

Alzheimer's disease: Viagra is seen as a potential treatment, but the research shows contradictory findings

February 21 2024, by Ian Maidment and Hayley Gorton



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A [recent study reported](#) that sildenafil, sold under the brand name Viagra, and other medicines from the same group called

[phosphodiesterase type-5 inhibitors](#) may reduce the risk of Alzheimer's disease. But [other research](#) has found no effect.

Why isn't the picture clear? And what can be concluded about whether drugs such as sildenafil reduce the risk of Alzheimer's if the available research has contradictory findings?

Dementia has been [described as a global pandemic](#). In 2022, it was the [biggest cause of death](#) in England and Wales.

Alzheimer's disease is the most common form of dementia, and current treatment is with [Acetylcholinesterase inhibitors](#) such as donepezil (sold as aricept) and memantine. These medications may relieve symptoms of Alzheimer's but [have no effect](#) on the underlying disease process.

Twenty-eight potentially disease-modifying treatments are currently being developed and one, lecanemab, has [recently been licensed in the US](#), China and Japan. However, lecanemab—and the related medication [donanemab](#), which is [likely to be available soon](#)—have a limited effect and simply slow any decline in symptoms.

There are also [key safety concerns](#) about these medications relating to brain bleeds and swelling. There is thus an urgent need for new treatments that are both effective and safe.

Drug repurposing: cheaper and quicker?

An alternative to the long and expensive process of discovering new medicines is [drug repurposing](#). This is when existing drugs or medications are used for alternative medical conditions.

[The most recent UK study](#) on the link between phosphodiesterase type-5 inhibitors (avanafil, sildenafil, tadalafil and vardenafil) and Alzheimer's

found they are associated with an 18% reduction in the risk of being diagnosed with Alzheimer's. But two earlier observational US studies found different results.

[One of these studies](#) found no link between the use of phosphodiesterase type-5 inhibitors and developing Alzheimer's. [The other](#) found sildenafil use was linked with a 69% reduced risk of the disease, significantly higher than the latest 18% finding.

So why the variability in results? The answer could be in the way the different studies were designed.

They were all [observational studies](#) that involved tracking large numbers of patients over time to see if they developed Alzheimer's disease and whether they were taking the medication. However, the three studies used different databases: U.S. insurance, U.S. Medicare Fee-For-Service claims, and UK primary care records.

Confounding variables

[Observational studies](#) are usually designed to account for other factors that might influence the results. For example, the reason someone was prescribed a medication might influence the likelihood of the event you are monitoring actually happening.

Therefore, studies need to [control for biases](#) and [confounding variables](#). These are factors that are separately related to both the medication and the outcome. They might explain why there appears to be an association between the medication and the outcome when there is, in fact, no link.

For example, children's IQ is associated with height. But the confounding variable is age: as children grow up, they become both taller and brighter.

All the studies exploring the link between phosphodiesterase type-5 inhibitors and Alzheimer's used advanced techniques to try to control for the potential impact of confounding variables. But they could only use what was recorded in the dataset.

For example, with the Medicare study, it was possible to control for potential signs of frailty and behavioural symptoms, whereas with the UK study, [socioeconomic status](#), alcohol use, blood pressure and body mass index could all be controlled for.

A problem with [observational studies](#) is they assume that participants took the medication as prescribed, which may not be correct. The US studies could at least confirm the medication was collected from the pharmacy, whereas this step was not known in the UK study.

Another issue is that medication may not always be recorded on these databases; for example, private prescriptions for sildenafil in the UK may not have been included in the data. Also, the [diagnosis of dementia may not be accurately recorded](#) on the electronic databases.

Multiple reasons for differing results

There are other reasons for the different results of the studies. Researchers selected certain populations and comparison medications to help them understand if any effect on Alzheimer's disease risk was related to the medicine, or a confounding variable.

The dose of phosphodiesterase type-5 inhibitors varies depending upon what is being treated. The 2022 US study included men and women with pulmonary hypertension only. The UK study only had men with [erectile dysfunction](#), whereas the 2021 US included both genders and both conditions. Because the dose is different for the different conditions, we cannot compare dose across the studies.

There are further factors that could also help explain the difference in findings between the studies.

First, the medication investigated wasn't the same in all three. In the 2021 US study, all participants received sildenafil, whereas in the UK study and 2022 US study, about 25% received other phosphodiesterase type-5 inhibitors.

Second, the duration of the study follow-up varied. This is an important factor to consider because Alzheimer's may take time to develop. For example, the disease is predominantly diagnosed in over-65s, so if a participant was only aged 40 on entry to the study, they are very unlikely to have a diagnosis during its time period, even when following people up for a long time.

We need new treatment for Alzheimer's disease. Observational studies can identify possible links between drugs and outcomes, and the latest study adds to the evidence that drugs such as sildenafil might protect against Alzheimer's disease. But for clear evidence that sildenafil and related drugs are effective at reducing the risk of dementia, clinical trials are needed.

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