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FROM THE ALZHEIMER'S ASSOCIATION INTERNATIONAL CONFERENCE 2020

FLU, PNEUMONIA VACCINATIONS TIED TO LOWER RISK OF ALZHEIMER'S DEMENTIA

CHICAGO, JULY 27, 2020 — Flu (influenza) and pneumonia vaccinations are associated with reduced risk of Alzheimer's disease, according to new research reported at the [Alzheimer's Association International Conference](#)® (AAIC®) 2020.

Three research studies reported at AAIC 2020 suggest:

- At least one flu vaccination was associated with a 17% reduction in Alzheimer's incidence. More frequent flu vaccination was associated with another 13% reduction in Alzheimer's incidence.
- Vaccination against pneumonia between ages 65 and 75 reduced Alzheimer's risk by up to 40% depending on individual genes.
- Individuals with dementia have a higher risk of dying (6-fold) after infections than those without dementia (3-fold).

“With the COVID-19 pandemic, vaccines are at the forefront of public health discussions. It is important to explore their benefit in not only protecting against viral or bacterial infection but also improving long-term health outcomes,” said Maria C. Carrillo, Ph.D., Alzheimer's Association chief science officer.

“It may turn out to be as simple as if you're taking care of your health in this way — getting vaccinated — you're also taking care of yourself in other ways, and these things add up to lower risk of Alzheimer's and other dementias,” Carrillo said. “This research, while early, calls for further studies in large, diverse clinical trials to inform whether vaccinations as a public health strategy decrease our risk for developing dementia as we age.”

Seasonal Flu Vaccine May Reduce Incidence of Alzheimer's Dementia

Previous research has suggested vaccinations may have a protective factor against cognitive decline, but there have been no large, comprehensive studies focused on the influenza (flu) vaccine and Alzheimer's disease risk, specifically. To address this gap, Albert Amran, a medical student at McGovern Medical School at The University of Texas Health Science Center at Houston, and team, investigated a large American health record dataset (n=9,066).

Amran and team found having one flu vaccination was associated with a lower prevalence of Alzheimer's (odds ratio 0.83, $p < 0.0001$), and among vaccinated patients receiving the flu vaccine more frequently was associated with an even lower prevalence of Alzheimer's (odds ratio 0.87, $p = 0.0342$). Thus, people that consistently got their annual flu shot had a lower risk of Alzheimer's. This translated to an almost 6% reduced risk of Alzheimer's disease for patients between the ages of 75-84 for 16 years.

The researchers found the protective association between the flu vaccine and the risk of Alzheimer's was strongest for those who received their first vaccine at a younger age — for example, the people who received their first documented flu shot at age 60 benefitted more than those who received their first flu shot at age 70.

“Our study suggests that regular use of a very accessible and relatively cheap intervention — the flu shot — may significantly reduce risk of Alzheimer's dementia,” Amran said. “More research is needed to explore the biological mechanism for this effect — why and how it works in the body — which is important as we explore effective preventive therapies for Alzheimer's.”

Pneumonia Vaccine May Reduce Alzheimer's Risk Later in Life

Repurposing of existing vaccines may be a promising approach to Alzheimer's disease prevention. Svetlana Ukraintseva, Ph.D., Associate Research Professor in the Biodemography of Aging Research Unit (BARU) at Duke University Social Science Research Institute, and team, investigated associations between pneumococcal vaccination, with and without an accompanying seasonal flu shot, and the risk of Alzheimer's disease among 5,146 participants age 65+ from the Cardiovascular Health Study. The team also took into account a known genetic risk factor for Alzheimer's — the rs2075650 G allele in the TOMM40 gene.

The researchers found that pneumococcal vaccination between ages 65-75 reduced risk of developing Alzheimer's by 25-30% after adjusting for sex, race, birth cohort, education, smoking, and number of G alleles. The largest reduction in the risk of Alzheimer's (up to 40%) was observed among people vaccinated against pneumonia who were non-carriers of the risk gene. Total number of vaccinations against pneumonia and the flu between ages 65 and 75 was also associated with a lower risk of Alzheimer's; however, the effect was not evident for the flu shot alone.

“Vaccinations against pneumonia before age 75 may reduce Alzheimer's risk later in life, depending on individual genotype,” Ukraintseva said. “These data suggest that pneumococcal vaccine may be a promising candidate for personalized Alzheimer's prevention, particularly in non-carriers of certain risk genes.”

