McMaster University | HEALTH FORUM

Living Evidence Synthesis

Effectiveness of trivalent and quadrivalent influenza vaccines in preventing infection, hospitalization, and severe outcomes in the 2023–2024 season onwards

7 November 2024

[MHF product code: LES 25.1]

Appendices listing

Appendix 1: Detailed search strategy

Databases searched:
- MEDLINE+ PUBMED via OVID: See detailed search strategy below
- Clinical trials registry: https://clinicaltrials.gov/

Search limits: 2023–current

Database retrieval:

Databases	10/09/2024
MEDLINE+ EMBASE via OVID	2,465
Preprint Citation Index	129
Clinical trials	179
TOTAL	2,773

MEDLINE+ EMBASE via OVID search:

#1	Influenza.mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kf, fx, dq, bt, nm, ox, px, rx, ui, sy, ux, mx]
#2	exp Influenza/
#3	exp vaccine/
#4	exp vaccination/
#5	vaccin*.mp.
#6	trivalent.mp.
#7	quadrivalent.mp.
#8	1 or 2
#9	3 or 4 or 5 or 6 or 7
#10	exp influenza vaccine/
#11	8 and 9
#12	10 or 11

#13	(effectiveness or efficacy or protection*).mp.
#14	12 and 13
#15	limit 14 to humans
#16	limit 15 to yr="2023-Current"
#17	remove duplicates from 16

Preprint Citation search:

#1	(TS=(Influenza)) AND TS=(vaccin* OR trivalent OR quadrivalent)) AND TS=((effectiveness OR efficacy OR protection))

Appendix 2: Summary of studies reporting on the effectiveness of trivalent and quadrivalent influenza vaccines in preventing infection, hospitalization, and severe outcomes

Reference (author year) with URL	Dimension of organizing framework	Study characteristics (type of publication, vaccine effectiveness analysis methods, setting and country)	Sample description and intervention	Summary of key findings in relation to the outcome

Lei 2024	• Population studied
	  ○ All age groups (from 6 months to 70+ years)
	• Type of vaccine
	  ○ Trivalent inactivated influenza vaccine (IIV3)
	  ○ Quadrivalent inactivated influenza vaccine (IIV4)
	  ○ Trivalent live attenuated vaccine (LAIV3)
	• Comparator
	  ○ Unvaccinated individuals
	• Testing
	  ○ Antigen detection
	  ○ RT-PCR
	• Outcome measures
	  ○ Vaccine effectiveness
	• Influenza related outcome
	  ○ Medically attended acute respiratory illness (hospital-attended influenza infection)
	• Timeframe (specimens collected)
	  ○ End of season 2023/24 (between 1 October 2023 and 31 March 2024)
		Type of publication: Preprint
		
		Study design: Test-negative case-control
		
		Analysis: Vaccine effectiveness (VE) was estimated using multivariate logistic regression models, adjusted for sex, age, influenza detection methods, and influenza testing timing
		
		Setting and country: Five tertiary hospitals in Hangzhou, China
			• The study included 157,291 patients with influenza-like illness across all age groups (from 6 months to 70+ years) who visited five tertiary hospitals in Hangzhou, China, between 1 October 2023 and 31 March 2024 with 36% testing positive for influenza and 7.1% having received the 2023/24 influenza vaccination
			• 86.3% of vaccinated participants received IIV4, 8.8% received IIV3, and 4.9% received LAIV3
				• Overall Vaccine VE:
				  ○ The estimated overall influenza VE against hospital-attended influenza infection in the 2023/24 season was 48% (95% CI: 46–51)
				• VE by Vaccine Type:
				  ○ IIV3 showed the highest overall VE at 59% (95% CI: 50–66)
				  ○ LAIV3 (3 to 17 years of age only) had a VE of 53% (95% CI: 42–62)
				  ○ IIV4 had a VE of 47% (95% CI: 45–50)
				• VE by Influenza Type:
				  ○ Influenza A 38% (95% CI: 34–42)
				  ○ Influenza B 57% (95% CI: 54–60)
				  ○ IIV3 provided significantly better protection against influenza B 87% (95% CI: 81–92) compared to IIV4 53% (95% CI: 50–57)
				• VE by Age Group:
				  ○ 0.5–2 years: 65% (95% CI: 54–72)
				  ○ 3–9 years: 43% (95% CI: 39–47)
				  ○ 10–17 years: 42% (95% CI: 36–48)
				  ○ 18–59 years: 52% (95% CI: 43–58)
				  ○ 60–69 years: 75% (95% CI: 59–85)
				  ○ ≥70 years: 28% (95% CI: 7–44)
				• VE by Vaccination Timing:
				  ○ Overall
				  ▪ Vaccination in the current season (2023/24) only provided the VE 52% (95% CI: 49–55)
				  ▪ Vaccination in both seasons (2023/24 and 2022/23) provided the VE 45% (95% CI: 41–49)
				  ○ Influenza A
				  ▪ Vaccination in the current season (2023/24) only provided the VE 47% (95% CI: 42–51)
				  ▪ Vaccination in both seasons (2023/24 and 2022/23) provided the VE 29% (95% CI: 23–35)
				  ○ Influenza B
				  ▪ Vaccination in the current season (2023/24) only provided the VE 56% (95% CI: 52–60)
				  ▪ Vaccination in both seasons (2023/24 and 2022/23) provided the VE 59% (95% CI: 55–63)

Reference (author year) with URL	Dimension of organizing framework	Study characteristics (type of publication, vaccine effectiveness analysis methods, setting and country)	Sample description and intervention	Summary of key findings in relation to the outcome

Costantino 2024	• Population studied
	  ○ General population (all ages)
	• Type of vaccine
	  ○ Quadrivalent inactivated influenza vaccine (IIV4)
	  ▪ Inactivated quadrivalent influenza vaccine standard dose (QIV-sd)
	  ▪ Cell culture-based inactivated quadrivalent influenza vaccine (QIV-cc)
	  ▪ High-dose inactivated quadrivalent influenza vaccine (QIV-hd)
	  ▪ Adjuvanted with MF59 inactivated quadrivalent influenza vaccine (QIV-a)
	  ▪ Live attenuated quadrivalent influenza vaccine (LAIV)
	• Comparator
	  ○ Unvaccinated individuals
	• Testing
	  o Nucleic acid testing-RT-PCR
	• Outcome measures
	  ○ Vaccine effectiveness
	• Influenza related outcome
	  o Medically attended acute respiratory illness (patients with influenza-like illness (ILI) seeking medical care)
	• Timeframe (specimens collected)
	  o Mid-season 2023/24 (between 1 October 2023 and 31 January 2024)
		Type of publication: Peer reviewed
		
		Study design: Test-negative case-control
		
		Analysis: VE was estimated by comparing the odds ratio of vaccination between cases and controls and using a logistic regression model to estimate VE adjusted by sex and at least one comorbidity overall and by age group
		
