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Shingles vaccine may slow progression of dementia, new study suggests

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By Jacqueline Howard



A pharmacist displays doses of a vaccine that protects against shingles, at a CVS Pharmacy in ...









The **shingles vaccine** not only offers protection against the painful viral infection, a new study suggests that the two-dose shot also may slow the progression of dementia.

Shingles, caused by the varicella-zoster virus, presents as a painful rash and it's estimated that about 1 in every 3 people in the United States will develop the illness in their lifetime. But the risk of shingles and serious complications increases with age, which is why in the United States, two doses of the shingles vaccine is recommended for adults 50 and older.

Vaccination is estimated to be more than 90% effective at preventing shingles in older adults, but recent research has shed light on some other potential benefits, too.

Emerging research suggests that getting the vaccine to protect against shingles may **reduce the risk of developing dementia**. A follow-up study, published Tuesday in **the journal Cell**, adds to that research by suggesting that the vaccine could also have therapeutic properties against dementia, by slowing the progression of the disease, leading to a reduced risk of dying from the disease.

"We see an effect on your probability of dying from dementia among those who already have dementia," Dr. Pascal Geldsetzer, assistant professor of medicine at **Stanford University** and senior author of the new study, said of the potential effects of the shingles vaccine.

"That means that the vaccine doesn't just have a preventive potential, but actually a therapeutic potential as a treatment, because we see some benefits already among those who have dementia," he said. "To me, this was really exciting to see and unexpected."

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The new study comes just months after Geldsetzer and his colleagues found evidence that shingles vaccination may offer a "dementia-preventing" or "dementia-delaying" effect.

In that study, the researchers analyzed the health records of older adults in Wales, where a **shingles vaccination program** for adults in their 70s was introduced September 1, 2013. The program indicated that anyone who was 79 on that date was eligible for the vaccine for one year, but those who were 80 or older were not eligible for the vaccine.

Those eligibility requirements allowed the researchers to examine data on the adults who were 79 and got vaccinated and then compare that data with the adults who were 80 and not eligible for vaccination but may have gotten the vaccine if they could.

"We are comparing groups of patients whose only difference is a tiny difference in age, just like a week or so, and they have this massive difference in the probability of ever getting vaccinated because of these unique eligibility rules," Geldsetzer said.

Among those adults in Wales, the researchers found that receiving the shingles vaccine reduced the probability of being newly diagnosed with dementia by 3.5 percentage points over a seven-year period, compared with not receiving the vaccine.

"We know they should have similar physical activity level, diets, et cetera," Geldsetzer said. "So, we're much more confident that what we're actually looking at here is cause and effect, rather than just correlation."

In the new follow-up study, the researchers analyzed the same data set of the adults in Wales, which included more than 282,500 adults. But this time, the researchers examined differences in the occurrence of mild cognitive impairment diagnoses and, among people living with dementia, differences in the incidence of deaths due to dementia, while comparing vaccinated versus unvaccinated groups.

"The key strength of our natural experiments is that these comparison groups should be similar in all characteristics except for a minute difference in age," the researchers wrote.

To strengthen their findings, the researchers also analyzed similar health records in Australia, which has a similar shingles vaccination program as Wales.

The researchers found that among older adults without any record of cognitive impairment prior to getting vaccinated, among those who received the shingles vaccine saw a reduction of 3.1 percentage points in their risk of being newly diagnosed with mild cognitive impairment over a nine-year period compared with those who did not receive the vaccine. And the protective effects appeared to be stronger among women than men, which was also found in the previous study.

Additionally, among older adults living with dementia, the researchers found that those who received the shingles vaccine had a drop of 29.5 percentage points in their risk of dying due to the disease over a nine-year period compared with those who did not get vaccinated – suggesting that the vaccine may play a role in slowing the progression of dementia.

"It seems to have these strong benefits across the entire disease course," Geldsetzer said of the shingles vaccine.

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While the new study turned a spotlight on the possible relationship between shingles vaccination and dementia outcomes, it did not specifically uncover why the vaccine may have these potential effects. But Geldsetzer had some theories.

"Broadly speaking, you can think about two mechanisms," Geldsetzer said.

For one, the <u>virus that causes shingles</u> also causes chickenpox. After someone has chickenpox in childhood, the virus remains dormant in the nervous system, and people get shingles when the virus reactivates.

But even while the virus is hibernating in the nervous system, "this causes a constant interplay with the immune system," Geldsetzer said. "We know this causes inflammation in the nervous system, and we know inflammation is a key process in so many chronic diseases, including dementia. So it makes sense that reducing these reactivations through shingles vaccination may have benefits for the dementia disease process."

The second possible mechanism, Geldsetzer said, is that the vaccine can provide a big boost to the immune system overall, strengthening it as a whole to fight off infections. And there is a growing body of research linking various **infections to increased dementia risk**, so being better fit to fight off any infection could help with lowering dementia risk.

"There's increasing evidence that vaccines have broader effects on the immune system, beyond just the specific antibody response that it has been designed to elicit," Geldsetzer said. "These kinds of broader immune system activations may well have benefits for dementia disease development as well, and we know the immune system plays a key role in dementia. So that's the other mechanism."

As a next step, he and his colleagues plan to raise funding to "conclusively test" this link between shingles vaccination and reduced dementia risks in a randomized clinical trial.

Overall, the new study shows that the shingles vaccine protects cognition from early to late stages of dementia, said Dr. Angelina Sutin, professor of behavioral sciences and social medicine at Florida State University College of Medicine, who was not involved in the research.

"When people find out that I study dementia, they often ask what I recommend to keep the brain healthy with age. I always respond with three things: exercise, be social, and do things you enjoy that make you feel purposeful. Now, I will add talk to your doctor about getting the shingles vaccine. There is no guarantee that doing these things means you will not get dementia, but all are relatively easy and accessible and help maintain healthy cognition for longer," Sutin wrote in an email.

But she added that what exactly may be driving this relationship between the shingles vaccine and reduced dementia risks remains a mystery.

"It is still unknown. This study is a very important advance in understanding because it provides the closest to causal evidence for the shingles vaccine that is possible. Unfortunately, it does not directly answer the why," she said. "This research sets a strong foundation for future research to find out why it is so protective."

Dr. Joel Salinas, a neurologist at NYU Langone, notes an important caveat about the study: The findings may not generalize to a newer vaccine that is now widely used.

"I would view these results as promising, providing unique evidence that shingles vaccination may have meaningful cognitive benefits, but not yet as definitive proof that we should vaccinate solely for dementia risk reduction," Salinas said. "It's reasonable to frame the connection as biologically plausible and increasingly well-supported by high-quality epidemiologic data, but still in need of mechanistic studies and replication before we can say definitively why shingles vaccination appears to be associated with lower dementia risk."





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