Infection Substantially Increases Mortality in People with Dementia

People living with dementia commonly experience other health conditions including viral, bacterial, and other infections. There is a growing trend in research to investigate whether infections might be worsening, more life-threatening or possibly causing dementia.

Janet Janbek, a Ph.D. student at the Danish Dementia Research Centre, Rigshospitalet and the University of Copenhagen in Denmark, and team, used data from national health registries to investigate mortality in Danish residents over age 65 (n=1,496,436) who had visited the hospital with an infection. They found that people with both dementia and such hospital visits died at a 6.5 times higher rate compared with people who had neither. Study participants with either dementia alone or infection-related contacts alone had a threefold increased rate. The rate of mortality was highest within the first 30 days following the hospital visit.

The researchers also found that for people living with dementia the mortality rates remained elevated for 10 years after the initial infection-related hospital visit, and mortality rates from all infections (including major infections like sepsis to minor ear infections) were higher compared with people without dementia or without an infection-related hospital visit.

“Our study supports the need to investigate these relations even further; to find out why infections are linked to higher mortality in people with dementia, specifically which risk factors and biological mechanisms are involved. This will help advance our understanding of the role of infections in dementia,” said Janbek.

“Our study suggests that the health care system — as well as relatives of people with dementia — should have increased awareness of people with dementia who get infections, so they get the medical care they need. People with dementia require more specialized treatment even when their hospital visits are not directly due to their dementia but to what might appear to be an unrelated infection,” Janbek added.

About the Alzheimer’s Association International Conference (AAIC)

The Alzheimer’s Association International Conference (AAIC) is the world’s largest gathering of researchers from around the world focused on Alzheimer’s and other dementias. As a part of the Alzheimer’s Association’s research program, AAIC serves as a catalyst for generating new knowledge about dementia and fostering a vital, collegial research community.

- AAIC 2020 home page: www.alz.org/aaic/
- AAIC 2020 newsroom: www.alz.org/aaic/pressroom.asp
- AAIC 2020 hashtag: #AAIC20

About the Alzheimer’s Association

The Alzheimer’s Association is a worldwide voluntary health organization dedicated to Alzheimer’s care, support and research. Our mission is to lead the way to end Alzheimer’s and all other dementia — by accelerating global research, driving risk reduction and early detection, and maximizing quality care and support. Visit alz.org or call 800.272.3900.

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- Albert Amran, et al. Influenza Vaccination is associated with a reduced incidence of Alzheimer’s Disease (Funder(s): U.S. National Institutes of Health, Christopher Sarofim Family Professorship, the CPRIT RR180012, UT Stars award)
- Svetlana Ukrainseva, PhD, et al. Repurposing of existing vaccines for personalized prevention of Alzheimer’s disease: Vaccination against pneumonia may reduce AD risk depending on genotype (Funded by U.S. National Institute on Aging)
- Janet Janbek, MSc, et al. Increased short- and long-term mortality following infections in dementia: A prospective nationwide and registry-based cohort study

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Influenza Vaccination is associated with a reduced incidence of Alzheimer's Disease

Background: AD is a devastating disease and its pathophysiology is still largely unknown. No treatment has been shown to be efficacious, so prevention remains a very valuable approach. The objective of this work is to statistically test the relationship between influenza vaccination and the incidence of AD to identify a candidate for AD prevention.

Method: We used the Cerner Health Fact EHR dataset and excluded patients less than 60 years of age and included patients with ICD9 code '331.0', i.e. Alzheimer's disease. From this population, we constructed a cohort (N=311,424) for statistical analysis. Then we did propensity score matching (PMS) on AD with regard to patients' demographics and then did PMS on influenza vaccine with regard to the age of AD onset and potential confounds such as prescribed medications. We obtained a balanced data set with respect to vaccinated patients and unvaccinated patients with PMS (N=9,066). To analyze the effects of frequency of vaccination, we divided the number of vaccinations by the length of time from the first vaccination timestamp to AD onset or the end of the observation. We performed a survival analysis on the entire cohort where development of AD was the end outcome.

Result: We obtained our results using chi-square test, uni-variate analysis, and time-to-event analysis. Our main outcomes are three aspects: (1) influenza vaccine significantly decreases AD prevalence (odds ratio 0.8309 with a p-value < 0.0001). (2) the frequency of influenza vaccine has a significant impact to inhibit AD onset (odds ratio 0.8736 with a p-value of 0.0342). (3) time-to-event analysis shows taking influenza vaccine at an earlier age leads to smaller AD risk than having vaccine at an older age (when the first vaccination age increases by 1, the hazard rate increases by 1.0924, p-value < 0.0001).