		Setting and country: Sicily, Italy
			• The study included 1,230 samples from participants of all age groups collected from general practitioners (GPs) and family pediatricians (FPs) in Sicily from 16 October 2023 to 7 January 2024 with 29.2% (n = 359) testing positive for influenza and 96.2% (n = 345) of these cases being influenza A(H1N1)pdm09
			• Of 191 vaccinated individuals, 29.4% received the QIV-sd, 11.1% received the QIV-cc, 25.4% received the LAIV, 23.1% received the QIV-hd, and 11.8% received the QIV-a
				• Overall VE:
				  ○ The overall influenza VE against influenza strain A(H1N1)pdm09: 41.4% (95% CI: 10.5–61.6)
				• VE by Age Group:
				  ○ 7 months–14 years: 37.9% (95% CI: –0.7–61.7)
				  ○ ≥65 years: 52.7% (95% CI: –38.0–83.8)

Choi 2024	• Population studied
	  ○ People aged 19 and over
	• Type of vaccine
	  ○ Quadrivalent inactivated influenza vaccine (IIV4)
	• Comparator
	  ○ Unvaccinated individuals
		Type of publication: Peer reviewed
		
		Study design: Test-negative case-control
			• The study included 2,632 patients who visited the emergency department or outpatient clinic with influenza-like illness, and those who were hospitalized with laboratory-confirmed	• VE against Influenza:
				  ○ Overall: 22.5% (95% CI: 6.6–35.8)
				  ○ 19–64 years: 24.3% (95% CI: 5.3–39.5)
				  ○ 65+ years: 17.4% (95% CI: –17.1– 41.8)
				• VE by Influenza Type:
				  ○ Influenza A
				  ▪ Overall: 22.3% (95% CI: 6.1–35.7)

Reference (author year) with URL	Dimension of organizing framework	Study characteristics (type of publication, vaccine effectiveness analysis methods, setting and country)	Sample description and intervention	Summary of key findings in relation to the outcome

	• Testing
	  ○ Antigen detection
	  ○ RT-PCR
	• Outcome measures
	  ○ Vaccine effectiveness
	• Influenza related outcome
	  ○ Medically attended acute respiratory illness (patients who visited emergency departments or outpatient clinics with influenza-like illness (ILI))
	  ○ Hospitalization (patients who hospitalized with either laboratory-confirmed influenza or ILI symptoms)
	• Timeframe (specimens collected)
	• Early-season 2023/24 (between 1 November 2023 and 31 December 2023)
		Analysis: VE was estimated using multivariate logistic regression models, adjusted for sex, age, and underlying comorbidities
		
		Setting and country: Eight hospitals in South Korea
			influenza or with symptoms consistent with influenza-like illness from ages 19 years and older who visited 8 hospitals in South Korea 1 November 2023 to 31 December 2023
			• RT-PCR testing confirmed 56.8% cases as influenza A/H1N1 and 38.4% cases as influenza A/H3N2
			• 32.4% test-positive cases were vaccinated, and 35.5% test-negative controls were vaccinated
				▪ 19–64 years: 23.9% (95% CI: 4.5–39.3)
				▪ ≥65 years: 17.4% (95% CI: –17.1–41.8)
				○ Influenza A/H1N1
				▪ Overall: 9.4% (95% CI: –51.3–45.7)
				▪ 19–64 years: 32.5% (95% CI: –128.7–80.1)
				▪ ≥ 65 years: 38.2% (95% CI: –15.6–67)
				○ Influenza A/H3N2
				▪ Overall: 0.3% (95% CI: –77–43.8)
				▪ 19–64 years: 84.1% (95% CI: –28.1–98.0)
				▪ ≥65 years: 0.0% (95% CI: –121.8–54.9)

Frutos 2024	• Population studied
	  ○ Older adults (aged ≥65 years)
	  ○ Children and adolescents aged six months to 17 years
	• Type of vaccine
	  ○ Not specified (vaccination status: ≥1 dose of any 2023-24 influenza vaccine in the United States received ≥14 days before illness onset or medical encounter)
	• Comparator
	  ○ Unvaccinated individuals
	• Testing
	  ○ Nucleic acid testing-RT-PCR
	• Outcome measures
	  ○ Vaccine effectiveness
	• Influenza related outcome
	  ○ Medically attended acute respiratory illness (outpatient visits including clinics, urgent care, emergency departments for ARI)
		Type of publication: Government report
		
		Study design: Test-negative case-control
		
		Analysis: VE was estimated to compare the odds ratio of vaccination against acute respiratory illness in different settings between cases and controls; a multivariable logistic regression model was used and adjusted for age, geographic region, and calendar time of illness
		
		Setting and country: 22 states in the United States
			• Control patients were those who had acute respiratory illness (ARI) who had received a negative influenza molecular assay result, and case patients were those who had ARI and had received a positive influenza assay result
			• Patients considered vaccinated in this study had received one or more dose of the 2023/24 influenza vaccine 14 days or more before an index date
			• Analyses were conducted using data from four CDC-affiliated VE networks, and VE estimates were calculated for influenza A subtypes A(H3N2) and
				• VE against Any Influenza:
				  ○ Medically Attended Acute Respiratory Illness
				  ▪ 0.5–17 years: NVSN 59% (95% CI: 48–67), US Flu VE 67% (95% CI: 48–80), VISION 60% (95% CI: 57–64)
				  ▪ ≥18 years: US Flu VE 33% (95% CI: 16–47), VISION 49% (95% CI: 47–51)
				  ▪ 18–64 years: US Flu VE 25% (95% CI: 3–42), VISION 52% (95% CI: 50–55)
				  ▪ ≥65 years: US Flu VE 51% (95% CI: 14–72), VISION 41% (95% CI: 36–45)
				  ○ Hospitalization
				  ▪ 0.5–17 years: NVSN 61% (95% CI: 40–75), VISION 52% (95% CI: 16–72)
				  ▪ ≥18 years: IVY 44% (95% CI: 32–54%), VISION 41% (95% CI: 34–47)
				  ▪ 18–64 years: IVY49% (95% CI: 33–61), VISION 40% (95% CI: 28–50)
				  ▪ ≥65 years: IVY 42% (95% CI: 23–56), VISION 42% (95% CI: 34–50)
				• VE against Any Influenza A:
				  ○ Medically Attended Acute Respiratory Illness

