McMaster University | Health Forum

Living Evidence Synthesis

Effectiveness of trivalent and quadrivalent influenza vaccines in preventing infection, hospitalization, and severe outcomes in the 2024–2025 season onwards

21 May 2026

[MHF product code: LES 25.3]

Context

- Seasonal influenza (the flu) is a globally common respiratory virus that spreads easily when someone with the flu coughs or sneezes.(1)
- Vaccination is considered the best method to prevent serious outcomes associated with influenza infection.(1)
- In Canada, influenza and pneumonia are ranked among the top 10 leading causes of death.
  - While most people recover from the flu in 7 to 10 days, some population groups are at increased risk of severe influenza illness.(2)
  - Each year, influenza causes an estimated 3,500 deaths and 12,200 hospital stays.(3)
  - Adults aged 65 years and older account for 46% of the reported hospitalizations.(4)
- Influenza viruses constantly evolve, requiring continuous global monitoring and frequent reformulation of vaccines.(5)
- While trivalent and quadrivalent vaccines show potential for influenza prevention, uncertainty persists about their effectiveness across different populations and influenza types.(6)
  - Factors such as age, health status, and the match between vaccine strains and circulating viruses can all influence vaccine efficacy and effectiveness.
- Given this, the effectiveness of influenza vaccines can vary from season to season, depending on factors such as the match between vaccine strains and circulating viruses, as well as the age and health status of vaccinated individuals.(7)
- Monitoring vaccine performance is crucial for understanding and improving vaccination benefits.
- This monitoring can be done through vaccine effectiveness (VE) studies that evaluate how circulating and evolving influenza viruses affect vaccine performance in real-world conditions, considering factors such as outcome, season, and population.
- The Public Health Agency of Canada (PHAC) aims to monitor the effectiveness and impact of influenza vaccines over time to support vaccine policy, enhance situational awareness, inform routine briefings, and ultimately protect Canadians from severe illness.
  - In synthesizing evidence about the effectiveness of trivalent and quadrivalent vaccines in preventing influenza, it is important to focus on effects at a population level, with particular emphasis on groups disproportionately affected by or at higher risk of contracting influenza.
  - Such evidence is crucial for supporting vaccine policy, enhancing situational awareness, and ultimately protecting vulnerable populations from severe influenza-related outcomes.
- This living evidence synthesis (LES) has been requested to inform those efforts.
  - It builds on previous versions (LES 25.1 and 25.2), which examined the effectiveness of influenza vaccines against influenza infection in older adults, infants and populations across all age group, while addressing a broader set of outcomes and research questions.

This current version of the LES introduces several refinements to that scope to strengthen the relevance of findings for vaccine policy decision-making, which describe in the research questions section below.

Questions

From the previous to the current version of this LES, the primary research question has been substantially refined and the secondary research questions removed. The earlier version assessed the effectiveness of trivalent and quadrivalent influenza vaccines across the general population and multiple age groups, whereas the current report narrows its focus to two priority populations: older adults aged ≥60 years and children aged 0–17 years (including subgroup analysis 0–5 years).

The scope of outcomes has also been updated. In addition to medically attended acute respiratory illness (MAARI), outpatient visits, hospitalization, ICU admission, and death included previously, emergency department (ED) visits have been added as a distinct outcome in this current version of the LES, reflecting evolving patterns of healthcare utilization.

Furthermore, the geographic and temporal scope has been restricted. This current version of the LES includes evidence from the northern hemisphere (2024–2025 season onwards) enhancing relevance to the current vaccine decision-making context.

All secondary research questions from the previous LES versions, including those addressing immunocompromised populations and candidate vaccine viruses (CVVs) against highly pathogenic Avian Influenza A(H5) viruses (have been removed from this update. These topics may be revisited in future reports.

The updated research question for this current report is as follows:

- What is the effectiveness of trivalent and quadrivalent influenza vaccines in preventing influenza-associated outcomes (medically attended influenza infection, outpatient visits, emergency department (ED) visits, hospitalization, intensive care unit (ICU) admission, and death) across different influenza types and subtypes (all types for 0-5 years old and subtypes, A, A(H1N1)pdm09, A(H3N2), and B) in the following populations: a) older adults aged ≥60 years; and b) children aged 0–17 years as reported in the northern and southern hemispheres in the 2024−2025 and 2025-2026 seasons, respectively?

High-level summary of key findings

Evidence identified

- We identified 7,602 records and included 22 studies for data from 2024/2025 onwards, of which 17 were newly identified in this version, and five studies carried over from previous versions of the LES:
  - 21 studies were test-negative case-control designs (17 were newly identified in this version) and one study used cohort design.
  - 17 studies were included for meta-analysis (12 were newly identified in this version).
- The risk of bias (ROBINS-I Version 2) among 22 studies was assessed as the following:
  - Moderate risk of Bias (n=12)
  - Serious Risk of Bias (n=10)
- Random-effects models were used to calculate pooled effects as we anticipated meaningful heterogeneity across studies and group comparisons.
- When data were available, subgroup analyses were computed to examine how findings varied according to different vaccine seasons and age groups.

Key findings in relation to the research question

- Of the 22 included studies covering the 2024/2025 season (n=17), the 2025/2026 season (n=4), Northern Hemisphere interim studies and the Southern Hemisphere 2025 season (n=1), 21 used a test-negative case-control design, while one

study used a cohort design with target trial emulation. The studies were conducted across diverse healthcare settings, including community laboratories, primary care, sentinel practitioner offices, emergency departments, and inpatient hospital facilities.

- The evidence spanned multiple geographic regions:
  - North America (the United States and Canada)
  - Europe (Italy, the United Kingdom, Germany, France, Denmark, Finland, and Sweden) and ten additional countries via European multi-centre networks (Belgium, Croatia, Hungary, Ireland, Lithuania, Malta, Netherlands, Portugal, Romania, Spain)
  - Asia (China, Japan, and South Korea)
  - Southern Hemisphere (Argentina, Australia, Brazil, Chile, New Zealand, Paraguay, Peru, Uruguay).
- Compared with previous LES versions, the meta-analysis included in this version broadened the evidence base by adding new studies and extending the geographic and healthcare-setting representation.
- This update incorporates preliminary 2025/26 Northern-Hemisphere interim data and Southern-Hemisphere 2025 data that were not available in the prior review, including the first vaccine effectiveness estimates against the antigenically distinct A(H3N2) subclade K (J.2.4.1).
- For the 2024/25 season, vaccine effectiveness against medically attended influenza A was moderate, and higher in children than in older adults:
  - A(H1N1)pdm09
    - Children and adolescents (<18 years): VE 45% (95% CI 32–55)
    - Older adults (≥60 years): VE 38% (95% CI 27–47)
  - A(H3N2)
    - Children and adolescents: VE 47% (95% CI −44 to 81), not statistically significant
    - Older adults: VE 30% (95% CI −21 to 60), not statistically significant.
- For the 2024/25 season, vaccination provided meaningful protection against influenza-associated hospitalisation:
  - Influenza A: VE 59% (95% CI 49–68) in children and adolescents, 46% (95% CI 35–54) in older adults
  - Protection was strongest against A(H1N1)pdm09-associated hospitalisation in children and adolescents (VE 67%, 95% CI 62–71), with moderate protection in older adults (VE 42%, 95% CI 32–51)

Box 1: Approach and supporting materials

We retrieved candidate studies by searching: 1) Medline, 2) Embase via OVID, 3) Preprint Citation Index (e.g. bioRxiv, medRxiv), and 4) ClinicalTrials.gov. We also included studies identified by subject-matter experts who reviewed the protocols and final report. Searches were conducted for studies reported in English, French, Spanish, Portuguese, Arabic, and Chinese conducted with humans and published between January 2023 and 03 March 2026. Our detailed search strategy is included in Appendix 1.

For efficacy/effectiveness outcomes, any experimental design such as interventional trials or observational designs including cohort, case-control, before-after studies, interrupted time-series, and case series were considered for inclusion. For all outcomes, evidence syntheses were tracked, and any relevant primary studies from them were pulled out for our analysis. A full list of included studies is provided in Appendix 2. Studies excluded at the last stages of reviewing are provided in Appendix 3.

Population of interest: General population older adults aged ≥65 years, children aged 0 to 17 years, individuals with immunocompromising conditions.

Intervention: Vaccination with trivalent or quadrivalent influenza vaccines.

Control: Unvaccinated individuals in current season.

Primary outcomes: Any of the following outcomes associated with influenza A, influenza A(H1N1) pdm09, influenza A(H3N2), and influenza B): 1) medically attended influenza infection 2) hospitalization; 3) ICU admission; and 4) death.

Data extraction: Data extraction was conducted by one team member.

Critical appraisal: The risk of bias (ROB) of individual studies was assessed using validate ROBINS-I. Judgements for the domains within these tools were decided by one reviewer and details are provided in Appendix 4. PRISMA flow diagram are provided in Appendix 5.

Summaries: We summarized the evidence by presenting narrative evidence profiles across studies by outcome measure. When appropriate, statistical pooling of results was performed using random effects methods. The presence of heterogeneity was measured with the I^2 estimator. When heterogeneity was higher than 50%, we suppressed the meta-analysis and reported the findings only narratively.

The next update to this document is to be determined.

- Moderate protection was also observed against A(H3N2)-associated hospitalisation (VE 39% in children and adolescents, 44% in older adults), with effectiveness very similar across age groups for this subtype.
- Vaccination reduced severe outcomes in older adults (one study):
  - One study reported 63% VE (95% CI 54–73) against influenza-related death among adults aged 65 year and older
  - Protection was highest among adults aged 75 years and older (VE 69%, 95% CI 59–78) compared with those aged 65 to 74 years (VE 45%, 95% CI 19–72).
- Enhanced vaccines consistently outperformed standard-dose vaccines against influenza-associated hospitalisation for the 2024/25 season
  - High-dose IIV4 with VE ~46–63% vs. adjuvanted IIV4: VE ~46–48% vs. standard-dose IIV4: VE ~31–44%.
- Early 2025/26 evidence suggested lower and more variable VE during a period of A(H3N2) subclade K dominance:
  - VE against medically attended influenza was lower, particularly in older adults
  - Protection against hospitalisation remained meaningful in children (single-study estimate: VE 74% against influenza A-associated hospitalisation in 2–17-year-olds, 73% against subclade K specifically), but was more modest and uncertain in older adults
  - Despite the antigenic distance of subclade K from the 2025/26 vaccine reference strain, three studies demonstrated measurable cross-protection in children, supporting continued vaccine recommendation.
- Severe outcomes were sparsely reported: no included study analyzed ICU admission or invasive ventilation as a VE outcome; and there was only one study reporting influenza-related death, finding more durable protection against death than against medically attended infection or hospitalization across the season.

Heterogeneity was low (I^2=0%) for influenza B and A(H1N1) hospitalization pools but substantial-to-considerable (I^2=73–85%) for influenza A medically attended infection and hospitalization pools, reflecting differences in vaccine products care settings across studies, and country-specific surveillance systems.

