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Highlights

- Retrospective cohort study of recombinant zoster vaccine (RZV) on dementia risk.
- Use of medical and pharmacy claims in the Optum Labs Data Warehouse.
- Herpes zoster infection is a significant risk factor for dementia.
- Fully vaccinated individuals had a 32 % reduced risk of dementia.
- Supports policy decisions to increase RZV vaccination rates for older adults.

Abstract

Background

Herpes zoster is a potential risk factor for dementia. The effectiveness of the recombinant zoster vaccine for preventing dementia is uncertain.

Methods

This retrospective cohort study used de-identified claims data from the Optum Labs Data Warehouse database from January 1, 2017, to December 31, 2022, to determine whether the recombinant zoster vaccine is associated with a reduced risk of dementia. Immunocompetent patients with ≥365 days of continuous enrollment were included, with the risk period starting upon age-eligibility for the recombinant zoster vaccination. Cox regression adjusted for time-fixed and time-updated measures every six months was implemented to estimate hazard ratios for dementia. Herpes zoster diagnosis and antiviral therapy were also assessed.

Results

There were 4,502,678 individuals (median [IQR] age, 62 [54–71] years; 51 % female) included in this study: 206,297 (4.6 %) were partially vaccinated, and 460,413 (10.2 %) were fully vaccinated. The incidence rate of dementia was 99.1 cases per 10,000 person-years in the fully vaccinated group, 108.2 cases per 10,000 person-years in the partially vaccinated group, and 133.0 cases per 10,000 person-years in the unvaccinated group. After adjustment, vaccination was significantly associated with a decreased risk of dementia for two doses (hazard ratio [HR]: 0.68; 95 % CI: 0.67–0.70; $P < .001$) and for one dose (HR 0.89; 95 % CI: 0.87–0.92; $P < .001$). Having a herpes zoster diagnosis before the first vaccination dose was associated with an increased hazard of dementia (HR 1.47; 95 % CI: 1.42–1.52; $P < .001$) compared to those with no diagnosis. Antivirals used to treat zoster infection were protective against dementia (HR 0.42; 95 % CI: 0.40–0.44; $P < .001$).

Conclusions

These findings suggest that the recombinant zoster vaccine is associated with a decreased risk of dementia and highlight an additional benefit of vaccination beyond preventing herpes zoster.

Introduction

Dementia is a neurocognitive disorder characterized by a decline in the domains of cognition, such as executive function, perceptual-motor skills, or social cognition [1]. This disorder affects over 55 million people globally, with 10 million new cases diagnosed per year [2]. While there are no established treatments to reverse the effects of dementia after onset, some environmental and lifestyle factors may be controlled to reduce the risk of developing dementia. One potential risk factor is herpes zoster (HZ) infection, a neurocutaneous disease caused by the reactivation of the varicella-zoster virus (VZV), commonly known as shingles. In the United States, about one in three people will develop HZ in their lifetime [3].

Multiple studies have shown that HZ may be implicated in dementia risk, perhaps through neuroinflammation or cerebral vasculopathy [4]. Two population-based cohort studies from 2017 and 2020 found that HZ was associated with an increased risk of dementia, while antiviral therapy following HZ infection reduced the risk [5,6]. There is less clarity on whether HZ vaccination lowers the risk of developing dementia. Some prior studies have shown that HZ vaccination is associated with lower rates of dementia [7], [8], [9], [10], [11], [12]], but these primarily explored the effects of the zoster live vaccine (ZVL; Zostavax), which was discontinued in 2020. The recombinant zoster vaccine (RZV; SHINGRIX), released in late 2017, is now the approved and recommended vaccine for preventing HZ infection by the Centers for Disease Control and Prevention (CDC), with 97 % efficacy in clinical trials [13,14].

The aim of our study was to determine the impact of RZV on developing dementia using a large claims database. Specific aims were to determine (1) whether vaccination with RZV has a protective effect on dementia and (2) how HZ infection and antiviral therapy are associated with the risk of developing dementia.

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Data source

This retrospective cohort study used medical and pharmacy claims data from the Optum Labs Data Warehouse (OLDW; Optum Labs, Eden Prairie, MN), a de-identified administrative claims and electronic health record (EHR) database consisting of enrollment information of commercial and Medicare Advantage enrollees of all ages since 1994 [15]. Medical claims comprised of diagnosis codes, i.e., International Classification of Disease 10th revision (ICD-10), Current Procedural Terminology (CPT) codes, ...

Results

Table 1 shows the characteristics of the cohort, which consisted of 4,502,678 individuals. Individuals were included if they reached age eligibility for RZV of 50 years or older with at least one year of continuous enrollment before the eligibility date and were excluded if they had dementia or a condition that made them immunocompromised in the baseline period. Cohort selection is outlined in Fig. 1. The cohort's median age was 62 years (interquartile range (IQR): 54–71 years). Approximately ...

Discussion

In this population-based cohort study, we found that RZV was associated with a significantly decreased risk of dementia. Full vaccination with RZV conferred the most protection against dementia (32 % decrease in risk; 95 % CI: 30–33 %; $P < .001$) compared to those classified as unvaccinated; but even partial vaccination was associated with an 11 % decrease in risk (95 % CI: 8–13 %; $P < .001$) compared to being unvaccinated. The relatively high percentage of patients who received only one dose ...

Conclusion

In conclusion, this study from a large claims database found that RZV is associated with a lower risk of dementia, with the greatest protection in fully vaccinated individuals. Patients who had HZ had an increased risk of dementia, while those receiving antiviral treatment exhibited a lower risk, irrespective of the reason for receiving antivirals. These findings underscore the importance of promoting RZV as a preventive measure against dementia, regardless of prior zoster infection status. ...

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Role of the Funder/Sponsor

The funding organizations had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication. ...

CRediT authorship contribution statement

Emily Tang: Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Project administration, Methodology, Formal analysis, Data curation, Conceptualization. **Isabel Ray:** Writing – review & editing, Writing – original draft. **Benjamin F. Arnold:** Writing – review & editing, Validation, Methodology, Conceptualization. **Nisha R. Acharya:** Writing – review & editing, Writing – original draft, Validation, Supervision, Software, Resources, Project administration, ...

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Nisha R. Acharya reports financial support was provided by National Eye Institute. Nisha R. Acharya reports financial support was provided by National Institutes of Health Office of Research on Women's Health. Benjamin F. Arnold reports financial support was provided by National Eye Institute. Nisha R. Acharya reports financial support was provided by Research ...

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