Reference (author year) with URL	Dimension of organizing framework	Study characteristics (type of publication, vaccine effectiveness analysis methods, setting and country)	Sample description and intervention	Summary of key findings in relation to the outcome
	○ Hospitalization (inpatient for ARI) • Timeframe (specimens collected) ○ Mid-season 2023/24 (between 1 October 2023 and 31 January 2024)		A(H1N1)pdm09 when possible • NVSN = New Vaccine Surveillance Network; US Flu VE = U.S. Flu Vaccine Effectiveness Network; VISION = Virtual SARS-CoV-2, Influenza, and Other respiratory viruses Network; and IVY = Investigating Respiratory Viruses in the Acutely Ill network	▪ 0.5–17 years: NVSN 55% (95% CI: 41–66), US Flu VE 46% (95% CI: 15–67), VISION 59% (95% CI: 55–62) ▪ ≥18 years: US Flu VE 27% (95% CI: 9–43), VISION 46% (95% CI: 44–48) ▪ 18–64 years: US Flu VE 13% (95% CI: –13–34), VISION 49% (95% CI: 46–51) ▪ ≥65 years: US Flu VE 52% (95% CI: 16–73), VISION 40% (95% CI: 36–45) ○ Hospitalization ▪ 0.5–17 years: NVSN 56% (95% CI: 30–73), VISION 46% (95% CI: 7–69) ▪ ≥18 years: IVY 42% (95% CI: 23–57), VISION 40% (95% CI: 34–47) ▪ 18–64 years: IVY 42% (95% CI: 13–61), VISION 40% (95% CI: 28–50) ▪ ≥65 years: IVY 42% (95% CI: 23–57), VISION 40% (95% CI: 33–47) • VE against Influenza A (H1N1)pdm09: ○ Medically attended acute respiratory illness ▪ 0.5–17 years: NVSN 54% (95% CI: 37–66), US Flu VE 61% (95% CI: 26–81), ▪ ≥18 years: US Flu VE 25% (95% CI: 1–43), ○ Hospitalization ▪ 0.5–17 years: NVSN 60% (95% CI: 32–77) ▪ ≥18 years: IVY 50% (95% CI: 30–64) • VE against Influenza A (H3N2): ○ Medically Attended Acute Respiratory Illness ▪ 0.5–17 years: NVSN 55% (95% CI: 20–74) ▪ ≥18 years: US Flu VE 54% (95% CI: 11–77) • VE against Influenza B: ○ Outpatient Medically Attended Acute Respiratory Illness ▪ 0.5–17 years: NVSN 64% (95% CI: 47–75), US Flu VE 89% (95% CI: 70–97), VISION 79% (95% CI: 71–85) ▪ ≥18 year: US Flu VE 78% (95% CI: 57–90), VISION 78% (95% CI: 74–81) ▪ 18–64 years: US Flu VE 75% (95% CI: 50–89), VISION 79% (95% CI: 75–82) ▪ ≥65 years: VISION 69% (95% CI: 51–80) ○ Hospitalization ▪ ≥18 years: VISION 60% (95% CI: 30–77) 18–64 years: VISION 50% (95% CI: 5–74)

Reference (author year) with URL	Dimension of organizing framework	Study characteristics (type of publication, vaccine effectiveness analysis methods, setting and country)	Sample description and intervention	Summary of key findings in relation to the outcome

Maurel 2024	• Population studied
	  ○ General population (all ages)
	  ○ Older adults (aged ≥65 years)
	  ○ Children and adolescents aged six months to 17 years
	• Type of vaccine
	  ○ Quadrivalent
	• Comparator
	  ○ Unvaccinated individuals
	• Testing
	  ○ Nucleic acid testing-RT-PCR
	• Outcome measures
	  ○ Vaccine effectiveness
	• Influenza related outcome
	  ○ Medically attended acute respiratory illness (primary care)
	  ○ Hospitalization
	• Timeframe (specimens collected)
	  ○ Mid-season 2023/24 (between September 2023 and January 2024)
		Type of publication:
		Peer reviewed
		
		Study design:
		Test-negative design
		
		Analysis: VE was estimated using multivariate logistic regression models, adjusted for sex, age, presence of chronic conditions, and onset date
		
		Setting and country: Europe
			• A total of 12,036 patients were collected between September 2024 to January 2024
			• Random influenza virus positive specimens were collected at eight primary care centres and three hospitals
			• In hospitals, 40% of controls. 39% of A(H1N1), and 57% of A(H3N2) were vaccinated
			• For the control population, the percentage of controls were 64% for hospitals, 62% influenza A(H1N1)pdm09, and 75% A(H3N2)
			• The study used various types of quadrivalent influenza vaccines, with the majority (73%) being standard dose, egg-propagated, inactivated vaccines, while smaller proportions were high-dose (12%), cell-based (9%), adjuvanted (5%), or live attenuated vaccines (1%)
				• Overall VE against Influenza A:
				  ○ Medically Attended Acute Respiratory Illness
				  ▪ All ages: 51% (95% CI: 41–59)
				  ▪ 0–17 years: 71% (95% CI: 55–82)
				  ▪ 18–64 years: 40% (95% CI: 22–55)
				  ▪ ≥65 years: 45% (95% CI: 22–62)
				  ○ Hospitalization
				  ▪ All ages: 38% (95% CI: 27–48)
				  ▪ 18–64 years: 53% (95% CI: 31–68)
				  ▪ ≥65 years: 36% (95% CI: 22–47)
				• VE against Influenza A (H1N1)pdm09:
				  ○ Medically Attended Acute Respiratory Illness
				  ▪ All ages: 53% (95% CI: 41–63)
				  ▪ 0–17 years: 85% (95% CI: 71–93)
				  ▪ 18–64 years: 40% (95% CI: 17–57)
				  ▪ ≥65 years: 41% (95% CI: 8–62)
				  ○ Hospitalization
				  ▪ All ages: 44% (95% CI: 30–55)
				  ▪ 18–64 years: 59% (95% CI: 30–77)
				  ▪ ≥65 years: 41% (95% CI: 23–54)
				• VE against Influenza A (H3N2):
				  ○ Medically Attended Acute Respiratory Illness
				  ▪ All ages: 30% (95% CI: –3–54)
				  ▪ 18–64 years: 35% (95% CI: –13–65)
				  ○ Hospitalization
				  ▪ All ages: 14% (95% CI: –32–43)
				  ▪ ≥65 years: 13% (95% CI: –42–45)
				• All age influenza vaccine effectiveness against medically attended acute respiratory illness was 53% (95% CI: –7–78) for clade 5a.2a and 39% (95% CI: –44–74) for 5a.2a.1

Whitaker 2024	• Population studied
	  ○ ≥ 2 years old
	• Type of vaccine
	  ○ All vaccines were quadrivalent
	  ○ Live-attenuated influenza vaccine (LAIV, for ages 2-17) via nasal spray
	  ○ Quadrivalent cell-based vaccine (QIVc for ages 18-64 years)
	  ○ Adjuvanted egg-based vaccine (QIVe for ages 65 years and older)
		Type of publication:
		Peer reviewed
		
