Health Information and Quality Authority

An tÚdarás Um Fhaisnéis agus Cáilíocht Sláinte

Scoping Review

The association between herpes zoster vaccination and the risk of dementia

20 May 2026

About the Health Information and Quality Authority

The Health Information and Quality Authority (HIQA) is an independent statutory authority established to promote safety and quality in the provision of health and social care services for the benefit of the health and welfare of the public.

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- **Regulating health services —** Regulating medical exposure to ionising radiation.

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- **National Care Experience Programme** — Carrying out national service-user experience surveys across a range of health and social care services, with the Department of Health and the HSE.

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The membership of the EAG was as follows:

Dr Sarah Geoghegan	Clinical Lead for National Immunisation Advisory Committee, HTA Directorate, HIQA
Dr Patricia Harrington	Deputy Director (HTA), HIQA
Dr Graham Hughes	Consultant Geriatrician and Clinical Lead for National Clinical Programme for Older People, HSE
Dr Conor Maguire	General Practitioner, Irish College of General Practitioners
Dr Máirín Ryan	Director of HTA and Deputy CEO, HIQA
Prof Corinna Sadlier	Consultant in Acute Medicine and Infectious Diseases, Cork University Hospital and National Immunisation Advisory Committee
Prof Susan Smith	Consultant in General Practice, Public Health and Primary Care, Trinity College Dublin
Dr Conor Teljeur	Chief Scientist, HTA Directorate, HIQA

Members of the Evaluation Team:

Members of HIQA's Evaluation Team were Dr Emma Reece, Joan Quigley, Dr Patricia Harrington, Dr Conor Teljeur, and Dr Máirín Ryan.

Conflicts of Interest

General practices derive a small portion of their income from administration of vaccines.

There were no reported potential conflicts of interest for members of the Evaluation Team.

List of abbreviations used in this report

AD	Alzheimer's disease
BCG	Bacillus Calmette-Guerin
CCA	corrected cover area
CI	confidence interval
HIQA	Health Information and Quality Authority
HTA	health technology assessment
HZ	herpes zoster
MCI	mild cognitive impairment
NMIBC	non-muscle-invasive bladder cancer
PHN	post-herpetic neuralgia
RCT	randomised controlled trial
RZV	recombinant zoster vaccine
SCD	subjective cognitive decline
SD	standard deviation
Tdap	low dose diphtheria and low dose acellular pertussis
VaD	vascular dementia
ZVL	live attenuated zoster vaccine

Advice to the Minister and the Health Service Executive

In 2024, following a request from the Department of Health, HIQA published a health technology assessment (HTA) of the addition of herpes zoster (HZ) vaccination to the adult vaccination programme. The HTA found clear and consistent evidence that the recombinant zoster vaccine is safe and effective at reducing HZ cases, also noting that effectiveness diminishes over time. At the submitted price, HZ vaccination was found not to represent an efficient use of healthcare resources in Ireland. Following a new request from the Department of Health, HIQA has been asked to determine whether any additional scientific information relevant to the policy question has been published.

Recent epidemiological studies have suggested that vaccination against HZ may be associated with a lower risk of dementia. This scoping review was undertaken to identify, collate, and summarise the existing literature specifically in relation to HZ and dementia. The scoping review considered three related research questions:

- the association between HZ infection and dementia
- the impact of HZ vaccination on dementia risk
- the broader links between vaccinations in general and dementia incidence.

Arising from the findings of this review, HIQA's advice to the Minister for Health regarding the potential inclusion of risk of dementia in the economic model of HZ vaccination is as follows:

- Herpes zoster (HZ), commonly known as shingles, is characterised by a painful, blistering rash that typically takes two to four weeks to resolve. The most frequent complication of HZ is post-herpetic neuralgia (PHN), referring to persistent chronic pain after the resolution of the acute rash. PHN can significantly alter individuals' lives, inflicting debilitating pain, disrupting daily activities, sleep, and emotional well-being.

- HZ vaccination reduces the risk of HZ, but is not currently provided as part of the publicly-funded healthcare system. The recombinant zoster vaccine is licensed for prevention of HZ and PHN only, and not for the prevention of dementia. Prompt antiviral treatment for HZ is recommended to reduce the risk of complications including PHN and is funded through the HSE's primary care reimbursement schemes.

- In relation to the three research questions posed:

- Twelve observational studies evaluated the association between HZ infection and dementia. Results were mixed. Seven studies reported a harmful association, with a 12% to 47% increase in the risk of dementia among individuals with a diagnosis of HZ. Four studies found no significant association, and one reported evidence to suggest that HZ may have a protective effect among frail individuals and females. Four of the twelve studies reported that antiviral treatment for acute HZ infection mitigated some of the additional risk, while one study reported no association.
- Ten non-randomised studies included in the review explored the potential association between HZ vaccination and risk of dementia. All ten studies reported a protective association, with the authors concluding that HZ vaccination reduced the risk of dementia.
- Five recent systematic reviews and meta-analyses of observational studies indicate that receipt of routine adult vaccinations may be associated with lower risk of dementia. The largest body of evidence related to seasonal influenza vaccination, with studies consistently reporting a protective effect against dementia.

- While there is no randomised controlled trial evidence to determine causation, observational evidence links HZ vaccination with a lower risk of dementia. The consistency of this association across multiple studies suggests a protective effect may exist.
  - These associations are confounded by underlying determinants of dementia, health seeking behaviour, co-vaccination, and other unmeasured factors. Evidence demonstrating an association between HZ incidence and increased dementia risk, lends plausibility to a protective effect of HZ vaccination, alongside broader findings that vaccination in general may be associated with a lower risk of dementia.
  - It is unclear if any reduced risk of dementia reflects prevention or delay in onset, and the extent to which such protection wanes over time. This would be an important factor in estimating the optimal age for vaccination.
  - While the available evidence suggests a positive impact, it is not possible to determine the contribution or magnitude of effect that HZ vaccination may have in reducing dementia risk, independent of other factors.

- While the current evidence base lacks robustness and causal certainty, the broadly consistent direction of association suggests that shingles vaccination as well as other routine adult vaccinations may offer some benefit against dementia. This evidence should be considered alongside an updated review of the clinical effectiveness of shingles vaccination, informing whether the impact on healthcare resources needs to be re-assessed.

Plain Language Summary

This review looked at whether shingles (herpes zoster) infection might increase the risk of developing dementia and if shingles vaccination might reduce that risk. We also looked at whether other adult vaccines reduce the risk of developing dementia.

Dementia is a major health challenge, that comes with substantial personal, societal and healthcare system burden. Even small reductions in dementia risk could have meaningful benefits for individuals, families, and society.

We carried out this review to understand the current evidence and to help decide whether we should update our economic evaluation of shingles vaccination we published in 2024.

What we found

The link between shingles infection and dementia

Some studies report that having shingles may increase the risk of dementia. These studies showed this risk was higher in more severe cases of shingles, and those involving the eye. However, other studies found no clear link. These findings come from studies that do not look for a cause of dementia, so they cannot prove that shingles infection by itself directly increases dementia risk.

People who got antiviral treatment for shingles tended to have a lower risk of dementia than those who did not. Prompt antiviral treatment is already routinely recommended for certain groups to reduce the risk of complications from shingles, including post-herpetic neuralgia. This antiviral treatment could also reduce any additional risk of dementia.

The link between shingles vaccination and dementia

All studies that looked at shingles vaccination reported that people who were vaccinated against shingles had a lower risk of developing dementia. The reduction in risk of dementia ranged from about 20% to nearly 40%. However, these studies cannot prove that shingles vaccination reduces the risk of dementia. The reduced risk may also be for other reasons, such as a healthy lifestyle and a lack of other risk factors.

The link between other adult vaccines and dementia

Many reviews show that routine vaccines for adults like flu, tetanus/diphtheria/pertussis, hepatitis, and others, are also linked with a lower risk of dementia. For example, the flu vaccine was linked with a lowered risk of 26% to 31%. However, these studies did not consider some key differences between

people, so the evidence does not show if vaccination alone caused the lower dementia risk.

Conclusion

None of the included studies were clinical trials. The information available was about people who chose to get vaccinated rather than those who did not. Often, people who choose to get vaccinated have healthier lifestyles and better access to healthcare, which also lowers dementia risk.

From the available evidence, it is difficult to know how much of the benefit was due to the vaccine itself, or the characteristics of people who got vaccinated. This means that the studies can show links but cannot prove cause and effect.