What we found

We identified 7,602 articles, and we screened 6,464 titles and abstracts. We reviewed 265 full-text articles and included 22 single studies, of which 17 were newly identified in this version, and studies carried over from the previous round:

- Of the 22 included studies, 21 studies used a test-negative case-control design, and one study used a cohort design with target trial emulation, and the studies were conducted across diverse healthcare settings, including primary care, outpatient clinics, emergency departments, and inpatient hospital facilities.
- The 22 studies spanned multiple geographic regions:
  - North America (United States and Canada)
  - Europe (Italy, U.K., Germany, France, Denmark, Finland, Sweden, Spain) and nine additional countries via European multi-centre networks (e.g. Belgium, Croatia, Hungary, Ireland, Lithuania, Malta, Netherlands, Portugal, Romania)
  - Asia (China, Japan, and South Korea)
  - Southern Hemisphere (Argentina, Australia, Brazil, Chile, New Zealand, Paraguay, Peru, Uruguay)
- 17 studies address the research questions about effectiveness and were included in the meta-analysis (12 were newly identified in this version).

The risk of bias in the included studies was moderate in 12 studies, and serious in ten studies.

Random-effects models were used to calculate pooled effects, as we anticipated meaningful heterogeneity across studies and group comparisons. When data were available, subgroup analyses were computed to examine how patterns of findings varied according to different age groups. All estimates, and their corresponding confidence intervals (CIs), were converted to risk ratios (RRs). RRs were then log-transformed for use in meta-analytic models, and the CIs were used to derive a standard error for each effect size. If a study only reported VE for each single influenza season, age group or influenza subtype/lineage without an overall estimate, we considered each season, age group, or influenza subtype/lineage as a separate cohort in the meta-analysis.

Key findings in relation to influenza vaccine effectiveness

Our comprehensive analysis examined influenza VE across two consecutive seasons, providing a detailed assessment of protection against medically attended influenza infection, hospitalization, and other severe outcomes. Medically-attended influenza infection means a laboratory-confirmed influenza case identified at the point of healthcare contact for a symptomatic acute respiratory illness, ascertained through a test-negative design (or comparable analytic framework), in any ambulatory or sentinel surveillance setting; it does not require hospital admission, but in most included studies it can include patients who were subsequently hospitalized if the test was performed at the encounter that captured them. A total of 17 studies covering the 2024/2025 and five studies covering the 2025/2026 influenza season met inclusion criteria. Random-effects meta-analyses using REML estimation of τ^2, with Hartung–Knapp–Sidik–Jonkman and Wald-type 95% confidence intervals were performed by outcome (medically-attended influenza and influenza-associated hospitalization), age group (children and adolescents <18 years and older adults ≥60 years), and influenza type/subtype.

Vaccine effectiveness in the 2024/2025 season

Medically attended influenza A infection

Eleven cohorts from six studies (8-13) were pooled in the meta-analysis evaluating effectiveness of influenza vaccine against medically attended influenza A among children and adolescents <18 years (Figure 1). The pooled odds ratio was 0.55 (95% CI 0.45–0.68), corresponding to a VE of 45% (95% CI 32–55), with moderate heterogeneity (τ^2 = 0.05; I^2 = 54%). Eleven cohorts from seven studies (8; 11; 14-18) were pooled for older adults ≥60 years (Figure 2). The pooled odds ratio was 0.62 (95% CI 0.53–0.73), corresponding to a VE of 38% (95% CI 27–47), with considerable heterogeneity (τ^2 = 0.04; I^2 = 85%).

Medically attended influenza A(H1N1)pdm09 infection

Six cohorts from four studies (8-11) were pooled for children and adolescents <18 years (Figure 3). The pooled odds ratio was 0.47 (95% CI 0.29–0.75), corresponding to a VE of 53% (95% CI 25–71), with substantial heterogeneity (τ^2 = 0.12; I^2 = 66%). Five cohorts from four studies (8; 11; 18; 19) were pooled for older adults ≥60 years (Figure 4). The pooled odds ratio was 0.75 (95% CI 0.44–1.26) (VE 25%, 95% CI –26 to 56), with substantial heterogeneity (τ^2 = 0.11; I^2 = 62%); the pooled estimate did not reach statistical significance.

Medically attended influenza A(H3N2) infection

Three studies (9-11) (four cohorts) were pooled for children and adolescents <18 years (Figure 5). The pooled odds ratio was 0.53 (95% CI 0.19–1.44), corresponding to a VE of 47% (95% CI –44 to 81), with considerable heterogeneity (τ^2 = 0.25; I^2 = 80%); the pooled estimate did not reach statistical significance. Two studies (11; 19) were pooled for older adults ≥60 years (Figure 6). The pooled odds ratio was 0.70 (95% CI 0.40–1.21), corresponding to a VE of 30% (95% CI −21 to 60), with no observed heterogeneity (τ^2 = 0.00; I^2 = 0%); the pooled estimate did not reach statistical significance and the confidence interval was wide owing to the small number of contributing studies.

Medically attended influenza B infection

Three cohorts (two studies) (11; 13) were pooled for children and adolescents <18 years (Figure 7). The pooled odds ratio was 0.36 (95% CI 0.26–0.49), corresponding to a VE of 64% (95% CI 51–74), with no observed heterogeneity (τ^2 = 0.00; I^2 = 0%). Four studies (14; 15; 17; 19) were pooled for older adults ≥60 years (Figure 8). The pooled odds ratio was 0.39 (95% CI 0.32–0.48), corresponding to a VE of 61% (95% CI 52–68), with no observed heterogeneity (τ^2 = 0.00; I^2 = 0%).

Medically attended any influenza in young children (0–5 years)

Four cohorts (three studies) (12; 20; 21) were pooled for medically-attended any influenza among children aged 0–5 years (Figure 9). The pooled odds ratio was 0.56 (95% CI 0.30–1.05), corresponding to a VE of 44% (95% CI –5 to 70), with no observed heterogeneity ($\tau^2 = 0.00$; $I^2 = 0\%$); the pooled estimate did not reach statistical significance.

Influenza A-associated hospitalization

Eight cohorts from five studies (9; 11; 12; 22; 23) were pooled for children and adolescents <18 years (Figure 10). The pooled odds ratio was 0.41 (95% CI 0.32–0.51), corresponding to a VE of 59% (95% CI 49–68), with substantial heterogeneity ($\tau^2 = 0.06$; $I^2 = 73\%$). Twelve cohorts from six studies (8; 11; 12; 16; 19; 24) were pooled for older adults ≥60 years (Figure 11). The pooled odds ratio was 0.54 (95% CI 0.46–0.65), corresponding to a VE of 46% (95% CI 35–54), with considerable heterogeneity ($\tau^2 = 0.04$; $I^2 = 83\%$).

A(H1N1)pdm09-associated hospitalization

Six cohorts from four studies (9; 11; 22; 23) were pooled for children and adolescents <18 years (Figure 12). The pooled odds ratio was 0.33 (95% CI 0.29–0.38), corresponding to a VE of 67% (95% CI 62–71), with no observed heterogeneity ($\tau^2 = 0.00$; $I^2 = 0\%$). Five cohorts from three studies (8; 11; 24) were pooled for older adults ≥60 years (Figure 13). The pooled odds ratio was 0.58 (95% CI 0.49–0.68), corresponding to a VE of 42% (95% CI 32–51), with no observed heterogeneity ($\tau^2 = 0.00$; $I^2 = 0\%$).

A(H3N2)-associated hospitalization

Three cohorts from three studies (9; 22; 23) were pooled for children and adolescents <18 years (Figure 14). The pooled odds ratio was 0.61 (95% CI 0.44–0.84), corresponding to a VE of 39% (95% CI 16–56), with no observed heterogeneity ($\tau^2 = 0.00$; $I^2 = 2\%$). Four cohorts from two studies (11; 24) were pooled for older adults ≥60 years (Figure 15). The pooled odds ratio was 0.56 (95% CI 0.52–0.60), corresponding to a VE of 44% (95% CI 40–48), with no observed heterogeneity ($\tau^2 = 0.00$; $I^2 = 0\%$).

Influenza B-associated hospitalization

Two studies (11; 23) were pooled for children and adolescents <18 years (Figure 16). The pooled odds ratio was 0.32 (95% CI 0.18–0.57), corresponding to a VE of 68% (95% CI 43–82), with substantial heterogeneity ($\tau^2 = 0.12$; $I^2 = 63\%$). Three cohorts from a single study (11)were pooled for older adults ≥60 years (Figure 17). The pooled odds ratio was 0.37 (95% CI 0.09–1.47), corresponding to a VE of 63% (95% CI −47 to 91) with moderate heterogeneity ($\tau^2 = 0.18$; $I^2 = 48\%$); the pooled estimate did not reach statistical significance.

Influenza-associated death

Faksova et al. (17) was the only included study reporting VE against influenza-related death. Using a target-trial-emulation cohort design with linked Nordic registry data (Denmark and Finland, ≥65 years), influenza-related death was defined as death within 30 days after a laboratory-confirmed influenza test, with follow-up to 18 weeks post-immunisation. The overall VE against influenza-related death was 63.2% (95% CI 53.6–72.8) for the overall ≥65 population. Effectiveness was greater in adults aged ≥75 years (68.5%, 58.7–78.3) than in those aged 65–75 years (45.3%, 19.1–71.6).

Product-specific vaccine effectiveness in the 2024/2025 season

Three studies (16; 17; 24) reported product-specific VE against unvaccinated comparators in adults aged ≥65 years during the 2024/25 influenza season. Across studies, enhanced vaccines generally showed higher VE than standard-dose vaccines. In Italy, Domnich et al. reported VE against influenza-associated hospitalisation of 40% (95% CI –14 to 68) for standard-dose IIV4 (sdIIV4), 46% (–3 to 72) for adjuvanted IIV4 (aIIV4), and 46% (8 to 68) for high-dose IIV4 (HD-IIV4), with only the high-dose estimate reaching statistical significance owing to limited brand-specific sample sizes. (24) In Denmark, Emborg et al. reported VE against influenza A-associated hospitalisation of 53% (35–66) for HD-IIV4, 47% (41–53) for aIIV4, and 36% (23–47) for sdIIV4; corresponding VE estimates against medically attended influenza A were 50%, 48%, and 33% respectively. (16) In the Nordic registry-based cohort study by Faksova et al., VE against influenza-associated hospitalisation was 63.4% (38.1–88.7) for Efluelda Tetra (HD-IIV4), 48.2% (40.8–55.6) for Fluad Tetra (aIIV4), 43.6% (23.7–63.6) for Vaxigrip Tetra (split-virion sdIIV4), and 30.6% (–7.8 to 69.1) for Influvac Tetra (subunit sdIIV4); the latter standard-dose estimate had wide confidence intervals reflecting smaller sample size. (17)

Vaccine effectiveness in the 2025/2026 season and Southern-Hemisphere 2025 season

Medically-attended influenza infection

Five studies (25-29) provide VE data for 2025/26 season with too few estimates per outcome, age and subtype for statistical pooling, and findings are therefore summarized narratively below. Among children seen in primary care in France, Clercq 2026 (25) reported a VE of 57% (95% CI 29–74) against any influenza in the 0–17-year stratum. In Beijing outpatients aged 6–17 years, where >99% of cases were H3N2 (mostly subclade K), Shen 2026 (29) reported a substantially lower VE of 20% (95% CI 3–33). In Canadian sentinel practitioner offices, Separovic 2026 (28) reported a VE of 35% (95% CI 10–54) against influenza A overall in the 1–17-year stratum, with consistent estimates against A(H3N2) (36%, 95% CI 10–55), subclade-K J.2.4.1 (32%, 95% CI –3 to 56), and a wide-CI estimate for A(H1N1)pdm09 (55%, 95% CI –19 to 83).

