

# Could HIV drugs help prevent Alzheimer's disease?

New research suggests that HIV drugs may have a protective effect against Alzheimer's. Willie B.

- Researchers at UVA Health have found that a class of HIV drugs called nucleotide reverse transcriptase inhibitors (NRTIs) may significantly reduce the risk of developing Alzheimer's disease.
- Their large-scale analysis of United States health insurance data revealed that patients taking these medications had up to a 13% lower risk of Alzheimer's disease each year.
- Based on these findings, the team is calling for clinical trials to test whether these drugs could be used to help prevent Alzheimer's.

Scientists are calling for clinical trials to investigate whether a class of HIV drugs known as nucleotide reverse transcriptase inhibitors (NRTIs) could help prevent Alzheimer's disease.

In their new research, they found that people taking these medications are significantly less likely to develop the condition.

The team had earlier discovered a possible biological mechanism explaining how the drugs might offer protection against Alzheimer's.

The findings were published in *Alzheimer's and Dementia: The Journal of the Alzheimer's Association* Trusted Source.

## Reduced risk by 6-13%

Alzheimer's disease is the leading cause of dementia, responsible for approximately 60% to 80% of all cases Trusted Source in the United States. It most commonly begins in individuals ages 65 and older.

Motivated by this, the researchers examined two major U.S. health insurance databases and found that the risk of developing Alzheimer's dropped by 6% per year in one dataset and by 13% per year in the other among patients on NRTIs.

Jayakrishna Ambati, MD, founding director of UVA's Centre for Advanced Vision Science and a professor in the Department of Ophthalmology at the University of Virginia School of Medicine, and senior of the study, explained the key findings to Medical News Today:

"We analysed health insurance databases of tens of millions of people and made the surprising discovery that people taking a group of anti-HIV drugs called NRTIs had a ~10% reduction in the risk of developing Alzheimer's disease for every year that they took these drugs."

— Jayakrishna Ambati, MD

## Investigating the link between NRTIs and Alzheimer's risk

NRTIs are commonly used to stop HIV from replicating in the body.

However, Jayakrishna Ambati and his research team had previously found that these drugs also block the activation of inflammasomes, key immune system components that have been linked to the development of Alzheimer's disease.

This discovery led them to investigate whether patients taking NRTIs, which also treat hepatitis B, might have a lower risk of developing Alzheimer's.

To explore this, the team analysed long-term health data from two major U.S. sources: 24 years of records from the Veterans Health Administration, which predominantly includes male patients, and 14 years from the MarketScan database, which covers a more diverse, commercially insured population.

They focused on individuals ages 50 and older who were being treated for HIV or hepatitis B and who had no prior diagnosis of Alzheimer's.

The researchers identified over 270,000 qualifying patients and assessed how many later developed Alzheimer's.

**After accounting for potential confounding factors, such as existing health conditions, they found that those taking NRTIs experienced a marked and meaningful reduction in Alzheimer's risk.**

## **Clinical trials needed to assess potential of NRTIs for Alzheimer's**

The researchers observed that the reduced risk of Alzheimer's was specific to patients taking NRTIs and was not seen in those using other types of HIV medications.

This distinction led them to conclude that NRTIs should be formally tested in clinical trials to assess their potential to prevent Alzheimer's disease. If proven effective, the impact could be substantial.

With nearly 7 million Americans currently affected by Alzheimer's and projections indicating that number could double to 13 million by 2050, the need for preventive treatments is growing.

In addition, the financial burden is expected to rise sharply, with the annual cost of care for Alzheimer's and related dementias projected to increase from \$384 billion today to nearly \$1 trillion in the coming decades, according to the Alzheimer's Association.

"It's estimated that 10 million people develop Alzheimer's disease around the world every year. A 10% reduction in risk could have a dramatic effect on the impact and burden of Alzheimer's," Dr Ambati explained.

"There are some ongoing clinical trials of NRTIs in Alzheimer's disease that are showing some interesting anti-inflammatory effects. Since NRTIs can have some rare but serious side effects, we have developed a modified version called K9 that has the beneficial anti-inflammatory effect without those side effects. K9 is already in clinical for eye diseases, and we are planning to start trials in Alzheimer's disease as well."

— Jayakrishna Ambati

### **How HIV drugs may reduce Alzheimer's risk**

James Giordano, PhD, Professor Emeritus of Neurology and Biochemistry, Georgetown University Medical Center, Washington, DC, who was not involved in the research, told MNT that "this is an interesting retrospective study."

"It provides evidence that use of nucleoside reverse transcriptase inhibitors (NRTIs) that have been used to treat human immunodeficiency virus (HIV), and which inhibit development of inflammasomes, is positively correlated to a reduced incidence of Alzheimer's disease."

"This is noteworthy in that several lines of converging evidence have shown that bodily and cerebral inflammatory states can induce production of both tau and amyloid proteins in brain that are contributory to the pathology of [Alzheimer's]," Giordano added.

"Inflammasomes are cellular proteins that aggregate and form discrete structures both in response to tau and amyloid aggregation, as well as following certain viral and bacterial infections, trauma, alterations in immune function, and exposure to various stressful environmental factors."

—James Giordano, PhD

"Inflammasomes induce changes in mitochondrial function, cell metabolism, calcium regulation, can contribute to the formation of neural plaques and tangles, and can induce a form of cell death, which has been implied in the genesis of Alzheimer's," Giordano explained.

## Inflammation, NRTIs, and Alzheimer's

“This study strengthens the hypothesis that inflammasome-mediated inflammatory processes are operative in Alzheimer's and offers potential direction for the development of NRTI type drugs and molecular agents aimed at mitigating inflammasome development as a viable treatment – or perhaps preventive intervention – for Alzheimer's.”

—James Giordano, PhD

### **News Source:**

<https://www.medicalnewstoday.com/articles/hiv-drugs-help-prevent-alzheimers-disease-nrti#How-HIV-drugs-may-reduce-Alzheimer-s-risk>