What this means

While shingles vaccination appears to be linked with a lower risk of dementia, the current evidence is not strong enough to say that the vaccine directly prevents dementia. Also, it is not possible to say by how much the shingles vaccine reduces this risk or what is the best age to get vaccinated. Other vaccines, such as the flu vaccine may also offer some protection against dementia, but again the extent to which they do this is uncertain.

Although the available information is not ideal, it is important to explore what it means for decision-making.

While it is possible that vaccines may offer some protection against dementia, they should be considered alongside other prevention strategies. These include managing blood pressure and cholesterol, staying physically active, not smoking, limiting alcohol, and keeping socially and mentally engaged. Seeking timely medical attention for shingles symptoms is also important. Early antiviral treatment can help reduce the risk of complications from the infection.

1 Introduction

Herpes zoster (HZ), commonly known as shingles, is characterised by a painful, blistering rash that typically takes two to four weeks to resolve. HZ occurs due to reactivation of latent varicella-zoster virus, usually decades after primary varicella (chicken pox) infection. Among those with a history of varicella, the individual life-time risk of developing HZ is approximately 30%. The most frequent complication of HZ is post-herpetic neuralgia (PHN), referring to persistent chronic pain after the resolution of the acute rash. PHN can significantly alter individuals' lives, causing debilitating pain, disrupting daily activities, sleep, and emotional wellbeing. The probability of PHN after HZ increases with age, increasing from a one in 10 chance in 50 to 59-year-olds to a one in five chance in those aged over 80 years.

In 2024, following a request from the Department of Health, HIQA published a health technology assessment (HTA) of the addition of HZ vaccination to the adult vaccination programme.[(1)] While the HTA found clear and consistent evidence that the recombinant zoster vaccine (RZV) is safe and effective at reducing HZ cases, it noted that effectiveness diminishes over time. Local and systemic adverse events were noted to be common, however serious adverse events are uncommon. At the submitted price, HZ vaccination was found not to represent an efficient use of healthcare resources in Ireland. The economic evaluation took into account the benefits arising from reductions in the incidence of HZ and PHN.

Recent epidemiological studies have suggested that vaccination against HZ may be associated with a lower risk of dementia. Following a new request from the Department of Health, HIQA has been asked to determine whether any additional scientific information relevant to the policy question has been published. The aim of this scoping review was to explore the current evidence regarding this potential association.

This scoping review was undertaken to identify, collate, and summarise the existing literature specifically in relation to HZ and dementia. The scoping review captures related aspects such as the association between HZ infection and dementia, as well as broader links between vaccinations in general and dementia incidence.

2 Methods

2.1 Search strategy

The scoping review was guided by three research questions (RQs):

RQ1 Is there a link between HZ and onset of dementia?

RQ2 Does HZ vaccination have an impact on onset of dementia?

RQ3 Is there a link between vaccination in general and onset of dementia?

Details of the search are outlined in Table 1. No date or language restrictions were applied.

Table 1. PubMed search strategies

Research question	Search date	Search terms
1. Is there a link between HZ and onset of dementia? 2. Does HZ vaccination have an impact on onset of dementia?	26 May 2025	(dementia[All Fields] OR Alzheimer's[All Fields] OR Alzheimer’s[All Fields]) AND (shingles[All Fields] OR herpes zoster[All Fields])
3. Is there a link between vaccination in general and onset of dementia?	26 May 2025	(((dementia[Title/Abstract] OR Alzheimer's[Title/Abstract] OR Alzheimers[Title/Abstract])) AND (vaccine[Title/Abstract] OR vaccination[Title/Abstract])) AND (systematic review[Title/Abstract] OR meta-analysis[Title/Abstract]

As a scoping review, this study aimed to provide a broad overview of the available evidence on the association between HZ and dementia. However, it may not have captured all relevant studies, and it did not include a formal assessment of study quality.

2.1.1 Eligibility criteria

For RQs 1 and 2, studies were eligible for inclusion if they:

- examined an association between HZ or HZ vaccination and dementia onset
- reported primary research data (for example, cohort, case-control, or cross-sectional studies).

Case reports, case series, narrative reviews, commentaries, editorials, and conference abstracts without sufficient data were excluded.

For RQ 3, an umbrella approach was adopted, in which only systematic reviews and meta-analyses examining vaccination and dementia onset were eligible. Primary studies, narrative reviews, and other non-systematic evidence were excluded for this question.

2.2 Data extraction and synthesis

Relevant data from the included studies were extracted into a Microsoft Excel spreadsheet. Extracted information included study characteristics, population details, type of vaccination, and key findings related to dementia onset. A narrative synthesis approach was used to summarise and integrate findings across studies.

To assess the degree of overlap in primary studies included in multiple systematic reviews addressing RQ3, the corrected covered area (CCA) was calculated. The CCA is a quantitative metric of overlap. It is calculated using the formula presented below.

The interpretation of CCA values is as follows:

- 0-5% = slight overlap
- 6-10% = moderate overlap
- 11-15% = high overlap
- >15% = very high overlap.[2]

$$CCA\ (Corrected\ CA) = \frac{N - r}{r\,c - r}$$

Key: where N is the number of included publications (including double counting, this is the sum of the ticked boxes in the citation matrix); where r is the number of rows (number of index publications) and c is the number of columns (number of reviews).[2]

3 Summary of findings

3.1 Association between herpes zoster infection and risk of dementia

A total of 12 studies investigating the association between HZ infection and the risk of dementia were included,[3-14] with a summary of these studies presented in Table 2. The studies varied in design and included nine retrospective cohort studies, two nested case-control studies, and one prospective cohort study, all assessing association. The studies spanned a range of countries, including the United States (n=4), United Kingdom (n=2), Taiwan (n=2), South Korea (n=2), Denmark (n=1), Italy (n=1). Populations generally comprised individuals aged 50 years and older, with total sample sizes ranging from approximately 3,500 to over 4.5 million individuals. The studies typically investigated the association between HZ infection and the risk of dementia based on administrative codes. One study each reported on the association between severe HZ (defined as hospitalisation due to HZ) and herpes zoster ophthalmicus (HZO) with risk of dementia.

Overall, seven studies reported a harmful association between HZ and dementia risk. These included populations from Italy,[3] South Korea,[4] Taiwan,[5, 10] and the United States.[6-8] Blandi et al. (2025) reported that individuals with severe HZ had an increased risk of dementia compared with two groups of unexposed matched controls: the general population and hospitalised controls (individuals hospitalised with a diagnosis other than HZ infection).[3] Bae et al. (2021) and Chen et al. (2018) similarly reported increased risk of dementia following HZ infection in large South Korean and Taiwanese cohorts, respectively, with both studies also noting that this increase was significantly mitigated if antiviral treatment was initiated.[4, 5] Ukraintseva et al. (2024) reported that HZ infection diagnosed between ages 65 and 75 years increased the risk of Alzheimer's disease later in life, in a US cohort,[6] while Tang et al. (2025) observed that having a HZ diagnosis before the first vaccination dose was associated with an increased risk of dementia.[7] Yeh et al. (2024) found that a history of HZ was associated with a higher long-term risk of subjective cognitive decline across multiple US cohorts.[8]

Across the studies that reported a harmful association between HZ and dementia, hazard ratios (HRs) ranged from 1.12 to 1.47, indicating between a 12% and 47% increased risk of developing dementia among individuals who had HZ compared with those who did not. In contrast to studies on general HZ infection, Tsai (2017) focused on patients with HZO and found a markedly increased risk of dementia, reporting an adjusted HR of 2.97, indicating a 197% higher risk compared with controls, with an even higher HR of 3.35 (235% increased risk) among male patients with HZO.[10]

One study reported mixed results. Warren-Gash et al. (2022) found no overall association between HZ infection and dementia risk among males who were otherwise fit; however, the study observed a slight decreased risk of dementia following HZ infection among frail individuals and females, indicating a protective association in these subgroups.[9]

Four studies found no significant link between HZ and dementia.[11-14] These included large cohort analyses from Denmark, the United States, and the United Kingdom, as well as a nested case-control study from South Korea. Although Weinmann et al. (2024) found no overall association, they reported that among some subgroups of individuals with a HZ diagnosis, the risk of dementia was lower in those who received antiviral treatment to treat the acute HZ infection, corresponding to a 12% reduction in risk, compared with those who did not receive an antiviral.[12] Similarly, Bae et al. (2021), Chen et al. (2018), and Tang et al. (2025) also found evidence that among individuals with a HZ diagnosis, receipt of antiviral therapy following acute HZ infection was associated with a lower risk of subsequent dementia, with a 24%, 45% and 58% reduction in risk, respectively compared with those who went untreated.[4, 5, 7] However, one other study also examined this association and did not find a statistically significant effect.[9] Where antiviral medication usage was recorded, it was generally through administrative data and on the basis of being prescribed within 7 to 30 days after HZ diagnosis.