		Study design: Test-negative case-control
		
		Analysis: VE was estimated using multivariate logistic regression models, adjusted for age, region, clinical risk status, sex, calendar time as week,
			• The GB-PC study included 1,193 case and 12,098 controls for A(H1N1)pdm09, A(H3N2), influenza A (untyped), influenza B, dual infections
			• The EN-H study included 1,359 cases and 22,539 controls with cases of influenza A (untyped), influenza B, and dual infections
				• VE against All Influenza (A and B):
				  ○ Medically attended ARI (GB-PC)
				  ▪ 2–17 years: 65% (95% CI: 41–79)
				  ▪ 18–64 years: 55% (95% CI: 43–65)
				  ▪ ≥65 years: 55% (95% CI: 32–70)
				  ○ Hospitalization (EN-H)
				  ▪ 2–17 years: 63% (95% CI: 46–75)
				  ▪ 18–64 years: 36% (95% CI: 20–49)
				  ▪ ≥65years: 40% (95% CI: 29–50)
				  ○ Hospitalization (SC-H)
				  ▪ 2–17 years: 65% (95% CI: 52–74)
				  ▪ 18–64 years: 55% (95% CI 43–65)

Reference (author year) with URL	Dimension of organizing framework	Study characteristics (type of publication, vaccine effectiveness analysis methods, setting and country)	Sample description and intervention	Summary of key findings in relation to the outcome

	• Comparator
	  ○ Unvaccinated individuals
	• Testing
	  ○ Not specified
	• Outcome measures
	  ○ Vaccine effectiveness
	• Influenza related outcome
	  ○ Medically attended acute respiratory illness (primary care)
	  ○ Hospitalization
	• Timeframe (specimens collected)
	• Mid-season 2023/24 (between 4 September 2023 and 28 January 2024)
		setting (community or hospital), and deprivation quintile
		
		Setting and country: Three sites in the U.K., including England, Scotland, and Wales (GB-PC study), England (EN-H), and Scotland (SC-H)
			• The SC-H study included 1,977 cases and 34,476 controls with influenza A (untyped), influenza A(H1N1)pdm09, influenza A(H3N2), and influenza B
			• 96% of controls between ages 2 and 17 years had live-attenuated influenza vaccine (remaining had quadrivalent)
			• 86–97% of controls aged 18–64 years received quadrivalent cell-based vaccine
			• 96–99% of controls aged 65 years and older received adjuvanted egg-based vaccine.
				▪ ≥65 years: 53% (95% CI 44–61)
				• VE against Influenza A(H1N1)pdm09:
				  ○ Medically Attended ARI (GB-PC)
				  ▪ 2–17 years: 65% (95% CI: 23–84)
				  ▪ 18–64 years: 62% (95% CI 46–74)
				  ▪ ≥65 years: 66% (95% CI: 35–82)
				  ○ Hospitalization (EN-H)
				  ▪ 18–64 years: 36% (95% CI: 20–49)
				  ▪ ≥65years: 60% (95% CI: 17–81)
				  ○ Hospitalization (SC-H)
				  ▪ 2–17 years: 71% (95% CI: 44–85)
				  ▪ 18–64 years: 64% (95% CI: 22–83)
				  ▪ ≥65 years: 61% (95% CI: 30–79)
				• VE against Influenza A(H3N2):
				  ○ Medically Attended Acute Respiratory Illness (GB-PC)
				  ▪ 2–17 years: 59% (95% CI: 18–79)
				  ▪ 18–64 years: 49% (95% CI 26–65)
				  ▪ ≥65 years: 44% (95% CI: –3–70)
				  ○ Hospitalization (EN-H)
				  ▪ 2–17 years: 80% (95% CI: 43–93)
				  ▪ 18–64 years: –3% (95% CI: –50–29)
				  ▪ ≥65 years: 39% (95% CI: 15–56)
				  ○ Hospitalization (SC-H)
				  ▪ 2–17 years: 64% (95% CI: 24–83)
				  ▪ 18–64 years: 74% (95% CI –1–72)
				  ▪ ≥65 years: 63% (95% CI 37–78)

Zhu 2024	• Population studied
	  ○ General population (all ages)
	• Type of vaccine
	  ○ For adults aged ≥65 years, high-dose, adjuvanted, or recombinant influenza
	• Comparator
	  ○ Unvaccinated individuals
	• Testing
	  ○ Nucleic acid testing-RT-PCR
	• Outcome measures
	  ○ Vaccine effectiveness
	• Influenza related outcome
	  ○ Infection (data from various healthcare settings (e.g.,
		Type of publication: Published study
		
		Study design: Test-negative case-control
		
		Analysis: Interim VE against influenza was estimated by comparing the odds of vaccination amongst patients who received a positive influenza laboratory-confirmed test result (case patients) and patients who received a negative influenza test result (control patients); a mixed
			• The study analyzed 678,422 individuals aged ≥6 months in California who underwent influenza testing between October 2023 and January 2024, with 11.4% testing positive for influenza
			• The intervention was 2023-24 seasonal influenza vaccination, received by 28.1% of the study population, with 88.8% of vaccinated adults aged ≥65 years receiving a high-dose, adjuvanted, or recombinant vaccine
				• VE against Influenza A and B:
				  ○ All ages: 45% (95% CI: 44–46)
				  ○ <18 years: 56% (95% CI: 54–57)
				  ○ 18–49 years: 48% (95% CI: 46–50)
				  ○ 50–64 years: 36% (95% CI: 33–39)
				  ○ ≥65 years: 30% (95% CI: 27–33)
				• VE against Influenza A:
				  ○ All ages 42% (95% CI: 41–43)
				  ○ <18 years: 52% (95% CI: 51–53)
				  ○ 18–49 years: 44% (95% CI: 42–46)
				  ○ 50–64 years: 35% (95% CI: 32–38)
				  ○ ≥65 years: 29% (95% CI: 26–32)
				• VE against Influenza B:
				  ○ All ages 76% (95% CI: 73–78)
				  ○ <18 years: 79% (95% CI: 76–82)
				  ○ 18–49 years: 75% (95% CI: 71–75)