Clercq 2026 (25) reported a VE of 28% (95% CI 17–37) against any influenza in adults ≥65 years. Shen 2026 found no significant protection among those aged ≥60 years (VE 13%, 95% CI –28 to 41). Separovic 2026 (28) reported a VE of 21% (95% CI –8 to 42) against influenza A overall in ≥65-year-olds, with 25% (95% CI –7 to 48) against A(H3N2), 26% (95% CI –21 to 55) against subclade K, and 6% (95% CI –71 to 48) against A(H1N1)pdm09, but none of which reached statistical significance.

Emergency department encounters

Kirsebom 2025 (26) reported VE against influenza A-related emergency department encounters in England during the autumn 2025 subclade K-dominant period. VE was highest in children 2–17 years (75%, 95% CI 66–81 against influenza A; 75%, 95% CI 52–88 specifically against subclade K), and intermediate in older adults ≥65 years (35%, 95% CI 22–45 against influenza A; 35%, 95% CI –9 to 63 against subclade K).

Influenza-associated hospitalization

Kirsebom 2025 (26) reported a VE of 74% (95% CI 63–82) against influenza A-associated hospitalization in children 2–17 years, with similar effectiveness specifically against subclade K (73%, 95% CI 48–87). For the Southern Hemisphere 2025 season, Russ 2025 (27) reported a VE of 51% (95% CI 44–57) against influenza A-associated hospitalization in young children, with comparable estimates against A(H1N1)pdm09 53% (95% CI 44–62) and lower against A(H3N2) 30% (95% CI 13–44); VE against influenza B-associated hospitalization was 64% (95% CI 41–79).

Kirsebom 2025 (26) reported a VE of 39% (95% CI 26–50) against influenza A-associated hospitalization in adults ≥65 years, with a similar non-significant estimate against subclade K (32%, 95% CI –14 to 61). Russ 2025 (27) reported lower estimates from the Southern Hemisphere, VE 35% (95% CI 29–41) against influenza A-associated hospitalization, 30%

(95% CI 22–37) against A(H1N1)pdm09, and 29% (95% CI 17–39) against A(H3N2). VE against influenza B-associated hospitalization in older adults was higher in the Russ study (82%, 95% CI 67–90). (27)

Next steps based on the identified evidence

The following recommended actions, synthesized from a comprehensive review of the evidence, address critical knowledge gaps in influenza VE. They provide a structured framework to enhance research and public-health responses to seasonal influenza outbreaks. These recommendations aim to strengthen our understanding of vaccine performance across different populations while improving outbreak management strategies.

- Research priorities
  - Develop strategies to enhance vaccine response in older adults where effectiveness is consistently lower
  - Study the impact of viral evolution on VE
  - Strengthen evidence on severe outcomes (ICU admission, invasive mechanical ventilation) beyond hospitalisation.
  - Conduct targeted research on populations with limited current data, including individuals with immunocompromising conditions and those with complex medical conditions
  - Continue and broaden A(H3N2) subclade K (J.2.4.1)-specific VE estimation as the 2025/26 season matures.
- Vaccine strategies
  - Develop specific approaches for populations showing lower vaccine protection
  - Prioritize enhanced vaccines (high-dose, adjuvanted, recombinant) in older adults, where standard-dose effectiveness was lowest in 2024/25
  - Strengthen vaccination campaigns in children (<18 years) given consistently higher effectiveness in this population group across outcomes
  - Explore potential booster or supplementary vaccination approaches for populations with lower protection
  - Evaluate next-generation vaccine platforms (mRNA-based influenza vaccines, broadly protective/universal candidates) in light of the demonstrated limits of current vaccines against drifted A(H3N2) variants, particularly in older adults.
- Policy implications
  - Strengthen healthcare capacity during periods of lower VE
  - Support the development of enhanced vaccines for populations with lower effectiveness
  - Encourage research into factors affecting end-season VE decline
  - Strengthen recommendations for enhanced vaccines (high dose, adjuvanted, recombinant) in adults ≥65 years

Table 1: Characteristics of all included studies

Reference and author year with URL	Research question addressed	Geographical location and trial name	Design	Population (add age of population)	Analysis	Type of vaccine	Risk of bias	Included in meta-analysis
Frutos 2025 (9)	• VE against medically attended influenza outpatient visits or influenza-associated hospitalizations	United States Trial Name: 1) Investigating Respiratory Viruses in the Acutely Ill (IVY) 2) New Vaccine Surveillance Network (NVSN) 3) U.S. Flu Vaccine Effectiveness (U.S. Flu VE) 4) Virtual SARS-CoV-2, Influenza, and Other respiratory viruses Network (VISION)	Test-negative case-control	• 3,175 adult participants were included from the IVY network • 4,611 participants <18 years were included from NVSN; 2,969 were outpatients and 1,642 were hospitalized • 3,344 participants were included from the U.S. Flu VE network; 1,134 were <18 years and 2,210 were adults • 139,558 outpatients were included from the VISION network; 36, 919 were patients <18 years and 102, 639 were adults • 32,671 hospitalized patients were included from the VISION network; 1,638 were <18 years, 31,033 were adults • Among control patients <18 years proportion of outpatients vaccinated against influenza ranged from 22% in the VISION network to 34% in the NVSN network; in hospitalized patients 27% (VISION) to 40% (NVSN) were vaccinated • Among adult controls 34% of outpatients were vaccinated against influenza; 35% (IVY) to 39% (VISION) of hospitalized patients were vaccinated	Multivariable logistic regression adjusted for geographic region, age, and calendar time of illness was used; VE was calculated using the following equation: VE = (1 – adjusted odds ratio) x 100%	• Trivalent inactivated influenza vaccine (IIV3) • Trivalent live attenuated vaccine (LAIV3) • Other (Trivalent recombinant influenza vaccine)	Serious	Yes

Reference and author year with URL	Research question addressed	Geographical location and trial name	Design	Population (add age of population)	Analysis	Type of vaccine	Risk of bias	Included in meta-analysis
				• Among controls 65 years or older 54% (VISION) to 59% (U.S. Flu VE) of outpatients were vaccinated against influenza; 45% (IVY) to 46% (VISION) of hospitalized patients were vaccinated				
Separovic 2025 (18)	• VE of influenza VE against ARI	Canada Trial name: Canadian Sentinel Practitioner Surveillance Network (SPSN)	Test-negative design	• 4,421 participants were included; 609 (14%) were positive for Influenza A and 3,812 (86%) were controls • 1,004 (23%) of participants were vaccinated for influenza including 101 (17%) cases and 903 (24%) controls)	No analysis section provided	• Variety of inactivated, egg based, cell based	Moderate	Yes
Blanquart 2025 (14)	• VE against influenza infection	France Trial name: Not reported	Test-negative design	• 59,472 patients presented at RELAB community laboratories; 44,420 were influenza-negative and 15,052 were influenza-positive • Among influenza-negative patients 10,875 (24%) were vaccinated; among influenza-positive patients, 1,916 (13%) were vaccinated • All ages were included	A logistic (binomial) linear model was fitted to the test result as a function of sex, age category, PCR technique, week, and vaccination status; VE was estimated using the odds ratio of the vaccine effect on testing positive for influenza	• Quadrivalent inactivated influenza vaccine (IIV4)	Moderate	Yes
Sun 2025 (20)	• VE against influenza infection	China Trial name: Not reported	Test-negative design	• 8,775 patients were included; 6,741 (76.8%) were influenza-negative and 2,034 (23.2%) were influenza-positive • Of 8,442 patients with available immunization information, 6.2% of cases (124/1,998) and 15.5%	Logistic regression was used to estimate odds ratios for vaccination status; VE was calculated with the following formula: (1 – OR) x 100%	• Trivalent inactivated influenza vaccine (IIV3) • Quadrivalent inactivated influenza	Moderate	Yes

Reference and author year with URL	Research question addressed	Geographical location and trial name	Design	Population (add age of population)	Analysis	Type of vaccine	Risk of bias	Included in meta-analysis
				(1,000/6,444) were vaccinated against influenza • All ages were included		vaccine (IIV4)		
Rose 2025 (11)	• VE against MAARI and influenza-like illness	Denmark, the United Kingdom, the European Union, Northern Ireland, Scotland Trial/network name: U-PC (European Union VEBIS primary care network)	Test-negative case-control	• Participants presenting with influenza-like illness or ARI had specimens collected • Vaccinated participants were defined as having received the 2024/25 influenza vaccine at least 14 days before symptom onset • Number of participants was not reported • All ages	VE was calculated using the formula (1 – OR) x 100; logistic regression adjusted for measured potential cofounding variables was used	• Trivalent inactivated influenza virus (IIV3) • Quadrivalent inactivated influenza virus (IIV4)	Serious	Yes
Choi 2026 (19)	• Vaccine effectiveness (VE) against influenza between November 2024 and April 2025	South Korea Trial name: Hospital-based Influenza Morbidity and Mortality (HIMM) Network	Test-negative case control	• A total of 3,954 patients (all adults), with 1,977 patients as influenza-positive cases and 1,977 patients as test-negative controls	VE against influenza between November 2024 and April 2025 was determined by using logistic regression to estimate the odds ratio of vaccination between influenza-positive cases and test-negative controls. Hospitalized patients presenting with sudden fever of ≥37.8 ◦C along with symptoms were assessed for VE against hospitalization.	• MF59-adjuvanted quadrivalent influenza vaccine (Fluad® Quad) (introduced in 2023), high-dose influenza vaccine (Efluelda®) (introduced in 2024)	Moderate	Yes
Clercq 2025 (15)	• Vaccine effectiveness against	France	Test-negative design	• 77,704 patients including test-positive (n = 20,650; 27%) and test-negative individuals	Vaccine effectiveness was measured as (1 – odds	• Quadrivalent inactivated influenza	Moderate	Yes

Reference and author year with URL	Research question addressed	Geographical location and trial name	Design	Population (add age of population)	Analysis	Type of vaccine	Risk of bias	Included in meta-analysis
	influenza infection • Vaccine effectiveness by influenza type (A and B), age group, vaccination timing	Trial name: RELAB Network		(n = 57,054; 73%) across all age groups (from 0 years to ≥65 years)	ratio) with 95% confidence intervals (CIs)	vaccine (IIV4)		
Clercq 2026 (25)	• Vaccine effectiveness against influenza infection • Vaccine effectiveness by age group, symptoms	France Trial name: RELAB Network	Test-negative design	• 24,267 individuals (n = 11,045 positives; 11.2%) across all age groups (from 0 years to ≥65 years)	Vaccine effectiveness was measured as (1 – odds ratio) with 95% confidence intervals (CIs)	• Quadrivalent inactivated influenza vaccine (IIV4)	Moderate	No
Domnich 2025 (24)	• Vaccine effectiveness against hospitalization • Vaccine effectiveness by influenza type (A and B), age group, dose of vaccine	Italy Trial name: Not reported	Retrospective case-control test-negative design	• 1339 participants were included with a mean age of 75.0 years of which 12.9 % (173/1339) of patients tested positive for ≥1 influenza virus	VE was estimated as (1–OR) × 100 %	• Quadrivalent inactivated influenza vaccine (IIV4)	Serious	Yes
Emborg 2025 (16)	• Vaccine effectiveness against infection for standard-dose QIV, an adjuvanted QIV, and a high-dose QIV for people	Denmark Trial Name: Danish National Microbiology Database	Test-negative design	• Among patients aged 65 and older, there were 11,006 non-hospitalised individuals (1,403 influenza A cases [12.7%] and 9,603 controls [87.3%]) and 21,937 hospitalised individuals (1,937 influenza A cases	Vaccine effectiveness was estimated by comparing vaccination odds between people who tested positive and negative, using adjusted logistic regression, and converting the resulting	• Quadrivalent inactivated influenza vaccine (IIV4)	Serious	Yes