Differences in findings across the cohort studies may reflect differences in follow-up duration, case definitions for both HZ and dementia, approaches to outcome ascertainment, population characteristics, and the proportion of individuals receiving antiviral treatment.

Overall, the evidence for an association between HZ infection and dementia risk is mixed. While over half of the studies suggest a harmful association between HZ and dementia, others report no significant link. Importantly, there is evidence across several studies that antiviral treatment for the acute HZ infection may mitigate any increased risk of dementia in individuals diagnosed with HZ infection.

Table 2. Summary of association between herpes zoster infection and risk of dementia in included studies

Author, year	Country	Study type	Population	Sample size	Follow-up	Results	Direction of effect (protective, harmful or no-link)
Schmidt, 2022[11]	Denmark	Retrospective cohort study	Individuals aged ≥40 years with HZ and matched general population comparators Median age 64 years (IQR 54-74)	247,305 individuals with HZ and 1,235,890 matched general population comparators	1-21 years (cohorts were followed from the day after the index date until the earliest of the following: first diagnosis of dementia, death, emigration, or end of the study)	The HR of all-cause dementia was 0.98; 95% CI: 0.92–1.04 during the first year post-HZ diagnosis and 0.93; 95% CI: 0.90–0.95 thereafter versus matched comparators. Dementia was diagnosed in 9.7% of patients with HZ and 10.3% of matched comparators by the end of follow-up.	No-link
Blandi, 2025[3]	Italy	Retrospective cohort study	Adults aged ≥50 years within the Lombardy Region Datawarehouse	132,968 individuals (12,088 with severe HZ; 60,440 matched general population	Up to 23 years	Severe HZ (hospitalised cases) was associated with a higher risk of developing dementia. Compared with the general population, the adjusted sub-distributed hazard ratio (SHR) was 1.13; 95% CI: 1.07–1.19, and compared with	Harmful link

Author, year	Country	Study type	Population	Sample size	Follow-up	Results	Direction of effect (protective, harmful or no-link)
			Mean age 74.6 years (range 50-104 years)	controls; 60,440 matched hospitalised controls)		hospitalised controls (individuals hospitalised with a diagnosis other than HZ infection), SHR was 1.08; 95% CI: 1.03–1.14.	
Weinmann, 2024[12]	United States	Retrospective cohort study	Individuals aged ≥50 years within Kaiser Permanente Northwest Median age (years) HZ unexposed: 64; HZ exposed: 64; HZ exposed with antiviral use: 64; HZ exposed without antivirals: 65	101,328 individuals (25,332 with HZ; 75,996 matched controls)	Median 4.8 years	HZ diagnosis was not associated with an increased risk of dementia (aHR: 0.99; 95% CI: 0.93–1.05) Among individuals with HZ, receipt of antiherpetic medication was associated with a lower risk of dementia in some subgroups (aHR: 0.88; 95% CI: 0.77–1.00)	No-link

Author, year	Country	Study type	Population	Sample size	Follow-up	Results	Direction of effect (protective, harmful or no-link)
Bae, 2021[(4)]	South Korea	Retrospective cohort study	Individuals aged ≥50 years from the National Health Insurance Service-National Sample Cohort Mean age 61.7 years (SD 9.4)	229,594 individuals (34,505 with HZ; 195,089 non-HZ group)	Study period 12 years	HZ was associated with a higher risk of dementia (adjusted HR: 1.12; 95% CI: 1.05–1.19). Among individuals with HZ, those who received antiviral treatment showed a significantly lower risk of dementia (HR 0.76; 95% CI 0.65–0.90).	Harmful link
Warren-Gash, 2022[(9)]	United Kingdom	Retrospective cohort study	Individuals aged ≥40 years in UK primary care practices Median age 65 years (IQR 55.1-75.0)	884,045 individuals (177,144 with HZ; 706,901 matched controls)	Median 4.6 years (IQR 2.0-8.1)	HZ was associated with a slight reduction in dementia diagnosis (adjusted HR: 0.92; 95% CI: 0.89–0.95), particularly among frail individuals and females. For patients who were fit, no association was seen (adjusted HR 0.97; 95% CI: 0.92–1.02). Dementia risk did not vary by prescription of antiviral agents.	No link (among those who were fit) Protective link (among frail individuals and females)

Author, year	Country	Study type	Population	Sample size	Follow-up	Results	Direction of effect (protective, harmful or no-link)
Tsai, 2017[10]	Taiwan	Retrospective cohort study	Patients diagnosed with herpes zoster ophthalmicus (HZO) aged ≥50 years from the Taiwan Longitudinal Health Insurance Database Mean age 62.2 years (SD 12.5) for HZO patients and 61.4 years (SD 13.3) for comparison patients	846 HZO patients and 2,538 matched controls	5 years	Patients with HZO had a significantly higher risk of developing dementia compared to controls (adjusted HR 2.97; 95% CI: 1.90–4.67). Male patients exhibited an even higher crude HR of 3.35; 95% CI: 1.79–6.28.	Harmful link (HZO)
Chen, 2018[5]	Taiwan	Retrospective cohort study	Individuals aged ≥50 years from Taiwan's National Health Insurance	78,410 individuals (39,205 with HZ; 39,205 matched controls)	6.2 years (SD 4.1)	HZ was associated with a slightly increased risk of dementia (adjusted HR: 1.11; 95% CI, 1.04–1.17). Prescriptions of antiviral therapy were associated with a lower risk of developing	Harmful link

Author, year	Country	Study type	Population	Sample size	Follow-up	Results	Direction of effect (protective, harmful or no-link)
			Research Database Mean age: individuals with HZ 63.5 years (SD 10); matched controls 63.5 years (SD 10)			dementia following the diagnosis of HZ (HR = 0.55; 95% CI, 0.40–0.77).	
Ukraintseva, 2024[6]	United States	Retrospective cohort study	Individuals aged 75 years from Health and Retirement Study (HRS) data.	6,001 individuals in the AD cohort. 5,548 AD/AD-related dementias and other dementias (ADRD+) cohort.	6.1 years 6.1 years (AD), 5.7 years (AD/ADRD+) and 6.3 (Death) years until exit	HZ infection showed a statistically significant association with AD (1.23; 95% CI: 1.06–1.41). HZ infection was not associated with the composite outcome of AD/ADRD+	Harmful link
Tang, 2025[7]	United States	Retrospective cohort study	Individuals aged ≥50 years in the Optum Labs Data Warehouse database	4,502,678 individuals (206,297 partially vaccinated; 460,413 fully vaccinated;	5 years	Having a HZ diagnosis before the first vaccination dose was associated with an increased hazard of dementia (HR 1.47; 95% CI: 1.42–1.52; P<0.001) compared to those with no diagnosis.	Harmful link

Author, year	Country	Study type	Population	Sample size	Follow-up	Results	Direction of effect (protective, harmful or no-link)
			Median age 62 years (IQR 54-71)	3,835,968 unvaccinated)		Antivirals used to treat HZ infection were protective against dementia (HR 0.42; 95% CI: 0.40–0.44; P<0.001).	
Choi, 2021[14]	South Korea	Nested case control study	Individuals aged ≥60 years from the Korean National Health Insurance Service-National Sample Cohort	11,445 dementia patients matched with 45,780 controls	12 years	The study found that past HZ infection did not increase the risk of neurodegenerative dementia. Adjusted OR for HZ infection in the dementia group: 0.90 (95% [CI]: 0.84–0.97), suggesting no increased risk. Subgroup analyses by age and sex also showed no significant associations.	No-link
Lophatananon, 2021[13]	United Kingdom	Nested case-control study	Individuals from UK biobank and primary care linkage health records	228,223 participants. 2,378 incident dementia cases and 225,845 controls	Up to 3 years	There was a small but non-significant increase in the risk of dementia in subjects with HZ diagnosed 3 years or more prior to dementia diagnosis (OR: 1.09 with 95% CI: 0.98–1.21).	No-link
Yeh, 2024[8]	United States	Prospective cohort study	Participants from Nurses' Health Study (NHS), NHS II, and Health Professionals	149,327 individuals (56,142 NHS, 66,966 NHS II, 26,219 HPFS)	Follow-up time since HZ occurrence: 1-4 years, 5-8 years, 9-12	A history of HZ was associated with higher long-term risk of SCD. In NHS, the multivariable-adjusted relative risk (MVRR) was 1.14 (95% CI: 1.01–1.32) for ≥ 13 years since HZ.	Harmful link

Author, year	Country	Study type	Population	Sample size	Follow-up	Results	Direction of effect (protective, harmful or no-link)
			Follow-Up Study (HPFS) NHS mean age: 64.6 years (SD 6.7) NHS II mean age: 47.2 years (SD 5.3) HPFS mean age: 68.5 years (SD 8)		years, ≥13 years	In NHS II, the MVRR was 1.34 (95% CI: 1.18–1.53) for 1-4 years and 1.20 (95% CI: 1.08–1.34) for ≥ 13 years since HZ. In HPFS, an elevated risk of SCD was suggested across all time points.	