Reference (author year) with URL	Dimension of organizing framework	Study characteristics (type of publication, vaccine effectiveness analysis methods, setting and country)	Sample description and intervention	Summary of key findings in relation to the outcome
	outpatient, inpatient, or intensive care unit) • Timeframe (specimens collected) ○ Mid-season 2023/24 (between 1 October 2023 and 31 January 2024)	effects logistic regression model was used and adjusted for age, race, and ethnicity Setting and country: California, United States		○ 50–64 years: 67% (95% CI: 55–76) ○ ≥65 years: 54% (95% CI: 34–67)
Smolarchuk 2024	• Population studied ○ General population (all ages) • Type of vaccine ○ Not specified • Comparator ○ Unvaccinated individuals • Testing ○ Nucleic acid testing-RT-PCR • Outcome measures ○ Vaccine effectiveness • Influenza related outcome ○ Medically attended acute respiratory illness • Timeframe (specimens collected) • Early-season 2023/24 (between 1 October 2023 and 31 December 2023)	Type of publication: Rapid communication Study design: Test-negative case-control Analysis: VE by influenza type and age group was estimated using multivariate logistic regression models, adjusted for age, gender, calendar time, hospitalization status, and presence of comorbidities Setting and country: Alberta, Canada	• The study included 38,136 patients across all age groups (6 months to 65+ years) who presented to physicians in Alberta, Canada, with influenza-like illness between 29 October 2023 and 30 December 2023 with 8,325, 310, and 312 patients testing positive for influenza A(H_1N_1)pdm09, influenza A(H_3N_2), and influenza B respectively	• VE by Influenza Type: ○ Influenza A(H_1N_1)pdm09: 61% (95% CI: 58–64) ○ Influenza A(H_3N_2): 49% (95% CI: 28–63) ○ Influenza B: 75% (95% CI: 58–85) • VE by Age Group for Influenza A(H_1N_1)pdm09: ○ 6 months–9 years: 74% (95% CI: 66–79) ○ 10–19 years: 62% (95% CI: 32–78) ○ 20–64 years: 62% (95% CI: 57–67) ○ ≥65 years: 57% (95% CI: 52–61)
Pérez-Gimeno 2024	• Population studied ○ Children aged six to 59 months • Type of vaccine ○ Quadrivalent ▪ inactivated influenza vaccine (IIV4) ▪ Intranasal live attenuated egg-based vaccine • Comparator ○ Unvaccinated individuals • Testing ○ Nucleic acid testing-RT-PCR • Outcome measures ○ Vaccine effectiveness • Influenza related outcome ○ ARI in primary care (Medically attended acute respiratory illness)	Study design: Test-negative case-control Analysis: VE was estimated by comparing the odds of vaccination between influenza cases and controls using logistic regression and Firth's method; estimates were adjusted for sex, age, week, chronic conditions, and region/hospital for both ARI and severe acute respiratory illness (SARI) models; VE was additionally estimated by influenza virus type, subtype, and clade	• 1,666 patients with ARI in primary care (n = 1,364) or SARI in hospital (n = 302); 292 patients tested positive for influenza (244 outpatient, 48 in hospital) • 33.2% of ARI patients and 33.1% of SARI patients had received a seasonal influenza vaccination	• VE for ARI Patients in Primary Care: ○ Against any influenza type: 70% (95% CI: 51–81) ○ Against A(H1N1)pdm09: 77% (95% CI: 56–88) ○ Against A(H3N2): 18% (95% CI: –97–65) ○ Against clade 5a.2a(H1N1): 96% (95% CI: 23–100) ○ Against 5a.2a.1 (H1N1): 49% (95% CI: –184–91) ○ Against 2a.3a.1 (H3N2): –116% (95% CI: –824–50) • VE for SARI Patients in Hospital: ○ Against any influenza type: 77% (95% CI: 21–93) ○ Against A(H1N1)pdm09: 75% (95% CI: –68–96) ○ Against A(H3N2): –3% (95% CI: –563–84)

Reference (author year) with URL	Dimension of organizing framework	Study characteristics (type of publication, vaccine effectiveness analysis methods, setting and country)	Sample description and intervention	Summary of key findings in relation to the outcome
	○ Hospitalisation • Timeframe (specimens collected) ○ End of season 2023/24 (between September 2023 and June 2024)	Setting and country: Primary care and 27 hospitals in 12 regions of Spain		
Shinjoh 2024	• Population studied ○ Children and adolescents aged six months to 15 years • Type of vaccine ○ Quadrivalent inactivated influenza vaccine (IIV4) • Comparator ○ Unvaccinated individuals • Testing ○ Nucleic acid testing-RT-PCR ○ Rapid influenza diagnostic tests • Outcome measures ○ Vaccine effectiveness • Influenza related outcome ○ Outpatients (medically attended acute respiratory illness) ○ Inpatients (hospitalization) • Timeframe (specimens collected) • End of season 2023/24 (between 1 November 2023 and 31 March 2024)	Study design: Test-negative case-control Analysis: VE was estimated using an adjusted odds ratio formula and adjusted for sex, age, comorbidity, area, month of onset, and diagnostic methods; VE was additionally estimated by age, presence of underlying disease, one dose versus two dose regimen, influenza strain, and method of testing Setting and country: Hospitals in Japan (17 sites for hospitalized patients, two sites for outpatients)	• 1,832 participants with fever were recruited from hospitals and outpatient clinics from November 2023 to March 2024 • 1,596 (20.4% positive) were involved in influenza A analysis; 1,497 (15.1% positive) were involved in Influenza B analysis • 35.8% of cases in the influenza A analysis were vaccinated with IIV4 against influenza; 36.2% of cases in the Influenza B analysis were vaccinated with IIV4 against influenza	• VE by for Influenza A: ○ In hospitalized cases (6 months–15 years): 51% (95% CI: 23–69) ▪ Age 1–2 years: 54% (95% CI: 1–79) ▪ Age 6–12 years: 59% (95% CI: 6–82) ▪ Without underlying disease: 58% (95% CI: 30–75) ▪ For one vaccine dose compared with none (6–12 months): 52% (95% CI: 4–76) ▪ For two vaccine doses compared with none (6–12 months): 47% (95% CI: 9–69) ○ In outpatient cases (6 months–15 years): 54% (95% CI: 27–71) ▪ Age 1–2 years: 81% (95% CI: 5–96) ▪ Age 3–5 years: 89% (95% CI 60–97) ▪ Without underlying disease: 69% (95% CI: 43–84) ▪ For one vaccine dose compared with none (6–12 months): 52% (95% CI: 2–77) ▪ For two vaccine doses compared with none (6–12 months): 59% (95% CI: 25–77) • VE for Influenza B: ○ In hospitalized cases (6 months–15 years): 60% (95% CI: 22–79) ▪ Age 6–12 years: 62% (95% CI: 11–84) ▪ With underlying disease: 90% (95% CI: 53–98) ▪ For two vaccine doses compared with none (6–12 months): 60% (95% CI: 15–81) ○ In outpatient cases (6 months–15 years): 56% (95% CI: 26–74) ▪ In age 3–5: 97% (95% CI: 67–100) ▪ In age 13–15: 87% (95% CI: 19–98) ▪ Without underlying disease: 53% (95% CI: 13–75) ○ For two vaccine doses compared with one (6–12 months old): 74% (95% CI: 10–93)
Mi 2024	• Population studied ○ General population (all ages) ○ Older adults (aged ≥65 years)	Study design: Test-negative case-control	• The study included 1,094 patients across all age groups (6 months and older) in four sentinel hospitals	• Overall VE against any Influenza (A or B) Infection: 54.7% (95% CI: 23.7, 73.1) • VE by influenza type ○ Influenza A: 62.3% (95% CI: 29.3–79.8)