Reference and author year with URL	Research question addressed	Geographical location and trial name	Design	Population (add age of population)	Analysis	Type of vaccine	Risk of bias	Included in meta-analysis
	aged 65 and older in Denmark			[8.8%] and 20,000 controls [91.2%]) • Patients were considered vaccinated if they received the vaccine at least 14 days before the sample date	odds ratio into VE as (1 − OR) × 100			
Erdwiens 2025 (8)	• Vaccine effectiveness against symptomatic ARI in PCR confirmed cases within primary and hospital care	Germany Trial Name: National Reference Center for Influenza Viruses (NRCI)	Test-negative case-control	• In primary care, 2,808 patients with acute respiratory infection (ARI) symptoms were enrolled, of whom 33% tested positive for influenza, mainly influenza A(H1N1)pdm09 and influenza B, with a small number of co-infections and untyped cases • In secondary care, 536 hospitalized patients with severe acute respiratory infection were analyzed after exclusions, and 19% tested positive for influenza, also predominantly A(H1N1)pdm09, followed by influenza B and A(H3N2) • All samples were collected from symptomatic patients in primary and hospital settings and tested using RT-PCR for influenza detection and subtyping.	Adjusted logistic regression was used to compare vaccination odds between cases and controls, accounting for factors like age, sex, underlying conditions, and symptom onset date, and then derived VE as 1 − OR × 100, both overall and by age group and virus type where possible	• Quadrivalent inactivated influenza vaccine (IIV4)	Serious	Yes
Faksova 2026 (17)	• Vaccine effectiveness of brand-specific influenza vaccines to prevent infection in	Denmark, Finland, Sweden Trial Name: Multiple registers in	Target trial emulation (primary), Test-negative case-control (secondary)	• Before matching, the study included over 1,611,962 influenza vaccine recipients across Denmark, Finland, and Sweden, with the largest group from Denmark (826,766) followed by Finland (752,350)	The Aalen-Johansen estimator was used to identify cumulative incidence to calculate vaccine effectiveness based on risk measures, including relative	• Quadrivalent inactivated influenza vaccine (IIV4)	Moderate	Yes

Reference and author year with URL	Research question addressed	Geographical location and trial name	Design	Population (add age of population)	Analysis	Type of vaccine	Risk of bias	Included in meta-analysis
	individuals aged 65 years or older	Denmark, Finland and Sweden		• After matching vaccinated and unvaccinated individuals aged ≥65 years, a substantial number of pairs were censored before follow-up due to rapid vaccine uptake among comparison individuals	effectiveness (1 − risk ratio) and absolute risk differences at 18 weeks, with results pooled across countries. In a supplementary analysis, vaccine effectiveness was also estimated using odds ratios, calculated as 1 − odds ratio (OR) from adjusted logistic regression models			
Kirsebom 2025 (26)	• The genetic and antigenic profiles of H3N2 viruses in England and assess vaccine effectiveness against influenza-related ED attendance and hospital admission	England Trial name: Respiratory Datamart surveillance system in England	Test-negative case-control	• Patients attending the ED or admitted to hospital who had a PCR test for influenza from 14 days before to 2 days after their visit Ages from 2 to 65+.	VE was estimated using multivariable logistic regression with test result as the outcome and vaccination status as the exposure, adjusting for week, age, region, and clinical risk, and stratified by age group and influenza type/subtype. The main analysis covered tests conducted between 29 September and 2 November 2025	• aIIV: adjuvanted inactivated influenza vaccine • IIV-HD: high-dose inactivated influenza vaccine • IIVc: cell-based inactivated influenza vaccine • IIVe: egg-based inactivated influenza vaccine • IIVr: recombinant influenza vaccine	Serious	No

Reference and author year with URL	Research question addressed	Geographical location and trial name	Design	Population (add age of population)	Analysis	Type of vaccine	Risk of bias	Included in meta-analysis
						• LAIV: live attenuated influenza vaccine		
Kwaah 2025 (10)	• Influenza VE against symptomatic laboratory-confirmed influenza	U.S.A Trial name: The Department of Defense Global Respiratory Pathogen Surveillance Program	Test-negative case-control	• Study sample: Military Health System (MHS) beneficiaries who sought outpatient care between November 24, 2024 and March 15, 2025 and met the influenza-like illness case definition • Cases were ILI patients who tested positive for any influenza virus (sub)type (n=295); controls were ILI patients who tested negative for influenza (n=965)	VE was estimated for influenza A (any subtype), A(H1N1)pdm09, and A(H3N2) in adults and children, adjusting for age group, month of illness, and region to estimate the Influenza VE against symptomatic laboratory-confirmed influenza. Service members, children <6 months, and those with unknown vaccination status were excluded	• Not reported	Moderate	Yes
Murphy 2025 (22)	• Influenza VE against symptomatic laboratory-confirmed influenza	China Trial name: Not reported	Prospective test negative study	• The study sample included 947 Children aged 9 months to 17 years (163 cases and 784 controls) hospitalized at Queen Mary or Princess Margaret Hospitals in Hong Kong between December 2024 and March 2025 with febrile acute respiratory illness (fever ≥38 °C plus a respiratory symptom within 72 hours)	Influenza VE was estimated using the odds ratio comparing vaccinated versus unvaccinated children (partially vaccinated children under 9 years and those younger than 9 months were excluded). Logistic regression included age (linear and quadratic), sex, underlying conditions, prior-season vaccination, and biweekly calendar time. Firth's penalized estimator addressed sparse data. VE was calculated as (1 − adjusted OR) × 100. VE	• Quadrivalent inactivated influenza vaccine (IIV4)	Serious	Yes

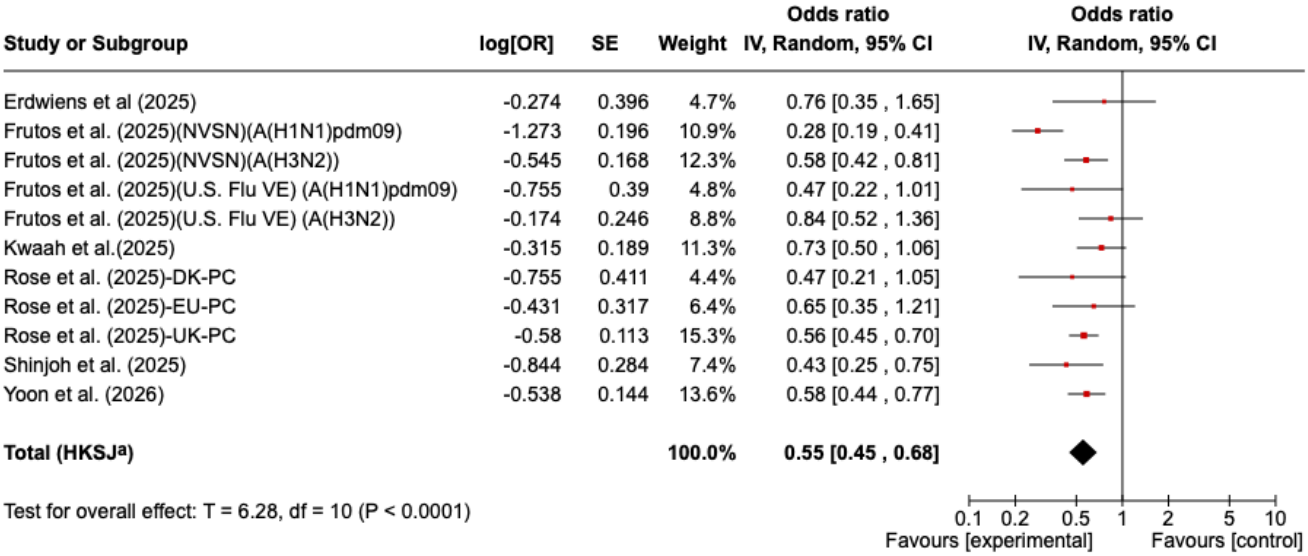
Reference and author year with URL	Research question addressed	Geographical location and trial name	Design	Population (add age of population)	Analysis	Type of vaccine	Risk of bias	Included in meta-analysis
					against influenza A hospitalization was estimated overall, by subtype, and by age group when possible. Analyses were conducted in R 4.2.3.			
Russ 2025 (27)	• Vaccine effectiveness (VE) against influenza-associated hospitalized and outpatient illness in the Southern hemisphere between March and September 2025	Eight Southern Hemisphere countries (Argentina, Australia, Brazil, Chile, New Zealand, Paraguay, South Africa, and Uruguay) Trial name: Multiple SARI and ILI Surveillance systems	Test-negative case control	• A total of 2,554 patients with ILI and 181,566 patients with SARI were identified through country surveillance networks, and of these, 2,122 patients with influenza-like illness (ILI) were included and 42,752 patients with severe acute respiratory infection (SARI) were included	VE against influenza-associated hospitalized and outpatient illness between March and September 2025 was determined by comparing the odds ratio of influenza vaccination between case patients who received a positive influenza RT-PCR test result and control patients who received a negative influenza RT-PCR test result. Vaccinated patients were those who received a 2025 influenza vaccine dose ≥14 days before symptom onset	• All countries used WHO-recommended egg-based, inactivated Southern Hemisphere influenza vaccine formulation, including trivalent, quadrivalent and adjuvanted vaccines	Serious	No
Shen 2026 (29)	• Vaccine effectiveness against influenza A(H3N2) subclade K in sentinel hospitals and network laboratories in Beijing, China	Beijing, China Trial Name: Influenza Surveillance System in Beijing	Test-negative case-control	• Among the 10,848 participants, 8.7% were aged ≤5 years (n=909), 26.1% were 6–17 years (n=2,737), 53.1% were 18–59 years (n=5,569), and 12.1% were ≥60 years (n=1,269), with a median age of 27.0 years (IQR 14.0–41.0); 93.3% (n=9,784) had no comorbidities, 14.0% (n=1,463) were vaccinated	The study estimated how well the vaccine worked by using a statistical model (logistic regression) to compare the odds of infection between vaccinated and unvaccinated people, then converting that into a percentage with the formula (1 − odds ratio) × 100%. The model accounted for	• Trivalent inactivated influenza vaccine (IIV3) • Quadrivalent inactivated influenza vaccine (IIV4) • Trivalent live attenuated	Moderate	No

