nine trials are registered in Europe, and four are taking place in Denmark. (See Fact Box).

Let's review some of these exciting new developments in turn.

Treatment 1: Targeting the protein, amyloid-beta

Numerous companies are producing potential treatments that target different aspects of the disease.

Many are developing drugs that target the reduction of a toxic substance, called amyloid-beta. This is a protein that is produced naturally by cells and is found in the brain. However, if amyloid-beta reaches very high levels it becomes toxic, causing cells to die. This is what happens in Alzheimer's.

Two drugs (sargramostim and AZD3293) are currently on trial to reduce the build-up of toxic levels of amyloid-beta. Sargramostim also has an

added benefit in helping to stimulate the immune system. AZD3293 is currently one of the drugs being trialled by Eli Lilly, here in Denmark.

Targeting this protein makes good sense in combating the disease since it is a key pathology of the disease. But so far, no drugs have been able to successfully counteract cognitive decline in the patients or prevent their death. We will have to wait and see whether these drugs fair any better.

Treatment 2: Targeting the immune system

Other companies are trialling pharmaceuticals (aducanumab, crenezumab, and gantenerumab) that target the immune system. They are referred to as passive immunity drugs and target amyloid-beta, either in the brain or in the blood, which provides short-term immunity from a few weeks to a few months.

One of these drugs, crenezumab is designed to only work on the cells in the brain that are affected by the disease, and not on other cell types, such as cells important for the immune system and for maintaining the blood-brain barrier. This drug is currently being tested in Phase 3 trials in several European countries and there are plans to initiate testing in Denmark. The trial expects to end in 2022 and the outcomes of it are still unknown.

Unfortunately, one such passive immunity drug, solanezumab from the pharmaceutical company, Eli Lilly, failed to deliver promising results in late phase clinical trials. The good news though, is that there are eight more drugs currently being tested in Eli Lilly's Clinical Trials pipeline, which may yet yield better results.

Treatment 3: Vaccines targeting amyloid-beta

A number of experimental vaccines are also being tested in order to train the body to fight against amyloid-beta in the brain.

These include CAD106, which provides immunity against amyloid-beta, and AADvac1, which is currently being developed to target tau—another substance that accumulates in the brain of patients.

CAD106 is currently in Phase 2 trials, but preliminary outcomes from one completed Phase 2 trial suggested that quite a few patients (25 per cent) suffered severe adverse affects.

In contrast, the AADvac1 has had relatively promising results following completion of a Phase 1 trial with a high efficiency in stimulating an immune response in patients and relatively good outcome for patient safety.

Treatments closest to approval stage are not "new"

Interestingly, of the seven pharmaceuticals that have entered Phase 4 trials (marketing and sales testing), none of them target Amyloid-beta. They consist of either natural compounds or drugs that are already approved and used to treat other diseases. Phase 4 trials run for at least two years so these could enter the market in the not too distant future.

These include:

- AVP-923: Consists of two drugs. It is an ingredient in cough syrup and used in combination with a drug currently used to treat irregular heartbeats.
- Carvedilol: Currently used to treat high blood pressure, but it has been shown to slow cognitive decline through its antihypertension effects.
- Prazosin: Has been shown to aid Alzheimer's disease by its

hypertension effects.

- Simvastatin: Currently used for [treatment](#) of hypercholesterol and cardiomyopathy. It demonstrates that drugs developed to treat cardiovascular disease and [high blood pressure](#) may have a beneficial effect in treating Alzheimer's.
- DHA: These are polyunsaturated fatty acids, naturally found in the brain. One study has shown that high ingestion of foods rich in DHA (fatty fish, walnuts, flax seeds) is correlated with a low incidence of Alzheimer's disease.
- Ketasyn: A nutritional drink derived from processed coconut or oils. It is suggested to provide an alternative glucose to the brain.
- Resveratrol: A natural bioactive polyphenol found in foods such as chocolate and red grapes, which has antioxidant properties and is also close to entering the market.

Alternative treatments and trials in development

There are also a number of other ongoing trials that do not involve drugs at all.

They instead target behaviour or focus on physical activities, such as yoga. Special programs such as, Describe, Investigate, Evaluate and Create (DICE) have been developed for caregivers to help cope and manage with their patient's changing behaviour. While alternative treatments such as acupuncture, electromagnetic treatment, and deep brain stimulation aim to stimulate the patient's brain or body activity and activate the cells that remain in the brain.

Some clinical trials even combine non-drug approaches with already approved pharmaceuticals such as the combination of electroacupuncture with donepezil. It is anticipated that this combination treatment may be more effective than just treatment with donepezil. The trial is ongoing and we still await the outcome.

New treatments are on the horizon

In summary, there are currently hundreds of trials ongoing around the world as part of a maximal effort to find new medications and treatments for Alzheimer's disease.

Despite the fact that no drugs have entered the market in the last 15 years, there is hope on the horizon that new drugs will emerge soon.

These new treatments will target the underlying pathology of the disease, and hopefully stop or limit its progression. However, at this stage, it is too soon to say whether any of these new and upcoming pharmaceuticals can reverse the effects of the disease.

Only long-term studies will reveal if any of these drugs can in fact completely halt the progression of Alzheimer's disease.

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