Conclusion: Analysis of a large clinical database suggests that there is a strong inverse relationship between AD and influenza vaccination. This result provides evidence that influenza vaccination may be a confounding factor in epidemiological studies of risk factors of Alzheimer's Disease. Future studies may shed light on biological mechanisms to more deeply understand a promising, readily available candidate for preventing AD.

Presenting Author

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Repurposing of existing vaccines for personalized prevention of Alzheimer's disease: Vaccination against pneumonia may reduce AD risk depending on genotype

Background: Repurposing of existing vaccines could be a promising approach to Alzheimer's disease (AD) prevention, exploiting potential heterologous effects of such vaccines. Adult vaccinations against pneumonia and the flu showed beneficial off-target effects on mortality and morbidity in some studies, including on dementia-related outcomes, suggesting that respective vaccines may be evaluated as repurposing candidates for prevention of AD and/or other dementias.

Method: We investigated associations between pneumococcal vaccine, with and without an accompanying flu shot, and the risk of AD among 5,146 elderly participants (65+) of the Cardiovascular Health Study, using covariates including sex, race, birth cohort, education, smoking, and rs2075650, a known genetic risk factor for AD in TOMM40 gene that may also be involved in brain vulnerability to infection through its connection to NECTIN2 (Yashin et al. 2018).

Result: Being vaccinated against pneumonia between ages 65-75 was associated with a reduction in the risk of AD afterwards (OR=0.70; P<0.04) in logistic model with all covariates. A largest reduction in the risk of AD (OR = 0.62; P<0.04) was observed in the vaccinated against pneumonia non-carriers of rs2075650 G allele (risk factor for AD). Total count of vaccinations against pneumonia and the flu between ages 65 and 75 was also associated with a lower risk of AD occurrence later in life (OR = 0.88; P<0.01); however, the effect was not seen for the flu alone.

Conclusion: Vaccination against pneumonia before the age 75 may reduce AD risk later in life, especially in people without genetic risk factor for AD (rs2075650, G allele). These results suggest that pneumococcal vaccine may be a promising candidate for repurposing for personalized AD prevention in carriers of particular genotypes. Validation of these effects in higher power datasets is warranted. The study was in part supported by NIH grants R56AG059428, 1R01AG062623, and 2R01AG046860.

Presenting Author

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Increased excess short- and long-term mortality following infections in dementia: A prospective nationwide and registry-based cohort study

Background: The role of infections in dementia remains to date insufficiently explored. Studies have reported that pneumonia and sepsis were either an immediate cause of death or increased mortality in people with dementia. However, it is unknown whether association with mortality is long-term and whether it is dependent on the type of infection. We aimed to investigate the association between several infections and the short- and long-term mortality in people with and without dementia.

Method: We conducted a nationwide registry-based prospective cohort study using data from Danish national registries. Follow up was from 1 January 2000 or the 65-year birthday (whichever came later) until death, immigration or 31 December 2015. Primary exposure was incident dementia and a first infection post start of follow-up. The primary outcome was all-cause mortality. Mortality rate ratios (MRR) were calculated in all exposure groups (Dementia/Infection; Infection before or after dementia, Dementia/No Infection, No Dementia/Infection and with No Dementia/No Infection as the reference group) and stratified by sex and infection site categories. MRRs were also calculated by time since first infection and by infection site.

Result: A total of 1,496,436 people were followed with a total of 12,739,135 person years. A total of 575,260 people died during follow-up (82,573 with dementia). MRR for the Dementia/Infection group (infection after dementia) was 6.52 (95% CI: 6.43 to 6.61) times higher compared with the reference group and was higher in men. MRRs for the Infection groups in all of the site categories were markedly higher in the Dementia than No Dementia group (highest ratios for sepsis and lowest for ear infections). MRRs were highest the first 30 days after onset of first infection in the Dementia group and remained higher than the No Dementia group until 10 years after first infection (similar trends in the analyzed infection site categories).

Conclusion: Mortality is substantially increased in people with dementia following infections of all sites. Excess mortality is both short- (within 30 days) and long-term (after 10 years). Our findings identify people with dementia and infections as a vulnerable group who need clinical attention.

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