Key: AD – Alzheimer's disease; ADRD – Alzheimer's disease and related dementias; CI – confidence interval; FDR – false discovery rate; HRS – Health and Retirement Study; HPFS – Health Professionals Follow-Up Study; HR – hazard ratio; HZ – herpes zoster; HZO – herpes zoster ophthalmicus; MVRR – multivariable-adjusted relative risk; NHS – Nurses' Health Study; OR – odds ratio; RZV – recombinant zoster vaccine; SCD – subjective cognitive decline; SHR – sub-distribution hazard ratio; UK – United Kingdom; US – United States.

3.2 Association between herpes zoster vaccination and risk of dementia

A total of 10 studies were included in this scoping review to explore the potential association between HZ vaccination and risk of dementia.[6-8, 13, 15-20] A summary of the characteristics of included studies is presented in Table 3. The studies included populations from the United States (n=6), the United Kingdom (n=3) and Australia (n=1). Study designs varied and included retrospective cohort studies (n=4), natural experiments leveraging changes to vaccination eligibility criteria (n=2), a quasi-experimental study (n=1), a prospective cohort study (n=1), a cross-sectional survey-based analysis (n=1) and a nested case-control design within a population-based cohort (n=1). Sample sizes ranged widely, from fewer than 300 participants in survey-based research to over 4.5 million individuals in population-level administrative databases.

Evidence for both types of HZ vaccines, the live attenuated zoster vaccine (ZVL) and recombinant zoster vaccine (RZV), was included, with some studies comparing outcomes between the two. The majority of studies evaluated populations aged 65 years and older, aligning with eligibility criteria for national HZ vaccination programmes. Outcomes assessed included all-cause dementia, Alzheimer's disease (AD), vascular dementia (VaD), mild cognitive impairment (MCI) and subjective cognitive decline (SCD).

Across all 10 studies, the findings consistently demonstrated a protective association: a lower risk of dementia or cognitive decline following HZ vaccination. No study reported a harmful effect (that is, an increased risk of dementia following vaccination) or a null association.

Two natural experiments provided evidence of vaccine benefit by comparing dementia incidence between vaccine-eligible and non-eligible cohorts. A UK-based study (n=282,541) by Eyting et al. (2025) exploited the Welsh eligibility rule whereby individuals born on or after 2 September 1933 were eligible for the HZ vaccine, while those born before this date were ineligible. Eligibility to receive the HZ vaccine was associated with a 20% relative reduction in the probability of a dementia diagnosis over a follow-up period of seven years (95% confidence interval [CI]: 6.5 to 33.4). This protective effect was stronger among women than men.[15] Another US-based natural experiment using data from before and after the discontinuation of ZVL (n=207,674), compared the risk of dementia in those who received RZV versus ZVL. Taquet (2024) reported that those individuals who received RZV had a significantly lower risk of developing dementia over the next six years compared with those who received ZVL (restricted mean time lost (RMTL) ratio, 0.83; 95% CI, 0.80–0.87; p<0.0001). This was estimated to equate to 17%

more time lived diagnosis-free, or 164 (95% CI: 124–202) additional diagnosis-free days among those affected.[20]

An Australian quasi-experimental study (n=101,219) by Pomirchy et al. (2025) used a date-of-birth eligibility threshold whereby individuals who turned 80 after 1 November 2016 were eligible for HZ vaccination, while those who turned 80 before that date were ineligible. Eligibility for HZ vaccination significantly decreased the probability of receiving a new dementia diagnosis by 1.8 percentage points (95% CI: 0.4 to 3.3, p=0.01) over 7.4 years, decreasing from 5.5% among vaccine-ineligible individuals to 3.7% among vaccine eligible individuals.[17]

Retrospective cohort studies also consistently reported significant protective associations. Harris et al. (2023) found a significant reduction in the risk of Alzheimer's disease among vaccinated individuals compared with unvaccinated individuals (RR 0.75, 95% CI: 0.73 to 0.76; 8.1% vs. 10.7%).[16] In Wales, Schnier et al. (2022) observed a 39% reduction in the risk of dementia diagnosis (adjusted HR: 0.72; 95% CI: 0.69 to 0.75), with reductions in risk reported for both Alzheimer's disease (HR: 0.81; 95% CI: 0.77 to 0.86) and vascular dementia (HR: 0.66; 95% CI: 0.61 to 0.71.).[19] Ukraintseva (2024) found that HZ vaccination was associated with a 21% lower risk of Alzheimer's disease (HR: 0.79; 95% CI: 0.68 to 0.93) in a population vaccinated between ages of 65 and 75 years compared with those who were not vaccinated between these ages.[6]

Tang et al. (2025) showed that full vaccination with RZV (two doses) was associated with a lower dementia risk by 32% (HR: 0.68; 95% CI: 0.67 to 0.70), while even partial vaccination (one dose) reduced risk by 11% (HR: 0.89; 95% CI: 0.87 to 0.92).[7] Lehrer et al. (2021) found that vaccinated individuals were significantly less likely to report cognitive impairment (p=0.03),[18] while Lophatananon (2021), using UK Biobank data, reported an odds ratio of 0.81 (95% CI: 0.66 to 0.99), indicating a 19% lower odds of dementia among vaccinated individuals.[13] Finally, Yeh (2024), using prospective cohort data, suggested a trend toward higher subjective cognitive decline among unvaccinated individuals, particularly in women, although this was not statistically significant (p=0.09).[8]

Overall, evidence from diverse methodological approaches and populations suggest a potentially protective relationship between HZ vaccination and a lower risk of dementia. Across the studies, the size of the effect differed, but dementia risk was consistently lower among vaccinated groups. Reported relative risk reductions ranged from 20% to 39%, depending on the vaccine type, number of doses, and how outcomes were defined. Follow-up periods in these studies ranged from 4.2 to 8 years.

Table 3. Summary of studies examining the association between herpes zoster vaccination and risk of dementia

Author, year	Country	Study type	Population	Sample size	Vaccine	Follow-up	Results	Direction of effect (protective, harmful or no-link)
Taquet, 2024[20]	United States	Natural experiment	Individuals aged 65 and older who received HZ vaccination	207,674 individuals (103,837 in each cohort: recombinant vs live vaccine recipients)	RZV and ZVL	4.2 years for RZV and 6 years for ZVL	Individuals who received RZV were at lower risk of developing dementia over the next six years (restricted mean time lost (RMTL) ratio, 0.83; 95% confidence interval (CI), 0.80–0.87; p<0.0001) compared to those who received ZVL, translating into 17% more time lived diagnosis-free, or 164 (95% CI: 124–202) additional diagnosis-free days among those affected.	Protective link
Eyting, 2025[15]	United Kingdom	Natural experiment	Individuals eligible for HZ vaccination based on date of birth	282,541 individuals	ZVL	7 years	Using regression discontinuity approach, it was estimated that eligibility for the HZ vaccine reduced the probability of a new dementia diagnosis over a follow-up period of 7 years by 3.5 percentage points, corresponding to a 20% (95% CI: 6.5–33.4) relative reduction.	Protective link
Pomirchy, 2025[17]	Australia	Quasi-experimental study (natural experiment)	Individuals eligible for HZ vaccination based on date of birth	101,219 individuals	ZVL	7.4 years	Eligibility for HZ vaccination decreased the probability of receiving a new dementia diagnosis over 7.4 years follow up by 1.8 percentage points (95% CI: 0.4-3.3; p=0.01).	Protective link