Reference (author year) with URL	Dimension of organizing framework	Study characteristics (type of publication, vaccine effectiveness analysis methods, setting and country)	Sample description and intervention	Summary of key findings in relation to the outcome
	○ Children and adolescents aged six months to 17 years • Type of vaccine ○ Not specified • Comparator ○ Unvaccinated individuals • Testing ○ Laboratory test (using nasal or nasopharyngeal specimens) • Outcome measures ○ Vaccine effectiveness • Influenza related outcome ○ Infection • Timeframe (specimens collected) • End of season 2023/24 (between 1 January 2024 and 7 April 2024)	Analysis: VE by influenza type and age group using Bayesian logistic regression models, adjusted for age, gender, ethnicity, calendar year, and time interval Setting and country: Ili, Xinjiang, China	across three cities in Ili, Xinjiang China between 1 January to 7 April 2024. During this period, five to 50 nasopharyngeal specimens were randomly collected weekly from hospital outpatients and laboratory tested for influenza virus, with 87 patients (7.95%) testing positive mainly for influenza B, seven (8.0%) of which were vaccinated	○ Influenza B: 51.2% (95% CI: 28.7–83.0) • VE against any influenza (A or B) stratified by age group ○ 6 months–6 years: 63.1% (95% CI: 33.2–79.6) ○ 7–17 years: –23.0% (95% CI: –56.0–34.8) ○ 18–59 years: 60.0% (95% CI: 25.5–78.5) • VE against influenza A by age group ○ 6 months–6 years: 38.8% (95% CI: –14.8–67.4) • VE against influenza B by age group ○ 6 months–6 years: 80.0% (95% CI: 62.6–89.2) ○ 7–17 years: –7.9% (95% CI: –62.2–38.4) ○ 18–59 years: 50.2% (95% CI: 7.3–73.2)
Domnich 2024	• Population studied ○ Adults (aged ≥18 years) ○ Older adults (aged ≥65 years) • Type of vaccine ○ Quadrivalent inactivated influenza vaccine (IIV4) • Comparator ○ Unvaccinated • Testing ○ Nucleic acid testing–RT-PCR • Outcome measures ○ Vaccine effectiveness • Influenza related outcome ○ Inpatient (Hospitalization) • Timeframe (specimens collected) • End of season 2023/24 (between 15 October 2023 and 15 April 2024)	Study design: Test-negative case-control study Analysis: VE was measured using logistic regression modelling, adjusted for age, sex, previous season vaccination, calendar week, and presence of comorbidities Setting and country: Hospital, Genoa, Italy	• 1,664 patients ages 18 years and older at the San Martino Hospital were included in the study where they were tested (RT-PCR) for influenza infection within five days of hospital referral • Inactivated influenza vaccine (IIV4) exposure was determined by linkage to the local vaccination registry; 114 patients tested positive for influenza (mostly influenza A(H1N1)pdm09) and were considered as cases	• VE against Influenza Type A: ○ For older adults (aged ≥65 years): 50.6% (95% CI: 7.7–73.6) ○ For adults aged ≥18 years: 40% (95% CI: –5–66) • VE against Influenza A(H1N1)pdm09: ○ For older adults (aged ≥65 years): 48.7% (95% CI: 1.9–73.2) ○ For adults aged ≥18 years: 35% (95% CI: –17–63) • VE against Influenza by Vaccine Type in Older Adults (aged ≥65 years): ○ High-dose vaccine (HD-IIV4): 58% effective (95% CI: 1–82) ○ Adjuvanted vaccine (aIIV4): 56% effective (95% CI: –22–84) ○ Standard egg-based vaccine (eIIV4): <25% effective
Gao 2024	• Population studied ○ General population (all ages) • Type of vaccine ○ Trivalent inactivated influenza vaccine (IIV3) ○ Quadrivalent inactivated influenza vaccine (IIV4)	Study design: Test-negative case-control Analysis: VE by influenza type and age group was estimated using multivariate logistic regression models, adjusted for age, gender, calendar month of	• Among 205,028 participants (aged ≥6 months) who presented with influenza-like illness in Yinzhou, southern China between September 2023 and March 2024, 13.4% of test-negative controls and 7.6% of test-	• VE against Any Influenza Cases (A and B): ○ All ages: 49.4% (95% CI: 47.8–50.9) ○ 6 months–6 years: 45.8% (95% CI: 42.6–48.9) ○ 7–17 years: 38.6% (95% CI: 35.7–41.5) ○ 18–64 years: 46.7% (95% CI: 36.8–55) ○ ≥65 years: 46.1% (95% CI: 33.7–48.7) ○ Inpatient (hospitalization): 46.5% (95% CI: 35.4–55.8) ○ Outpatient and emergency: 49.7% (95% CI: 48.1–51.2)

Reference (author year) with URL	Dimension of organizing framework	Study characteristics (type of publication, vaccine effectiveness analysis methods, setting and country)	Sample description and intervention	Summary of key findings in relation to the outcome
	○ Trivalent live attenuated vaccine (LAIV3) • Comparator ○ Unvaccinated individuals • Testing ○ Antigen ○ Nucleic acid testing-RT-PCR • Outcome measures ○ Vaccine effectiveness • Influenza related outcome ○ Infection (outpatient and emergency, and inpatient) ○ Inpatient (hospitalization) ○ Outpatient and emergency (medically attended acute respiratory illness) • Timeframe (specimens collected) • End of season 2023/24 (between 4 September 2023 and 25 March 2024)	specimen collection, hospitalization status, and presence of comorbidities Setting and country: Community and hospital, Yinzhou, China	positive cases had received any type of influenza vaccine (IIV3, IIV4, or LAIV3) at least 14 days before specimen collection	• VE against Influenza A: ○ All ages: 41.9% (95% CI: 39.8–44.0) ○ 6 months–6 years: 38.7% (95% CI: 34.6–42.6) ○ 7–17 years: 33.2% (95% CI: 29.4–36.8) ○ 18–64 years: 42.9% (95% CI: 32.6–51.5) ○ ≥65 years: 40.4% (95% CI: 33.5–46.7) ○ Inpatient (hospitalization): 39.8 (25.8–51.1) ○ Outpatient and emergency: 42.1% (95% CI: 40.0–44.2) • VE against Influenza B: ○ All ages: 59.9% (95% CI: 57.9–61.9) ○ 6 months–6 years: 61.0% (95% CI: 57.0–64.6) ○ 7–17 years: 48.4% (95% CI: 44.7–51.9) ○ 18–64 years: 67.3% (95% CI: 58.7–74.1) ○ ≥65 years: 62.6% (95% CI: 54.1–69.5) ○ Hospitalization: 60.5% (95% CI: 42.1–73.1) ○ Outpatient and emergency: 59.7% (95% CI: 57.6–61.7)
Zeno 2024	• Population studied ○ Older adults (aged ≥65 years for Argentina, Chile, and Uruguay; ≥60 years for Brazil and Paraguay) ○ Children and adolescents (6 months to 2 years in Argentina, 6 months to 3 years in Paraguay, 6 months to 5 years in Chile and Uruguay, 6 months to 6 years in Brazil) • Type of vaccine ○ Trivalent inactivated influenza vaccine (IIV3) ○ Quadrivalent inactivated influenza vaccine (IIV4) • Comparator ○ Unvaccinated individuals • Testing ○ Nucleic acid testing-RT-PCR • Outcome measures ○ Vaccine effectiveness	Study design: Test-negative case-control study Analysis: Interim VE was measured by comparing the odds of influenza vaccination between case patients and control patients using multivariable logistic regression, adjusted for sex, age, country, week of symptom onset, and presence of at least one comorbidity Setting and country: Hospitals, Argentina, Brazil, Chile, Paraguay, and Uruguay	• In this study, 11,751 patients (all age groups) with SARI from 2,535 hospitals in the target countries were identified through the SARInet Plus between 13 March 2024 and 19 July 2024 and tested for influenza using RT-PCR testing • VE against influenza-associated hospitalization was measured by comparing patients who tested positive for influenza (case patients) with patients who tested negative (control patients) for influenza and SARS-CoV-2 • Trivalent vaccines containing antigens were used in Argentina, Brazil, Chile, and	• VE against Any Influenza (A or B) by Age Group ○ Overall: 34.5% (95% CI: 26.4–41.6) ○ 6 months–6 years: 39.0 (95% CI: 25.6 –50.0) ○ 60+ years: 31.2% (95% CI: 18.3–42.0) ○ Comorbidities: 58.7% (95% CI: 43.4– 69.8) • VE Against Influenza A by Age Group ○ Overall: 34.2% (95% CI: 26.0–41.4) ○ 6 months–6 years: 38.1 (95% CI: 24.4–49.2) ○ 60+ years: 31.4% (95% CI: 18.5–42.2) ○ Comorbidities: 58.3% (95% CI: 42.6–69.7) • VE Against Influenza A(H3N2) by Age Group ○ Overall: 36.5% (95% CI: 25.8–45.7) ○ 6 months–6 years: 38.4% (95% CI: 17.3–54.1) ○ 60+ years: 30.8% (95% CI: 14.4–44.0) ○ Comorbidities: 67.4% (95% CI: 49.3–79.0) • VE against Influenza A(H1N1)pdm09 by Age Group ○ Overall: 37.1% (95% CI: 21.9–49.4) ○ 6 months–6 years: 27.8% (95% CI: 5.1–45.0) ○ 60+ years: 30.8% (95% CI: 14.4–44.0) ○ Comorbidities: 57.6% (95% CI: 19.1–77.8)