Reference and author year with URL	Research question addressed	Geographical location and trial name	Design	Population (add age of population)	Analysis	Type of vaccine	Risk of bias	Included in meta-analysis
					factors like age, sex, underlying health conditions, where people lived, and the time period	vaccine (LAIV3)		
Shinjoh 2025 (12)	• Vaccine effectiveness against Influenza A and B infection in youth aged 6 months to 17 years old	Japan Trial Name: Not reported	Test-negative case-control	• Among children who tested negative for influenza, IIV uptake was 40% (307/760) in hospitalized patients and 43% (118/277) in outpatients, while LAIV use was very low at 0.8% and 1.8%, respectively • Overall, out of 1,351 children, 35% (479) received IIV and only 1.2% (16) received LAIV. Of those given LAIV, 5 later developed influenza A (all confirmed by rapid testing), with symptom onset ranging from 2 weeks to under 3 months after vaccination, while the remaining 11 did not become infected	Vaccine coverage in children was calculated as the percentage of vaccinated individuals among all patients (including both influenza-positive and negative cases). Vaccine effectiveness (VE) was estimated using a test-negative case–control design, defined as 100%×(1−adjusted odds ratio). The odds ratio compared infection rates between vaccinated and unvaccinated groups based on positive and negative test results	• Trivalent inactivated influenza vaccine (IIV3) • Quadrivalent inactivated influenza vaccine (IIV4) • Trivalent live attenuated vaccine (LAIV3) • Cell-based/recombinant Influenza vaccines	Serious	Yes
Separovic 2026 (28)	• Vaccine effectiveness in preventing influenza A(H1N1)pdm09 and A(H3N2), subclade K	Canada Trial Name: Canadian Sentinel Practitioner Surveillance Network	Test-negative case-control	• Out of 4,448 individuals with acute respiratory illness, 784 (18%) were aged 1–8 years, 602 (14%) were 9–17, 1,604 (36%) were 18–49, 665 (15%) were 50–64, and 793 (18%) were 65 or older. The median age was 35 years (IQR: 13–58) • Among all participants, 1,696 (38%) tested positive for influenza A(H3N2), while	VE against medically attended acute respiratory illness (ARI) involved comparing the odds of testing positive for influenza (cases) versus testing negative (controls) between vaccinated and unvaccinated individuals, while accounting for potential confounding factors. VE was then	• Trivalent inactivated influenza vaccine (IIV3) • Trivalent live attenuated vaccine (LAIV3) • Cell-based/recombinant	Moderate	No

Reference and author year with URL	Research question addressed	Geographical location and trial name	Design	Population (add age of population)	Analysis	Type of vaccine	Risk of bias	Included in meta-analysis
				2,752 (62%) tested negative and served as controls. Of the influenza A(H3N2) cases, 303 (18%) had received the 2025/2026 seasonal influenza vaccine	calculated using the formula: (1 − odds ratio) × 100%	Influenza vaccines		
Yoon 2026 (13)	• Vaccine effectiveness of cell-based quadrivalent influenza vaccine among children between the ages of 6 months to 18 years old	South Korea Trial Name: Not reported	Test-negative case-control	• Among a total of 1476 participants, in participants aged 6 months to 13 years, there were 585 cases (77.90%) and 597 controls (82.34%); within this group, ages 6–35 months included 28 cases (3.73%) and 150 controls (20.69%), while ages 36 months to 13 years included 557 cases (74.17%) and 447 controls (61.66%). Among those aged 14–18 years, there were 166 cases (22.10%) and 128 controls (17.66%)	Crude vaccine effectiveness (VE) was determined using the formula (1 − odds ratio) × 100, along with 95% confidence intervals. Adjusted VE was calculated through logistic regression, accounting for factors like age, sex, location, existing health conditions, and when the sample was collected.	• Quadrivalent inactivated influenza vaccine (IIV4) • Cell-based/recombinant Influenza vaccines	Moderate	Yes
Yu 2026 (23)	• Vaccine effectiveness in hospitalized children in Hong Kong stratified by influenza subtypes	Hong Kong, China Trial Name: Not reported	Test-negative case-control	• Between October 2015 and July 31, 2025, a total of 34,919 children hospitalized with fever and acute respiratory symptoms were enrolled. Among those who tested negative for influenza, 682 were positive for SARS-CoV-2 and excluded • This left 34,237 children aged 1-17 years for analysis. Of these, 5,245 (15.3%) had influenza: 41.0% were A(H1N1)pdm09, 31.9%	Vaccine effectiveness (VE) for each of the three vaccinated groups was calculated as (1−adjusted odds ratio)×100%, using individuals who were never vaccinated as the reference group. VE was also analyzed overall and by specific influenza types and subtypes through stratified analyses	• Trivalent inactivated influenza vaccine (IIV3) • Quadrivalent inactivated influenza vaccine (IIV4) • Trivalent live attenuated vaccine (LAIV3)	Serious	Yes

Reference and author year with URL	Research question addressed	Geographical location and trial name	Design	Population (add age of population)	Analysis	Type of vaccine	Risk of bias	Included in meta-analysis
				A(H3N2), 24.1% influenza B, and fewer than 3% were of unknown subtype				
Zhang 2025 (21)	• Vaccine effectiveness against influenza associated infection outpatient sentinel hospitals across Beijing, China stratified by age group, influenza virus type and epidemic phase	Beijing, China Trial Name: Etiological Surveillance System of Sentinel Hospitals in Beijing	Test-negative case-control	• A total of 18,405 patients were enrolled into the study, consisting of 1850 (10.1%) individuals between the ages of 0-5 years, 4024 (21.9%) between the ages of 6-17 years, 10,563 (57.4%) between the ages of 18-59 years, 1968 (10.7%) that are ≥60 years. • From this group, 295 (15.9%) 0-5 years old, 467 (11.6%) 6-17 years old, 2334 (22.1%) 18-59 years old, and 594 (30.2%) ≥60 years tested positive for influenza • In the sample 15,176 (82.5%) were not vaccinated for both 2024/2025 and 2023/2024 season, 696 (3.8%) vaccinated for 2024/2025 season only, 945 (5.1%) vaccinated for 2023/2024 season only and 1588 (8.6%) vaccinated for both seasons	Multivariable logistic regression models were used, adjusting for potential confounders such as age, sex, geographic region, epidemic period, underlying chronic conditions, pneumonia status, and the time between symptom onset and sample collection. Vaccine effectiveness (VE) and its 95% confidence interval (CI) were calculated as follows: unadjusted and adjusted VE = (1 − unadjusted or adjusted odds ratio) × 100%, and the 95% CI for VE = (1 − CI of the odds ratio) × 100%.	• Trivalent inactivated influenza vaccine (IIV3) • Quadrivalent inactivated influenza vaccine (IIV4) • Trivalent live attenuated vaccine (LAIV3)	Moderate	Yes

Figure 1. Effectiveness of influenza vaccine against medically attended Influenza A infection among children & adolescents (<18 years)



Test for overall effect: T = 6.28, df = 10 (P < 0.0001)

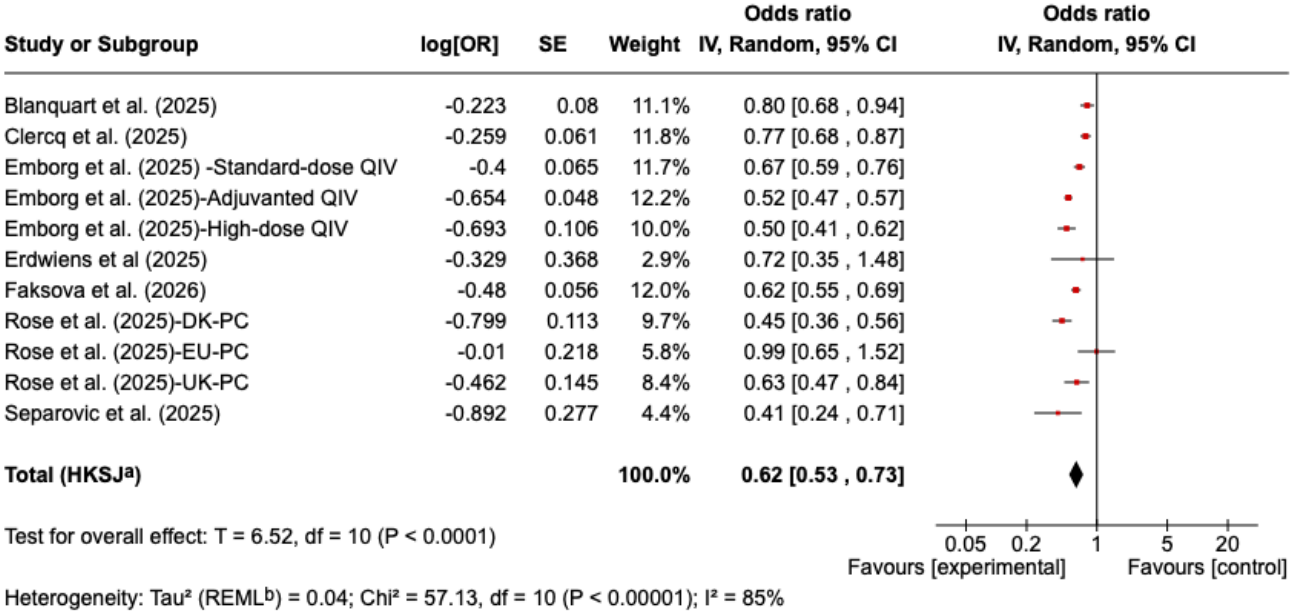
Heterogeneity: Tau² (REML[b]) = 0.05; Chi² = 19.36, df = 10 (P = 0.04); I² = 54%

Footnotes

[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.

[b]Tau² calculated by Restricted Maximum-Likelihood method.

Figure 2. Effectiveness of influenza vaccine against medically attended Influenza A infection among older adults (≥60 years)



Test for overall effect: T = 6.52, df = 10 (P < 0.0001)

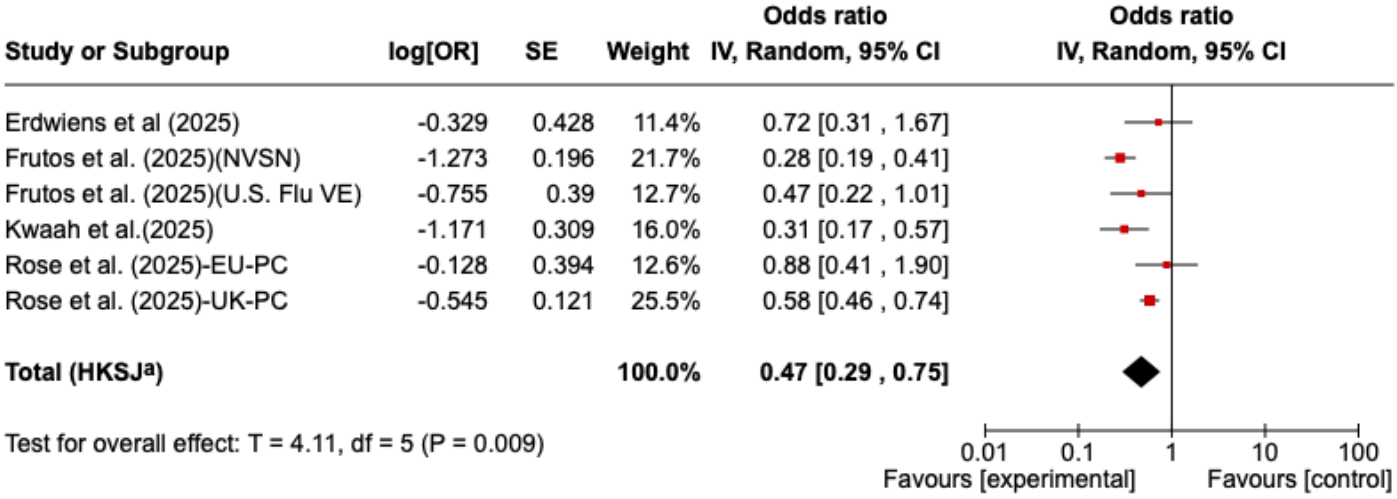
Heterogeneity: Tau² (REML[b]) = 0.04; Chi² = 57.13, df = 10 (P < 0.00001); I² = 85%

Footnotes

[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.

[b]Tau² calculated by Restricted Maximum-Likelihood method.