Author, year	Country	Study type	Population	Sample size	Vaccine	Follow-up	Results	Direction of effect (protective, harmful or no-link)
			Mean age 77 years (SD 4.7)					
Harris, 2023[16]	United States	Retrospective cohort study	Individuals aged 65 years and older with and without HZ vaccination Mean age (SD) of vaccinated: 73.1 years (5.6) Unvaccinated: 72.2 years (5.1)	212,417 individuals with HZ vaccination	RZV and ZVL	8 years	Individuals who received the HZ vaccine were associated with a 25% lower risk of developing Alzheimer's disease compared to unvaccinated individuals (8.1% of vaccinated patients vs. 10.7% of unvaccinated patients developed AD during 8-year follow up. RR 0.75, 95% CI: 0.73–0.76 and ARR 0.02, 95% CI: 0.02–0.02).	Protective link
Lehrer, 2021[18]	United States	Cross-sectional analysis using survey data	Older adults participating in the 2017 Behavioural Risk Factor Surveillance System (BRFSS) survey	275 individuals with social activity impairment HZ vaccinated cohort: 99	Primarily ZVL, but maybe some RZV	Not applicable (cross-sectional study)	61.6% of vaccinated individuals reported no social activity impairment due to disorientation or memory loss, compared to 46.6% of unvaccinated individuals p=0.025. Multivariate linear regression analysis, adjusting for sex and education level (but not age), confirmed the significance of vaccination in reducing the risk of cognitive impairment (p=0.03).	Protective link

Author, year	Country	Study type	Population	Sample size	Vaccine	Follow-up	Results	Direction of effect (protective, harmful or no-link)
			Mean age of vaccinated: 70±7 years Unvaccinated: 65±10 years p<0.001	Non-vaccinated cohort: 176				
Schnier, 2022[19]	United Kingdom	Retrospective cohort study	Individuals aged ≥70 years with and without HZ vaccination and free of dementia	336,341 individuals. HZ vaccine cohort: 155,972	Primarily ZVL, but some RZV	7 years	HZ vaccine recipients were at lower risk of being diagnosed with dementia (aHR: 0.72; 95% CI: 0.69–0.75; univariable HR: 0.78; 95% CI: 0.75–0.81). HZ vaccination resulted in a lower risk of being diagnosed with AD (aHR: 0.81; 95% CI: 0.77–0.86) and at lower risk of being diagnosed with VaD (aHR: 0.66; 95% CI: 0.61–0.71). Individuals exposed to the vaccine had a 39% reduced hazard of dementia diagnosis after vaccination.	Protective link
Ukraintseva, 2024[6]	United States	Retrospective cohort study	Individuals aged 75 years from Health and Retirement Study (HRS) data	6,001 individuals in the AD cohort. 5,548 AD/AD-related dementias	ZVL	6.1 years 6.1 years (AD), 5.7 years (AD/ADRD+) and 6.3	Vaccination against HZ was associated with a lower risk of AD by approximately 21% (HR: 0.79; CI: 0.68–0.93). After pseudorandomisation (a statistical method that uses weighting based on demographic, socioeconomic, and health-related factors to simulate	Protective link

Author, year	Country	Study type	Population	Sample size	Vaccine	Follow-up	Results	Direction of effect (protective, harmful or no-link)
				and other dementias (ADRD+) cohort.		(Death) years until exit	randomised group assignment and reduce confounding) it was also associated a lower risk of AD/ADRD+ (HR:0.90; CI:0.81–0.99).	
Tang, 2025[7]	United States	Retrospective cohort study	Individuals aged ≥50 years eligible for RZV vaccination, in the Optum Labs Data Warehouse database Median age 62 years (IQR 54-71)	4,502,678 individuals. Unvaccinated: 3,835,968. Partially vaccinated: 206,297. Fully vaccinated: 460,413	RZV	5 years	HZ vaccination was associated with a decreased risk of dementia for two doses (aHR: 0.68; 95% CI: 0.67–0.70; p<.001) and for one dose (aHR 0.89; 95% CI: 0.87–0.92; p<0.001). Full vaccination with RZV conferred the most protection against dementia (32% decrease in risk; 95% CI: 30–33%; p<0.001) compared to those classified as unvaccinated), but even partial vaccination was associated with an 11% decrease in risk (95% CI: 8–13%; p<0.001) compared to being unvaccinated.	Protective link
Lophatananon, 2021[13]	United Kingdom	Nested case-control study within the UK Biobank cohort	Individuals aged ≥70 from UK biobank and primary care linkage health records.	228,223 participants. 2,378 incident dementia cases and	ZVL	3 years	The odds ratio for dementia in vaccinated individuals was 0.81 (95% CI: 0.66–0.99).	Protective link

Author, year	Country	Study type	Population	Sample size	Vaccine	Follow-up	Results	Direction of effect (protective, harmful or no-link)
				225,845 controls				
Yeh, 2024[8]	United States	Prospective cohort study	Participants from Nurses' Health Study (NHS), NHS II, and Health Professionals Follow-Up Study (HPFS) NHS mean age: 64.6 years (SD 6.7) NHS II mean age: 47.2 years (SD 5.3) HPFS mean age: 68.5 years (SD 8)	149,327 individuals (56,142 NHS, 66,966 NHS II, 26,219 HPFS)	HZ vaccine (does not specify)	Follow-up time since HZ occurrence: 1-4 years, 5-8 years, 9-12 years, ≥13 years	Long-term risk of SCD may be greater among women who were not vaccinated against HZ (p=0.09, NHSII) Based on data in the NHSII, the risk of SCD following HZ may potentially be greater among those who have not been vaccinated against HZ.	Protective link

Key: aHR – adjusted hazard ratio; AD – Alzheimer's disease; ADRD+ – Alzheimer's disease and related dementias plus other cognitive disorders; BRFSS – Behavioral Risk Factor Surveillance System; CI – confidence interval; HPFS – Health Professionals Follow-Up Study; HR – hazard ratio; HZ – herpes zoster; MCI – mild cognitive impairment; NHS – Nurses' Health Study; OR – odds ratio; p-value – probability value (statistical significance); RZV – recombinant zoster vaccine; SCD – subjective cognitive decline; VaD – vascular dementia; ZVL – live attenuated zoster vaccine.

3.3 Association between vaccinations in general and risk of dementia

Several recent systematic reviews and meta-analyses have examined the potential relationship between adult vaccinations and the risk of developing dementia. Five relevant systematic reviews published between 2022 and 2024 were identified.[21-25] These reviews provide evidence on specific vaccines, including influenza and Bacillus Calmette-Guérin (BCG), as well as the broader impact of routine adult immunisation. Two of the included studies focussed on use of the BCG vaccine in the context of bladder cancer, where BCG is administered as an immunotherapy. A summary of the characteristics and results of these studies is presented in Table 4. For the five systematic reviews included in this scoping report, the corrected covered area (CCA) was calculated at 18.5%, indicating a very high level of overlap, with the corresponding citation matrix provided in the Appendix.

A systematic review and meta-analysis by Veronese et al. in 2022 investigated the association between seasonal influenza vaccination and the risk of developing dementia.[24] This review included five observational studies, with a total of 292,157 older adults (mean age 75.5 years; 46.8% female) who did not have a recorded diagnosis of dementia at baseline. Over a mean follow-up period of nine years, influenza vaccination mitigated the risk of a dementia diagnosis by 3% (RR: 0.97; 95% CI: 0.94 to 1.00; $I^2 = 99\%$). After adjustment for a mean of nine potential confounders (for example, age, sex, diabetes), influenza vaccination at baseline was associated with a significantly lower risk of dementia during follow-up of approximately 29% (RR: 0.71; 95% CI: 0.60 to 0.94; $p<0.0001$; $I^2 =95.9\%$). These findings suggest that influenza vaccination may play a role in reducing the risk of dementia among older adults.

A 2023 study[22] systematically evaluated whether influenza vaccination reduces the risk of developing dementia in older adults. The meta-analysis included six cohort studies comprising 2,087,195 individuals without a recorded dementia diagnosis at baseline, with a follow-up period ranging from 4 to 13 years. The pooled analysis found that individuals who received at least one influenza vaccination had a 31% lower risk of developing dementia (RR: 0.69; 95% CI: 0.57 to 0.83). Sensitivity analyses confirmed the robustness of the findings, although there was high heterogeneity ($I^2 = 98.9\%$), mainly driven by two large US studies. The authors concluded that influenza vaccination in older adults was associated with a marked reduction in the risk of dementia.