Reference (author year) with URL	Dimension of organizing framework	Study characteristics (type of publication, vaccine effectiveness analysis methods, setting and country)	Sample description and intervention	Summary of key findings in relation to the outcome
	• Influenza related outcome ○ Hospitalization • Timeframe (specimens collected) • End of season 2023/24 (between 13 March 2024 and 19 July 2024, southern hemisphere flu season)		Uruguay while quadrivalent vaccines were used in Paraguay during each country's vaccination campaign	

Skowronski 2024	• Population studied
	  ○ General population (all ages)
	• Type of vaccine
	  ○ Trivalent inactivated influenza vaccine (IIV3)
	  ○ Quadrivalent inactivated influenza vaccine (IIV4)
	• Comparator
	  ○ Unvaccinated individuals = Never vaccinated individuals in the studied seasons
	• Testing
	  ○ Nucleic acid testing-RT-PCR
	  ○ Multiplex assays
	• Outcome measures
	  ○ Vaccine effectiveness
	• Influenza related outcome
	  ○ Medically attended acute respiratory illness
	  ○ Influenza-like illness (ILI)
	• Timeframe (specimens collected)
	  ○ Mid-season 2023/24 (between 1 October 2023 and 31 January 2024)
		Study design: Test-negative case-control
		
		Analysis: VE was calculated using the formula 1 – OR x 100%, adjusted for age group, province, and calendar time; Firth's penalized logistic regression was additionally used
		
		Setting and country: Community-based sentinel practitioners in Alberta, British Columbia, Ontario, and Quebec, Canada
			• 3,139 specimens were eligible for inclusion; 766 (24%) tested positive for influenza
			• 3,095 participants were included in the influenza A analysis; 722 (23%) tested positive for influenza A
			• 823 (27%) were vaccinated against influenza, 115 (16%) vaccinated individuals tested positive for influenza A, and the remaining 708 (30%) were influenza controls
				• VE against Medically Attended ARI Type Influenza A: 59% (95% CI: 48-68)
				  ○ Age 1–19 years: 60% (95% CI: 34–76)
				  ○ Age 20–64 years: 54% (95% CI: 38–66)
				  ○ Age ≥ 65 years: 70% (95% CI: 48–83)
				• VE against Medically Attended ARI Type Influenza A(H_1N_1)pdm09: 63% (95% CI: 51–72)
				  ○ By clade:
				  ▪ Vaccine-matched clade 5a.2a.1: 56% (95% CI: 33–71)
				  ▪ Alternate clade 5a.2a: 67% (95% CI: 48–80)
				  ○ By age:
				  ▪ 1–19 years old: 68% (95% CI: 42–83)
				  ▪ 20–64 years old: 56% (95% CI: 38–69)
				  ▪ ≥65 years old: 72% (95% CI: 47–85)
				• VE against Medically Attended ARI Type Influenza A(H_3N_2): 40% (95% CI: 5–61)
				• VE against ILI by Influenza Type:
				  ○ Influenza A: 58% (95% CI: 45–67)
				  ○ Influenza A(H_1N_1)pdm09: 61% (95% CI: 47–71)
				  ○ Influenza A(H_3N_2): 46% (95% CI: 11–67)
				• VE Estimates in Patients ≥12 Years Old in B.C., Ontario, and Quebec against Medically Attended ARI:
				  ○ Against influenza A: 59% (95% CI: 45–69)
				  ○ Against influenza A(H_1N_1)pdm09: 63% (95% CI: 48–74)
				  ▪ Clade 5a.2a.1: 51% (95% CI: 18–71)
				  ▪ Clade 5a.2a: 73% (95% CI: 48–86)
				  ○ Against influenza A(H_3N_2): 44% (95% CI: 5–67)