Figure 3. Effectiveness of influenza vaccine against medically attended Influenza A(H1N1)pdm09 infection among children & adolescents (<18 years)



Test for overall effect: T = 4.11, df = 5 (P = 0.009)

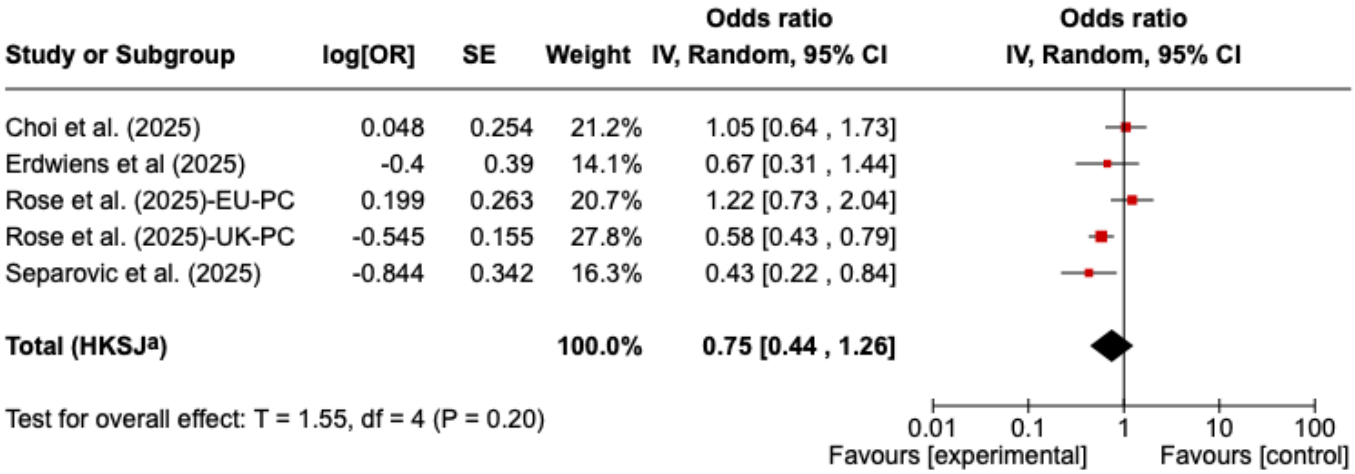
Heterogeneity: Tau² (REML[b]) = 0.12; Chi² = 15.27, df = 5 (P = 0.009); I² = 66%

Footnotes

[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.

[b]Tau² calculated by Restricted Maximum-Likelihood method.

Figure 4. Effectiveness of influenza vaccine against medically attended Influenza A(H1N1)pdm09 infection among older adults (≥60 years)



Test for overall effect: T = 1.55, df = 4 (P = 0.20)

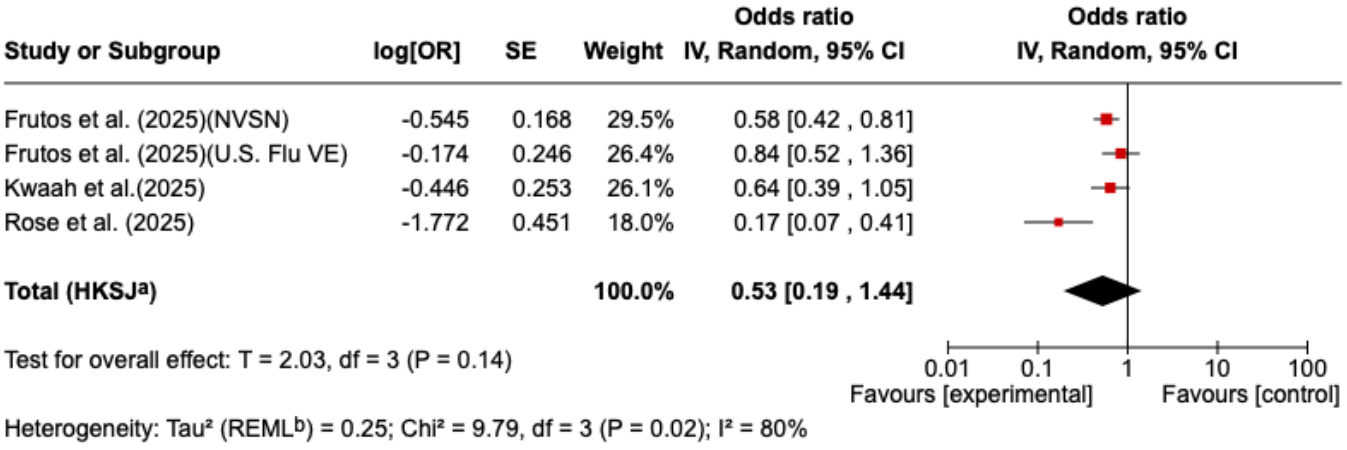
Heterogeneity: Tau² (REML[b]) = 0.11; Chi² = 10.47, df = 4 (P = 0.03); I² = 62%

Footnotes

[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.

[b]Tau² calculated by Restricted Maximum-Likelihood method.

Figure 5. Effectiveness of influenza vaccine against medically attended Influenza A(H3N2) infection among children & adolescents (<18 years)

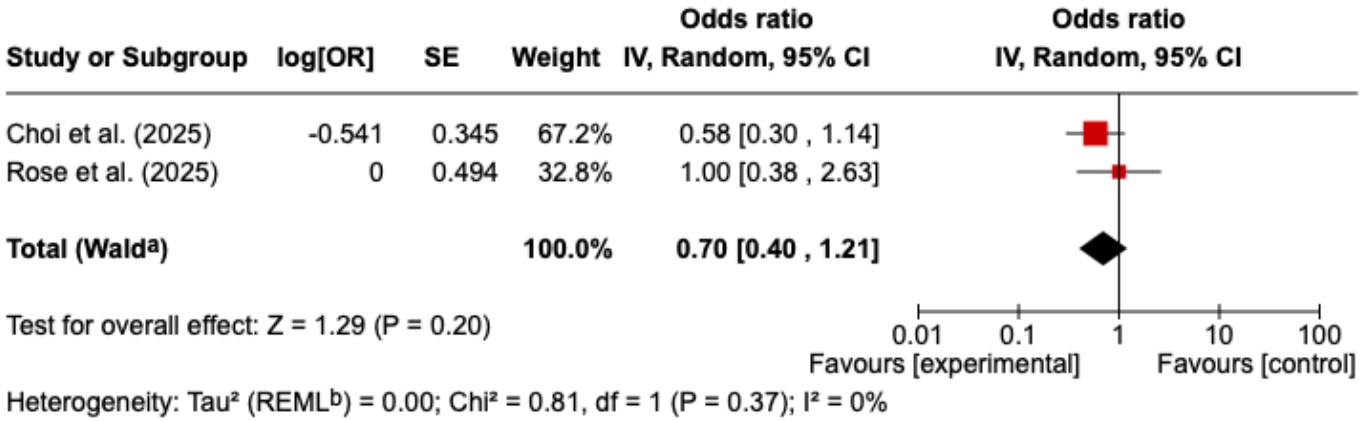


Footnotes

[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.

[b]Tau² calculated by Restricted Maximum-Likelihood method.

Figure 6. Effectiveness of influenza vaccine against medically attended Influenza A(H3N2) infection among older adults (≥60 years)

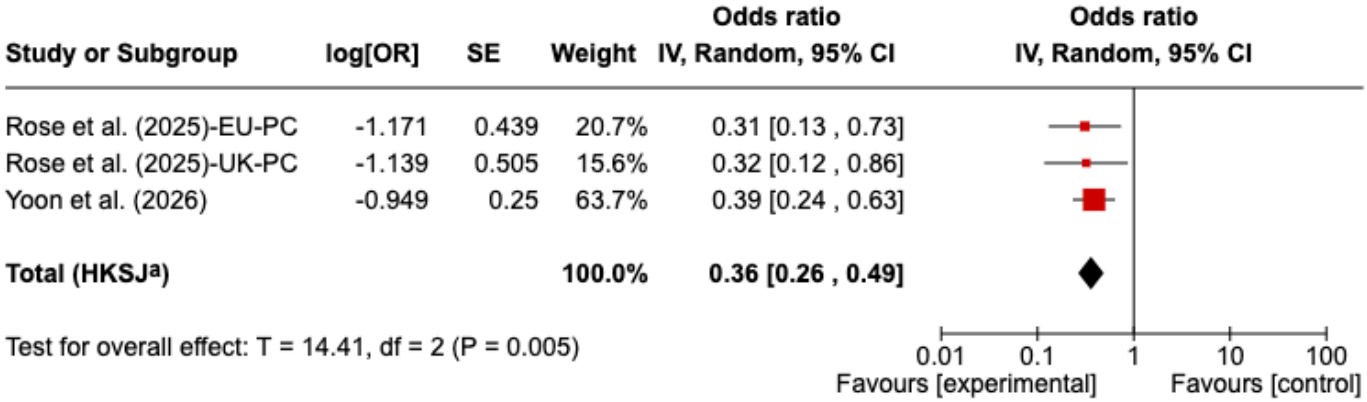


Footnotes

[a]CI calculated by Wald-type method.

[b]Tau² calculated by Restricted Maximum-Likelihood method.

Figure 7. Effectiveness of influenza vaccine against medically attended influenza B infection among children & adolescents (<18 years)

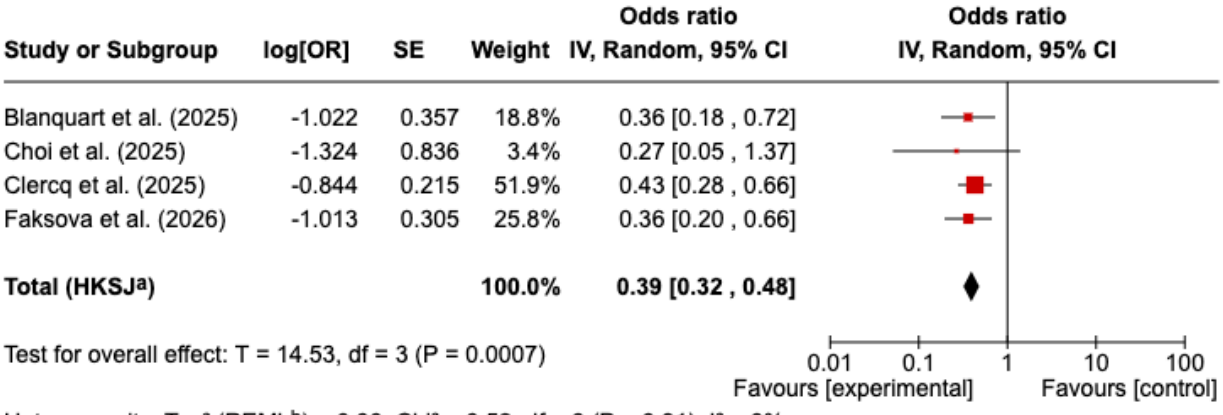


Footnotes

[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.

[b]Tau² calculated by Restricted Maximum-Likelihood method.