A 2022 systematic review and meta-analysis[25] investigated the association between routine adult vaccinations and the risk of developing dementia. This review included 17 observational studies, with a total of 1,857,134 participants. Multiple vaccines were included in the analysis, including vaccines for seasonal influenza; herpes

zoster; tetanus, low dose diphtheria and low dose acellular pertussis (Tdap); Bacillus Calmette-Guérin (BCG); pneumococcal; poliomyelitis vaccines; hepatitis A; hepatitis B; typhoid; rabies; yellow fever; cholera; and meningitis. The pooled results indicated that adult vaccinations were associated with a 35% reduction in dementia risk (HR: 0.65; 95% CI: 0.60 to 0.71), p overall effect <0.001; $I^2 = 91.8\%$, p heterogeneity<0.001). Significant protective effects were observed for several vaccines, including rabies (HR: 0.43); Tdap (HR: 0.69); herpes zoster (HR: 0.69); influenza (HR: 0.74); hepatitis A (HR: 0.78); typhoid (HR: 0.80); and hepatitis B (HR: 0.82). The study also reported a greater reduction in the risk of dementia in individuals who received multiple types of vaccines or received the seasonal influenza vaccine more frequently. The association between vaccination and reduced dementia risk did not vary significantly by age, gender, or type of dementia. The authors concluded that routine adult vaccinations are associated with a significant reduction in dementia risk and may be an effective strategy for dementia prevention. However, they emphasised the need for further research to establish causality and understand the underlying mechanisms of this association.

A systematic review and meta-analysis of the impact of the BCG vaccine on the risk of dementia in bladder cancer patients was published by Ibrahim et al. in 2024.[21] When used to treat bladder cancer, the treatment involves intravesical BCG administration, delivered directly into the bladder to induce a local immune response. While some systemic absorption occurs, administration in this manner is inherently different to intradermal BCG administration for active immunisation against tuberculosis. Eight observational studies were included; due to overlapping populations in some of the studies, two separate main analyses were conducted. In the first analysis, which pooled data from five studies that were non-overlapping (n=88,852). an association with lower risk of dementia was observed with BCG vaccination, although this was not statistically significant (HR: 0.65; 95% CI: 0.40 to 1.06; $I^2 = 85\%$). In contrast, the second analysis, pooling six studies (n=70,025), reported a statistically significant reduction in dementia risk (HR: 0.63; 95% CI: 0.40 to 0.97; $I^2 = 83\%$). A sensitivity analysis excluding unpublished studies did not significantly alter the outcomes. Additionally, a separate meta-analysis focusing on Alzheimer's disease found no significant risk reduction associated with BCG vaccination. The authors concluded that BCG administration in bladder cancer patients may reduce dementia risk, but that the treatment effect is likely to be small.

A study[23] examined whether BCG vaccination could reduce the risk of Alzheimer's disease, particularly in patients with non-muscle-invasive bladder cancer (NMIBC). Based on six cohort studies with 47,947 individuals, the meta-analysis found that BCG vaccination was associated with a 26% reduction in the risk of developing Alzheimer's disease (p<0.00001). Subgroup analyses suggested that the protective effect was more pronounced among adults over 75 years of age and female

participants. However, the results showed considerable heterogeneity among studies, especially in male participants and those under 75 years of age. The authors concluded that BCG vaccination may offer a protective effect against Alzheimer's disease progression in certain populations, though they cautioned that further research was needed.

Overall, evidence from the five systematic reviews suggests that receipt of routine adult vaccinations may be associated with lower risk of dementia. Seasonal influenza vaccination was linked with reductions of approximately 26% to 31% over follow-up periods ranging from 4 to 13 years, while analyses that considered a broader range of adult vaccines was associated with a pooled reduction of 35%. Findings for intravesical BCG vaccination used as a treatment for bladder cancer reported reductions in dementia risk ranging from 26% to 37%, however there were mixed findings with respect to Alzheimer's disease**.**

Table 4. Summary of systematic reviews and meta-analysis examining the association between adult vaccination and risk of dementia

Author, year	Country	Population	Number of studies included and sample size	Vaccine	Results	Direction of effect (protective, harmful or non-link)
Veronese, 2022[24]	Populations from Taiwan, US and Canada	Older adults (mean age 75.5 ± 7.4 years; 46.8% female) without dementia at baseline.	5 studies 292,157 individuals	Influenza vaccine	Influenza vaccination mitigated the risk of dementia by 3% (RR:0.97; 95% CI: 0.94– 1.00; I^2 =99%). When adjusted for confounders (for example age, sex, diabetes), influenza vaccination was associated with a 29% lower risk of dementia (RR=0.71; 95% CI: 0.60–0.94; I^2 =95.9%).	Protective link
Wu, 2022[25]	Populations from US, China, UK, Canada and Israel	Adults aged 50 years and older, numerous populations including those with bladder cancer, COPD, CKD, CHF, periodontitis, patients who underwent transurethral resection, those from cardiovascular health study,	17 studies 1,857,134 individuals	Multiple vaccines, including influenza, herpes zoster, tetanus & diphtheria & pertussis (Tdap), Bacillus Calmette-Guerin (BCG), pneumococcal, and poliomyelitis vaccines. Hepatitis A, hepatitis B, typhoid, rabies, yellow fever, cholera, and meningitis vaccines	The overall pooled results showed that vaccinations were associated with a 35% lower risk of dementia (HR: 0.65; 95% CI: 0.60–0.71, p <0.001; I^2=91.8%, p heterogeneity <0.001). All types of vaccination were associated with a lower risk of dementia, with a statistically significant difference observed with rabies (HR:0.43), tetanus & diphtheria & pertussis (Tdap) (HR:0.69), herpes zoster (HR:0.69), influenza (HR:0.74), hepatitis A (HR:0.78), typhoid (HR:0.80), and hepatitis B (HR:0.82) vaccination.	Protective link

Author, year	Country	Population	Number of studies included and sample size	Vaccine	Results	Direction of effect (protective, harmful or non-link)
		those on Medicare database and Veterans Health Administration.				
Ibrahim, 2024[21] *	Populations from US, Israel, Denmark and Sweden	Patients with bladder cancer who received Bacillus Calmette–Guérin (BCG) as therapy. Most patients were males (>70%) and mean age ranged from 69 to 83	8 studies 98,879 individuals	BCG vaccine	The first analysis showed that compared to controls, BCG did not reduce dementia risk (5 studies pooled, n=88,852, HR: 0.65; 95% CI: 0.40–1.06, I^2 = 85%) whereas there was a marginally significant risk reduction in the second analysis (6 studies pooled, n=70,025, HR: 0.63; 95% CI: 0.40–0.97, I2 = 83%). Additional meta-analysis showed that BCG did not reduce the risk of Alzheimer's disease.	No-link
Sun, 2023[22]	WHO regions: three from a region of the Americas and three	Participants without dementia at baseline. mean age: 61.8–75.5 years, 57.05% males, and 149,804 (7.18%) cases of dementia	6 studies 2,087,195 individuals	Influenza vaccine	When adjusted for age and sex, influenza vaccination was associated with a 31% reduction in dementia risk based on pooled analysis (RR: 0.69; 95% CI: 0.57– 0.83).	Protective link

Author, year	Country	Population	Number of studies included and sample size	Vaccine	Results	Direction of effect (protective, harmful or non-link)
	from Western Pacific region	occurred during 4.00–13.00 years of follow-up				
Umar, 2024[23]	Populations from US and Israel	Individuals with and without BCG vaccine	6 studies 47,947 individuals	BCG vaccine	BCG vaccine administration lowered the risk of AD by 26% in non-muscle-invasive bladder cancer (HR 0.74; 95% CI: 0.67–0.82, $p < 0.00001$, $I^2 = 28\%$)). Subgroup analyses showed that BCG vaccination showed a potentially notable preventive effect on AD in older adults (>75 years) and female participants. Conversely, no preventative effect was observed among male participants and those aged <75 years.	Protective link

Key: AD – Alzheimer's disease; BCG – Bacillus Calmette–Guérin; CHF – congestive heart failure; CI – confidence interval; CKD – chronic kidney disease; COPD – chronic obstructive pulmonary disease; HR – hazard ratio; I^2 – I-squared statistic (a measure of heterogeneity in meta-analyses); NMIBC – non-muscle-invasive bladder cancer; RR – relative risk; Tdap – Tetanus, low dose diphtheria, and low dose acellular pertussis.
* As some included studies contained overlapping populations, two separate main analyses were undertaken when pooling data.