Figure 8. Effectiveness of influenza vaccine against medically attended influenza B infection among older adults (≥60/65 years)

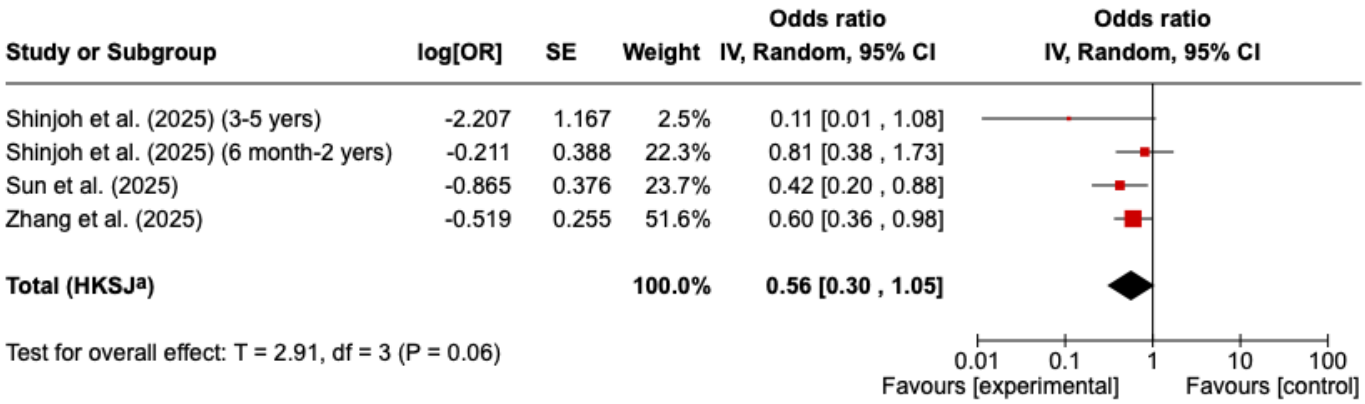


Footnotes

[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.

[b]Tau² calculated by Restricted Maximum-Likelihood method.

Figure 9. Effectiveness of influenza vaccine against medically attended (any) influenza infection among children (0 to 5 years)



Test for overall effect: T = 2.91, df = 3 (P = 0.06)

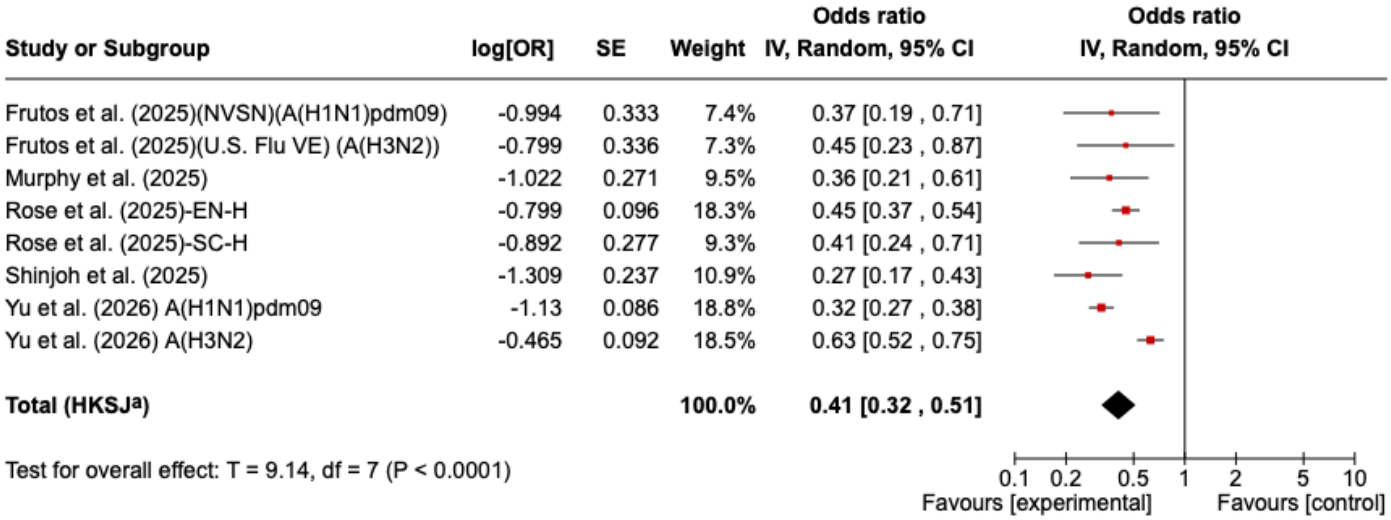
Heterogeneity: Tau² (REML[b]) = 0.00; Chi² = 3.48, df = 3 (P = 0.32); I² = 0%

Footnotes

[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.

[b]Tau² calculated by Restricted Maximum-Likelihood method.

Figure 10. Effectiveness of influenza vaccine against Influenza A-associated hospitalization among children & adolescents (<18 years)



Test for overall effect: T = 9.14, df = 7 (P < 0.0001)

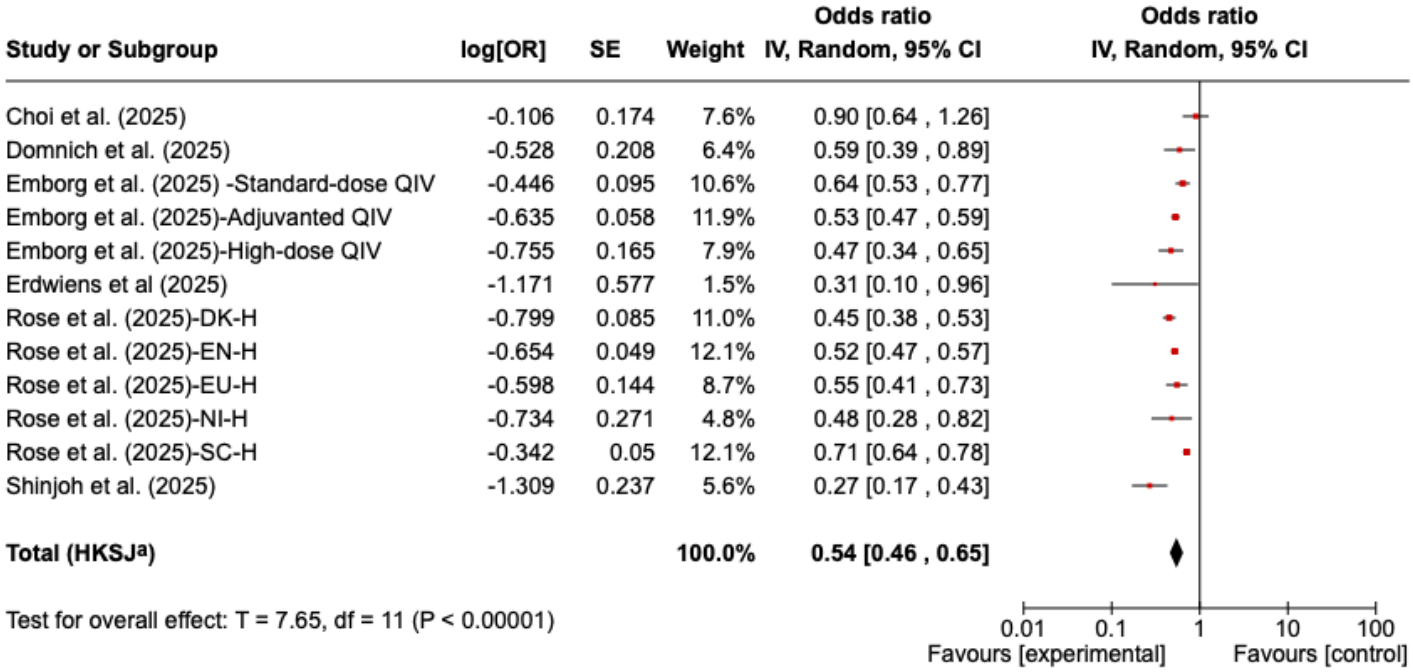
Heterogeneity: Tau² (REML[b]) = 0.06; Chi² = 32.78, df = 7 (P < 0.0001); I² = 73%

Footnotes

[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.

[b]Tau² calculated by Restricted Maximum-Likelihood method.

Figure 11. Effectiveness of influenza vaccine against Influenza A-associated hospitalization among older adults (≥60 years)



Test for overall effect: T = 7.65, df = 11 (P < 0.00001)

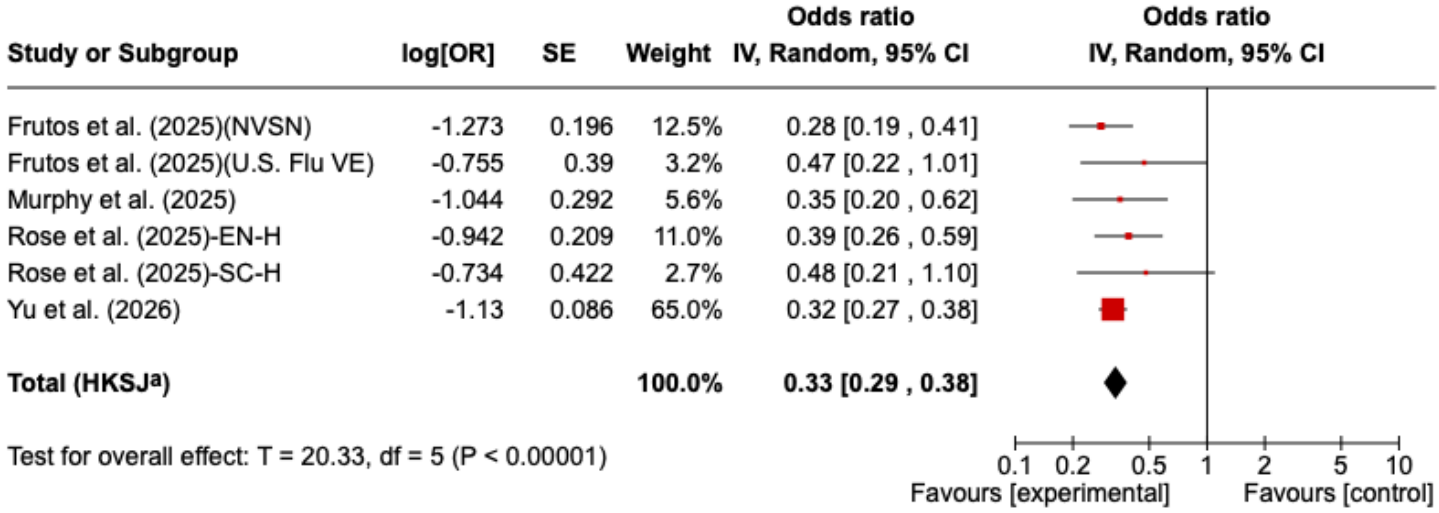
Heterogeneity: Tau² (REML[b]) = 0.04; Chi² = 53.51, df = 11 (P < 0.00001); I² = 83%

Footnotes

[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.

[b]Tau² calculated by Restricted Maximum-Likelihood method.

Figure 12. Effectiveness of influenza vaccine against Influenza A(H1N1)pdm09-associated hospitalization among children & adolescents (<18 years)



Test for overall effect: T = 20.33, df = 5 (P < 0.00001)

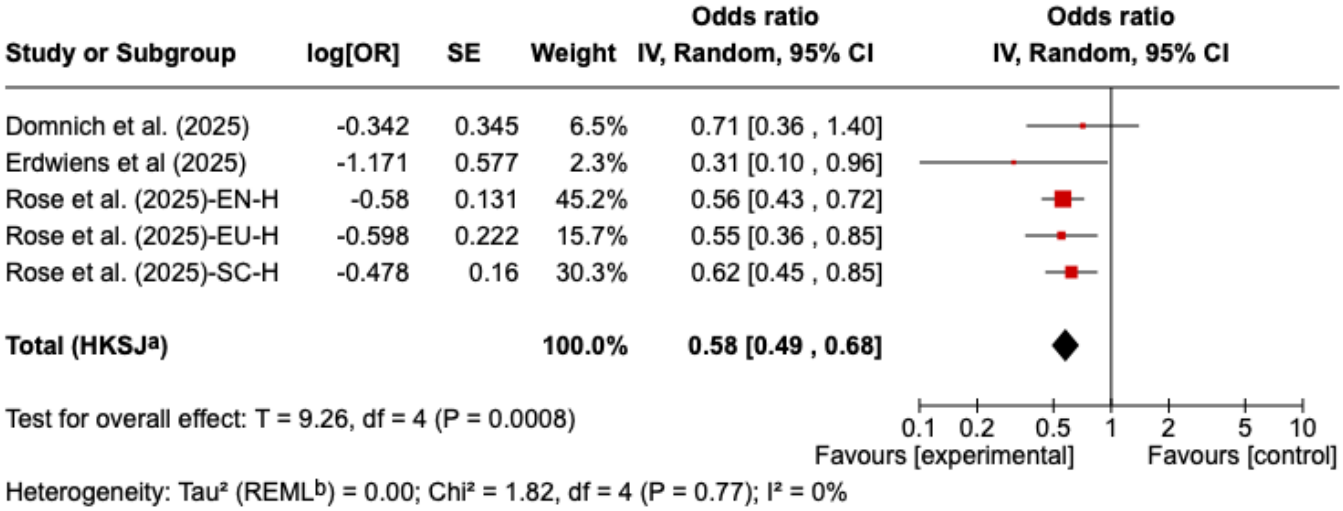
Heterogeneity: Tau² (REML[b]) = 0.00; Chi² = 3.04, df = 5 (P = 0.69); I² = 0%

Footnotes

[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.

[b]Tau² calculated by Restricted Maximum-Likelihood method.

Figure 13. Effectiveness of influenza vaccine against A(H1N1)pdm09-associated hospitalization among older adults (≥60 years)

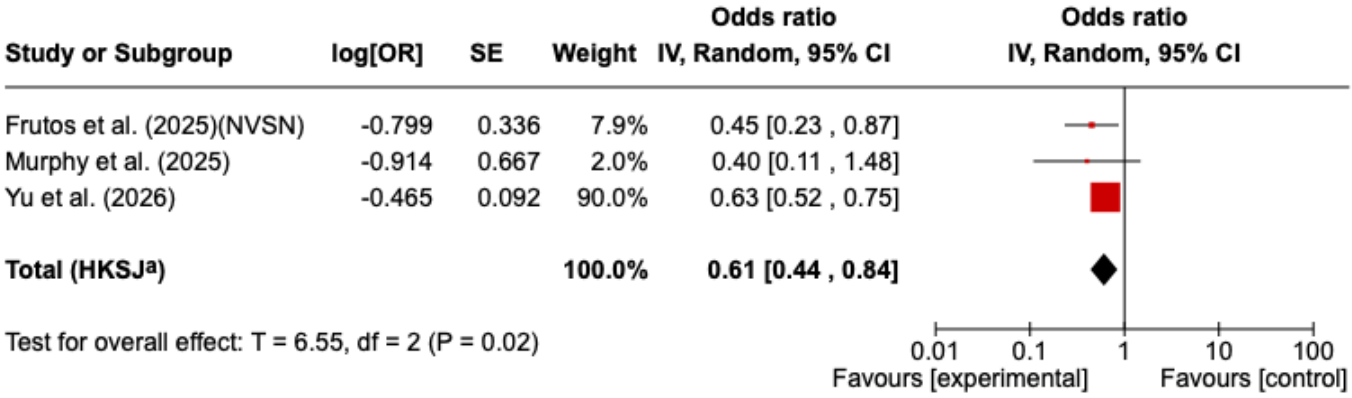


Footnotes

[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.

[b]Tau² calculated by Restricted Maximum-Likelihood method.

Figure 14. Effectiveness of influenza vaccine against Influenza A(H3N2)-associated hospitalization among children & adolescents (<18 years)

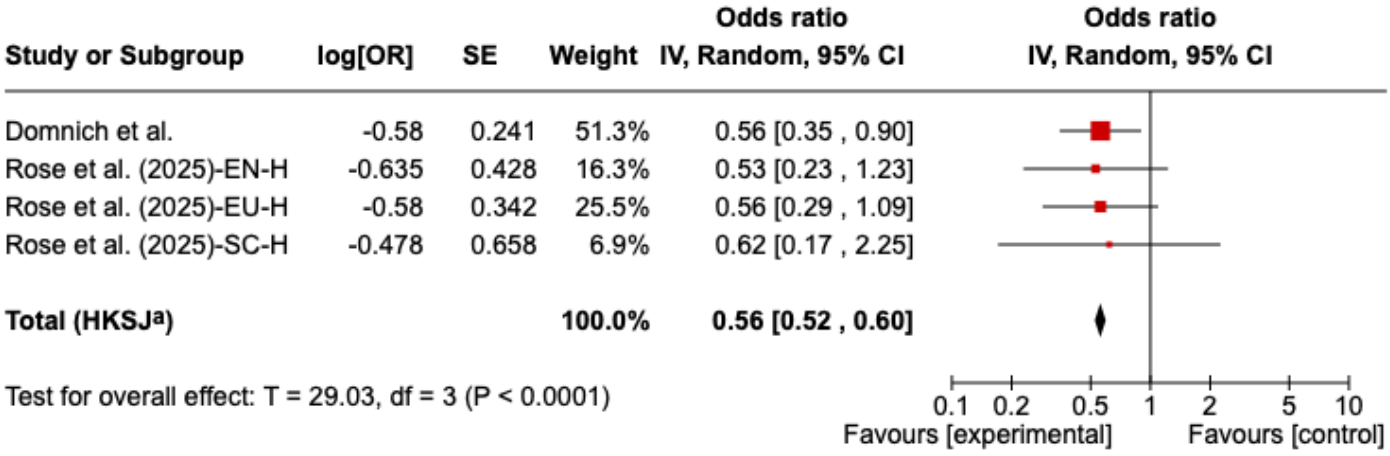


Footnotes

[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.

[b]Tau² calculated by Restricted Maximum-Likelihood method.

Figure 15. Effectiveness of influenza vaccine against Influenza A(H3N2)-associated hospitalization among older adults (≥60/65 years)



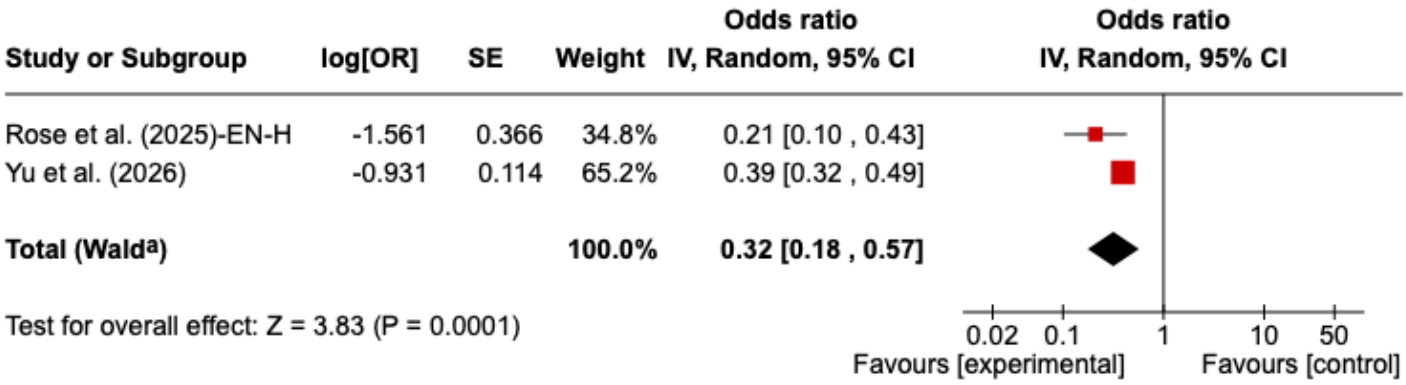
Heterogeneity: Tau² (REML[b]) = 0.00; Chi² = 0.04, df = 3 (P = 1.00); I² = 0%

Footnotes

[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.

[b]Tau² calculated by Restricted Maximum-Likelihood method.

Figure 16. Effectiveness of influenza vaccine against Influenza B-associated hospitalization among children & adolescents (<18 years)



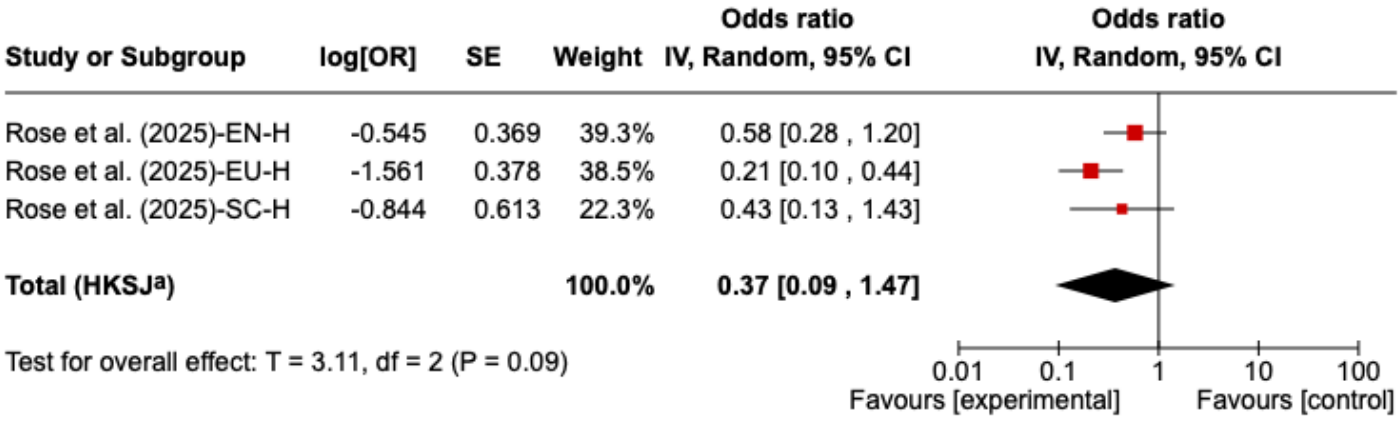
Heterogeneity: Tau² (REML[b]) = 0.12; Chi² = 2.70, df = 1 (P = 0.10); I² = 63%

Footnotes

[a]CI calculated by Wald-type method.

[b]Tau² calculated by Restricted Maximum-Likelihood method.

Figure 17. Effectiveness of influenza vaccine against Influenza B-associated hospitalization among older adults (≥60 years)



Footnotes

[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.

[b]Tau² calculated by Restricted Maximum-Likelihood method.

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This living evidence synthesis was funded through a grant from the Canadian Institutes of Health Research (funding reference number: FP7-203225) to the McMaster Health Forum for the Evidence synthesis hub of the Evidence Support Network for Canada (ESN-CA) with a focus on pandemics and health emergencies. The McMaster Health Forum receives both financial and in-kind support from McMaster University. The views expressed in the living evidence synthesis are the views of the authors and should not be taken to represent the views of the funder or McMaster University.