4 Overall summary of findings

This scoping review explored the potential associations between HZ infection, HZ vaccination and general adult vaccinations and the onset of dementia. The following findings emerged:

- **Herpes zoster infection and dementia risk**
  Twelve studies evaluated the link between HZ infection and dementia. Results were mixed. Four studies found no significant association, and one reported evidence to suggest that HZ may have a protective effect among frail individuals and females. Seven studies reporting a harmful association, indicating a 12% to 47% increase in the risk of dementia among individuals with a diagnosis of HZ. Two studies considered severe disease, specifically, hospitalisation due to HZ and herpes zoster ophthalmicus, with the latter associated with a markedly higher risk of dementia (hazard ratio of 2.97). Notably, four of five studies that reported on the impact of HZ treatment observed that the risk of dementia was reduced in those who were issued antiviral treatment, compared with those who were not, suggesting that timely treatment may mitigate some or all of the potential neurocognitive consequences of the infection. The findings in terms of the association between HZ infection and dementia risk all come from observational studies that are highly susceptible to confounding and bias, and cannot be used to confirm if HZ infection itself causes changes in dementia risk.
- **Herpes zoster vaccination and dementia risk**
  All ten studies included in the review reported a protective association between HZ vaccination, with the authors concluding that HZ vaccination (live attenuated zoster vaccine (ZVL) and the recombinant zoster vaccine (RZV)), reduced the risk of dementia. Relative reductions in dementia risk ranged from 20% to 39%, with stronger protective effects often observed with RZV and among fully vaccinated individuals. No study reported a harmful or null effect. These findings were consistent across a mix of study designs, including natural experiments, retrospective cohorts, and prospective data, reinforcing the credibility of the observed protective association. However, while a number of the studies accounted for possible confounding factors, none did so comprehensively, so the observed protective associations cannot be interpreted as evidence that HZ vaccination directly reduced dementia risk.
- **General vaccinations and dementia risk**
  Five recent systematic reviews and meta-analyses indicate a broad protective association between routine adult vaccinations and dementia risk. These reviews included vaccines such as influenza, HZ, Tdap, hepatitis A, hepatitis B as well as intravesical BCG vaccination administered as treatment for bladder cancer. While acknowledging the high degree of overlap in the included studies across the systematic reviews, the largest body of evidence related to seasonal influenza

vaccination with studies consistently reporting a protective effect against dementia, with relative risk reductions of 26% to 31% over follow-up periods ranging from four to 13 years, and with evidence of a greater reduction in risk in individuals who received the seasonal influenza vaccine more frequently. However, these findings are also based on observational evidence that did not adjust for important confounders, making it unclear whether the reduced dementia risk reflects the biological effects of the vaccination.

5 Discussion

The current body of evidence suggests that HZ vaccination may play a protective role in reducing the risk of dementia. However, it is unclear if this protective effect is specific to HZ vaccination or part of a broader protective effect of other lifestyle and health behaviours, decision-making and uptake of vaccination in older adults. While HZ infection itself may elevate the risk of dementia, the findings across studies are inconsistent, with evidence also suggesting that timely antiviral therapy may mitigate some of this risk. More generally, routine adult vaccination may contribute to dementia prevention, warranting further investigation into shared immunological or inflammatory mechanisms that could explain these associations and a better understanding of the wider underlying determinants of dementia.

The therapeutic indication of both the currently authorised HZ vaccine (recombinant adjuvanted vaccine (RZV) and the live attenuated zoster vaccine (ZVL) which has been discontinued) is limited to the prevention of HZ and post-herpetic neuralgia, as demonstrated in randomised placebo-controlled clinical trials. The HIQA HTA, published in July 2024, concluded that that there was clear and consistent evidence that the recombinant adjuvanted vaccine (RZV) is safe and effective at reducing HZ cases, but that its effectiveness diminishes over time.[1] Protection against dementia is not a licensed indication, possibly reflecting the fact that the existing evidence base is not yet sufficient to support regulatory approval for this outcome. Internationally, dementia prevention has not been incorporated into formal HTAs or cost-effectiveness assessments for HZ vaccination, and, to date, no national immunisation technical advisory group (NITAG) has included dementia outcomes in economic modelling. Recent discussions, including those of the UK Joint Committee on Vaccination and Immunisation (JCVI) in June 2025, have considered the emerging observational evidence only at a horizon-scanning level and concluded that the effect is not currently quantifiable for economic evaluation. The JCVI minutes also emphasised that existing data are derived largely from younger cohorts and observational designs, and that further real-world evidence would be required before dementia prevention could be considered within programme evaluations.[26]

From an epidemiological and public health perspective, even modest relative reductions in dementia risk could translate into meaningful absolute benefits at the

population level. According to the Health Service Executive (HSE), approximately 64,000 people are currently living with dementia in Ireland.[27] If the associations observed in the literature were causal, a 5% reduction in dementia incidence or prevalence would correspond to roughly 3,000 fewer individuals living with dementia, while a 10% reduction would equate to over 6,000 fewer cases. While these figures are illustrative rather than predictive, they highlight the potential population-level implications of interventions that confer even small protective effects. Given the substantial personal, societal, and healthcare system burden associated with dementia, such reductions could have important implications for quality of life, caregiver burden, and long-term health and social care planning. However, it is also possible that experimental studies could also lead to smaller or non-significant estimates of benefit, particularly if the benefit relates to underlying confounding determinants of health.

Several important limitations must be considered when interpreting the findings from these studies. Most included studies were observational in nature, for example retrospective cohort studies. Such observational designs are inherently prone to confounding and bias; while many studies adjusted for some covariates, residual confounding remains possible.[28] An especially important confounder in these studies is the "healthy vaccinee effect", a well-documented source of bias in observational vaccine studies.[29, 30] Individuals who seek vaccination typically differ to those who do not: they are more likely to regularly engage with healthcare services, adhere better to prescribed treatments, maintain healthier diets, exercise more and are less likely to smoke — all behaviours independently linked to a lower risk of cognitive decline and dementia.[31] These favourable baseline characteristics skew risk estimates, often exaggerating the apparent benefit of vaccination. Techniques such as propensity score matching and extensive covariate control can attenuate, but do not eliminate this bias. As a result, the current evidence cannot separate how much of an observed risk reduction is due to the biological effect of vaccination from the healthier profile of vaccine recipients. In addition, several studies may be affected by time-related biases, including differences in the timing of cohort entry, exposure classification and follow-up, which can distort associations if not appropriately addressed. Also, none of the included studies conducted a systematic cognitive assessment at baseline to confirm the absence of dementia or any cognitive impairment. Instead, baseline status was determined by the presence or absence of a recorded dementia diagnosis, which does not preclude the possibility that individuals had undiagnosed dementia or early cognitive decline at study entry.

Another challenge is the significant overlap in uptake among different adult vaccines. For reference, the uptake of seasonal influenza vaccine in Ireland for the 2024/25 season increased with age, ranging from 49% in 60 to 69-year-olds, to 89% in those aged 75 years and over.[32] Recipients of an HZ vaccine are also likely to be up to

date with other vaccinations like influenza, pneumococcal, and if indicated, Tdap.[33, 34] Similarly, individuals who receive antiviral therapy for HZ infection are often those with better access to care, have higher health literacy and greater socioeconomic advantage.[35] Because few databases capture a comprehensive lifetime vaccination record,[36, 37] it is not possible to fully adjust for the confounding introduced by other immunisations or by past or concurrent infections. From the available evidence it is not possible to determine whether the observed reductions in dementia risk are due to the specific immunological impact of the HZ vaccine itself or the combined influence of overall vaccine uptake and associated health-seeking behaviours.

Considerable heterogeneity exists across the studies reviewed, including differences in population characteristics, type of vaccine administered (ZVL vs RZV), dementia definitions (all-cause dementia, specific subtypes of dementia, Alzheimer's disease), length of follow-up, and analytical approaches. This variation limits the direct comparability of effect sizes and complicates synthesis of findings. Several studies used administrative health databases or self-reported survey data, which may be subject to coding errors, misclassification of outcomes, and incomplete detection of confounders such as comorbidities or lifestyle factors. The majority of studies examining the association between HZ vaccination and dementia evaluated populations aged 65 years and older, aligning with eligibility criteria for national HZ vaccination programmes. Where reported, the mean age of participants ranged from 47.2 to 77 years. It is unclear if any benefit associated with HZ vaccination would apply equally across all age bands. Differences in follow-up duration between vaccinated and unvaccinated groups may also introduce bias if attrition is related to both exposure and dementia risk. Importantly, it is not clear whether these confounders would consistently bias in a single direction across studies. For studies examining the broader question of adult vaccination, the umbrella review identified a high degree of overlap in primary studies included across systematic reviews, which may give an inflated impression of the volume of evidence.

Since the completion of our search, several new studies have been published that align with the existing evidence base. These include additional quasi-experimental analyses from Canada (Pomirchy, 2026)[38] and Wales (Xie, 2025)[39], which strengthen the natural-experiment literature, but do not resolve the underlying concerns regarding residual confounding. A very large US cohort study (Polisky, 2025)[40] incorporated extensive covariate adjustment (~400 variables), representing one of the most rigorous attempts to date to account for confounding in this literature. The study reported patterns consistent with waning vaccine-derived protection, and the authors emphasised that the return of dementia risk towards a relative risk of approximately 1.0 suggests vaccination delays progression rather than prevents dementia diagnoses, an import nuance when interpreting the magnitude and nature of any potential effect. Despite this extensive adjustment, the

authors noted that unmeasured confounding could not be excluded. A US study by Rayens et al. (2026)[41] reported that vaccination with two doses of the RZV was associated with a significant reduction in the risk of dementia, which persisted after accounting for healthy vaccinee bias (using Tdap as an active comparator). In addition, a large nationwide Korean cohort study (Oh et al., 2026)[42] involving over two million adults aged ≥50 years reported that live HZ vaccination was associated with lower risks of memory disorders (aHR 0.88) and Alzheimer's disease (aHR 0.75), with restricted mean survival analyses indicating only modest gains in event-free time (restricted mean survival time gains of 15.5 and 11.3 days per decade). The authors interpreted these findings as evidence of delayed onset rather than complete prevention of cognitive decline, and noted that protective associations attenuated over time and varied by behavioural risk factors such as smoking and alcohol use. A large US Medicare cohort study of RZV recipients (dos Reis et al., 2026) found a 26% to 33% lower risk of new-onset dementia, Alzheimer's disease, and vascular dementia compared with unvaccinated comparators matched on age, sex and ethnicity.[43]

While these newer studies reinforce the overall direction of association, they do not alter the fundamental uncertainties and still do not provide the effect-size precision desirable for economic modelling. Substantial imprecision in effect size generally translates into notable uncertainty in outcomes, in this case cost-effectiveness. A recent Delphi consensus on drug repurposing for Alzheimer's disease identified HZ vaccination as one of only three high-priority candidates for further evaluation.[44] This reflects growing interest among experts in its potential relevance to neurodegenerative pathways and population-level dementia risk reduction. However, the consensus highlighted the need for formal clinical trials for the treatment and prevention of Alzheimer's disease.

Several mechanistic hypotheses have been proposed to explain how vaccination, whether targeting HZ, influenza, or other pathogens, might influence neurocognitive health. One proposed mechanism involves the reduction of systemic inflammation. Vaccines help prevent infections that would otherwise trigger chronic systemic inflammation, a well-established contributor to neurodegeneration.[45] Another hypothesis focuses on trained innate immunity. Some vaccines, such as BCG, appear to induce broad epigenetic reprogramming of innate immune cells, which enhances the body's antiviral and anti-inflammatory responses beyond the specific pathogen targeted by the vaccine.[46] A third proposed mechanism involves antigenic mimicry and cross-reactivity, in which antibodies generated in response to certain viral antigens may inadvertently interfere with pathological processes in the brain, such as amyloid-β aggregation.[47] While these mechanisms are biologically plausible, they remain largely speculative and are unlikely to act in isolation. Importantly, the presence of a plausible mechanism does not mean that all vaccines will have

identical or additive effects on dementia risk. These hypotheses could be tested through mechanistic studies and well-controlled human trials to better understand the complex interactions between vaccination, immune function, and neurodegenerative disease. In recognition of the need for more definitive evidence, a large-scale, four-year research initiative was launched in March 2025 by GSK, the UK Dementia Research Institute, and Health Data Research UK to explore the association between RZV and a reduced risk of dementia.[48] This research initiative will leverage real-world health data to examine whether receipt of RZV is linked with changes in dementia incidence at the population level.

As this was a scoping review, several methodological limitations should be acknowledged. Scoping reviews are designed to provide an overview of the existing literature rather than to assess the quality or strength of the evidence. As such, we did not conduct a formal critical appraisal of the included studies. While our search strategy was targeted and inclusive, relevant studies may still have been missed. In addition, this scoping review represents a point-in-time assessment of the literature, and we acknowledge that further studies have been published and that additional research is ongoing since the completion of our search.

From a public health perspective, while general adult immunisation is not currently promoted as part of a multifactorial strategy to prevent dementia, the emerging evidence suggests that it may play a supportive role in maintaining cognitive health. However, expectations should remain measured, introducing an HZ vaccination programme on its own may not lead to substantial or clearly measurable reductions in dementia incidence. Instead, general vaccination may be considered as a potentially complementary measure within a broader, multifactorial approach to promoting healthy cognitive ageing.

6 Conclusion

Observational evidence links HZ vaccination with a lower risk of dementia, and the consistency of this association across multiple studies suggests a protective effect may exist. However, these associations are confounded by underlying determinants of dementia, health-seeking behaviour, co-vaccination, and other unmeasured factors. Evidence demonstrating an association between HZ incidence and increased dementia risk, lends plausibility to a protective effect of HZ vaccination, alongside broader findings that vaccination in general may be associated with a lower risk of dementia. There is also evidence that timely antiviral treatment for acute HZ infection may mitigate some of the elevated dementia risk associated with HZ infection, suggesting that prompt management of HZ could be relevant to long-term neurocognitive outcomes. However, this scoping review of the existing evidence shows that although the direction of association is encouraging, it is not possible to determine the precise contribution or magnitude of effect that HZ vaccination alone

may have in reducing dementia risk. While the direction of association is broadly consistent, the current evidence base lacks robustness and causal certainty. A major real-world data study is now underway to more definitively examine whether receipt of HZ vaccination is associated with changes in dementia incidence. The results of this work are expected to strengthen the evidence base and may help clarify whether dementia outcomes could be considered in future evaluations. The evidence of a protective effect of vaccination generally against dementia suggests that staying up to date with all recommended vaccines complements established lifestyle and vascular strategies for healthy cognitive ageing. There is substantial uncertainty in the effect size, and what it might be independent of other vaccinations currently included in the adult immunisation programme in Ireland. The evidence outlined in this scoping report should be considered alongside an updated review of the clinical effectiveness of shingles vaccination, informing whether the impact on healthcare resources needs to be re-assessed.

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Appendix

Overlap of primary studies included in systematic reviews investigating the association between adult vaccination and dementia risk

Primary studies included	Veronese, 2022[24]	Wu, 2022[25]	Ibrahim, 2024[21]	Sun, 2023[22]	Umar, 2024[23]
Weimken, 2021[49]	✓	✓		✓	
Lee, 2020[50]	✓	✓		✓	
Liu, 2016a[51]	✓	✓		✓	
Liu, 2016b[52]		✓			
Luo, 2020[53]	✓	✓		✓	
Verreault, 2001[54]	✓	✓		✓	
Liu, 2016[52]		✓			
Amran, 2020[55]		✓			
Tyas, 2001[56]		✓			
Wilkinson, 2021[57]		✓			
Scherrer, 2021a[58]		✓			
Klinger, 2021[59]		✓	✓		✓
Kim, 2021[60]		✓	✓		✓
Gofrit, 2019[61]		✓	✓		✓
Ukraintseva, 2020[62]		✓			
Wiemken, 2022[63]		✓			
Scherrer, 2021b[64]		✓			
Sørup, 2022‡			✓		
Han, 2023[65]			✓		
Weinberg, 2023[66]			✓		✓
Bukhbinder, 2022[67]				✓	
Dow, 2022[68]					✓
Makrakis, 2022[69]					✓

‡ A precise reference was not given for this study in the citing review, on the grounds that it was published in conference proceedings and did not undergo peer-review.

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For further information please contact:

Health Information and Quality Authority

George's Court

George's Lane

Smithfield

Dublin 7

D07 E98Y

+353 (0)1 8147400

info@hiqa.ie

www.hiqa.ie

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