Appendix 3: Documents excluded at the final stage of reviewing

Author (year of publication) with hyperlink	Title	Reason for exclusion
Murphy et al. (2024)	Influenza vaccine effectiveness against hospitalizations associated with influenza A(H3N2) in Hong Kong children aged 9 months to 17 years, June-November 2023	Wrong timeline
Prasert et al. (2023)	Influenza virus circulation and vaccine effectiveness during June 2021–May 2023 in Thailand	Duplicate study
Broad et al. (2023)	Adapting COVID-19 research infrastructure to capture influenza and respiratory syncytial virus alongside SARS-CoV-2 in UK healthcare workers Winter 2022/23 and beyond: Protocol for a pragmatic sub-study	Wrong study design
Yuan Ma et al. (2024)	Association between influenza vaccination and one-year all-cause and cardiovascular mortality risk: A self-controlled case series and matched case-control study	Wrong outcomes
Maurel et al. (2024)	Exploring the effect of clinical case definitions on influenza vaccine effectiveness estimation at primary care level: Results from the end-of-season 2022-23 VEBIS multicentre study in Europe	Wrong intervention
Stein et al. (2024)	Relative vaccine effectiveness of cell- vs egg-based quadrivalent influenza vaccine against test-confirmed influenza over 3 seasons between 2017 and 2020 in the United States	Wrong comparator
McLean et al. (2023)	Comparison of influenza vaccine effectiveness estimates from the US influenza vaccine effectiveness network and electronic health record source population data, 2021-2022	Wrong study design
Noble et al. (2023)	Effectiveness of influenza vaccination against influenza-associated emergency department (ED) visits and hospitalizations among children with and without underlying medical conditions, new vaccine surveillance network (NVSN), 2015-2016 through 2019-2020	Wrong study design
Zemlianskaia et al. (2023)	Substantially elevated influenza risk in vaccinated immunocompromised adults and high-risk patients relative to all vaccinated	Wrong comparator
Imran et al. (2024)	Relative effectiveness of the MF59-adjuvanted influenza vaccine versus high-dose and non-adjuvanted influenza vaccines in preventing cardiorespiratory hospitalizations during the 2019–2020 US influenza season	Wrong comparator
Palmu et al. (2024)	High-dose quadrivalent influenza vaccine for prevention of cardiovascular and respiratory hospitalizations in older adults	Wrong comparator
Platas-Abenza et al. (2024)	Effectiveness of influenza vaccine in preventing severe cases of influenza: Season 2022/2023	Wrong timeline
Johansen et al. (2024)	Effectiveness of high-dose versus standard-dose quadrivalent influenza vaccine against recurrent hospitalizations and mortality in relation to influenza circulation: A post-hoc analysis of the DANFLU-1 randomized clinical trial	Wrong comparator
Sui et al. (2023)	Research progress of influenza vaccination, pneumococcal vaccination and COVID-19 vaccination among cancer patients	Wrong study design
Levin et al. (2024)	A clinical and economic assessment of adjuvanted trivalent versus standard egg-derived quadrivalent influenza vaccines among older adults in the United States during the 2018-19 and 2019-20 influenza seasons	Wrong comparator
Akhtar et al. (2023)	Optimal timing of influenza vaccination among patients with acute myocardial infarction – Findings from the IAMI trial	Wrong outcomes
Music et al. (2023)	Perspectives of older adults on COVID-19 and influenza vaccination in Ontario, Canada	Wrong interventions
Brennan et al. (2023)	Influenza vaccination: Simple, safe, and effective for patients with ischaemic heart disease and heart failure	Wrong outcomes
Zysman et al. (2023)	Impact of pharmacological and non-pharmacological interventions on mortality in chronic obstructive pulmonary disease (COPD) patients	Wrong study design
Sookaromdee et al. (2023)	Concurrent administration of COVID-19 vaccine and seasonal influenza vaccine: No increased estimated vaccine-related mortality rate	Wrong study design
Liu et al. (2023)	Timing and sequence of vaccination against COVID-19 and influenza	Wrong study design
Shinjoh et al. (2023)	Effectiveness of inactivated influenza and COVID-19 vaccines in hospitalized children in 2022/23 season in Japan - The first season of co-circulation of influenza and COVID-19	Wrong patient population

Author (year of publication) with hyperlink	Title	Reason for exclusion
Imran et al. (2023)	Relative effectiveness of the cell-based quadrivalent influenza vaccine in preventing cardiorespiratory hospitalizations in adults aged 18–64 years during the 2019–2020 US influenza season	Wrong comparator
Biering-Sørensen et al. (2023)	DANFLU-1: Feasibility of a pragmatic randomised trial to assess the relative effectiveness of high-dose (QIV-HD) vs standard-dose quadrivalent influenza vaccine (QIV-SD) on severe cardio-respiratory outcomes in elderly adults	Wrong study design
Mazagatos et al. (2023)	Impact of influenza vaccination on the burden of severe influenza in the elderly: Spain, 2017–2020	Wrong outcomes
Frühwein et al. (2023)	Enhanced targeted influenza vaccines – New evidence shows higher effectiveness in older adults	Wrong study design
Zeevat et al. (2023)	Reducing hospital capacity needs for seasonal respiratory infections: The case of switching to high-dose influenza vaccine for Dutch older adults	Wrong comparator
Escandell Rico et al. (2023)	Effectiveness of the influenza vaccine in the prevention of influenza in people over 65 years of age	Wrong interventions
Andrejko et al. (2023)	Receipt of COVID-19 and seasonal influenza vaccines in California (USA) during the 2021–2022 influenza season	Wrong outcomes
Johansen et al. (2023)	A pragmatic randomized feasibility trial of influenza vaccines	Wrong comparator
Shrestha et al. (2024)	Influenza epidemiology and vaccine effectiveness following funded influenza vaccine in Queensland, Australia, 2022	Wrong timeline
Chatzilena et al. (2024)	Winter 2022-23 influenza vaccine effectiveness against influenza-related hospitalised aLRTD: A test-negative, case-control study	Wrong timeline
Laniece et al. (2024)	Corrigendum to "Effectiveness of COVID-19 vaccines administered in the 2023 autumnal campaigns in Europe: Results from the VEBIS primary care test-negative design study, September 2023-January 2024" [Vaccine 42(19) (2024)]	Wrong interventions
Yang et al. (2024)	Repeated vaccination does not appear to significantly weaken the protective effect of influenza vaccine in the elderly: A test-negative case-control study in China	Wrong timeline
Tenforde et al. (2024)	Influenza vaccine effectiveness against Influenza A-Associated emergency department, urgent care, and hospitalization encounters among US adults, 2022–2023	Wrong timeline
McGovern et al. (2024)	Relative vaccine effectiveness of MF59-adjuvanted vs high-dose trivalent inactivated influenza vaccines for prevention of test-confirmed influenza hospitalizations during the 2017–2020 influenza seasons	Wrong timeline
Tenforde et al. (2023)	Vaccine effectiveness against influenza-associated urgent care, emergency department, and hospital encounters during the 2021-2022 season, VISION network.	Wrong timeline
Shinjoh et al. (2022)	Trends in effectiveness of inactivated influenza vaccine in children by age groups in seven seasons immediately before the COVID-19 era	Wrong timeline
Yildirim et al. (2021)	A retrospective test-negative case-control study to evaluate influenza vaccine effectiveness in preventing hospitalizations in children	Wrong timeline
Grijalva et al. (2021)	Influenza vaccine effectiveness for prevention of severe influenza–associated illness among adults in the United States, 2019-2020: A test-negative study	Wrong timeline
Chung et al. (2021)	Influenza vaccine effectiveness against all-cause mortality following laboratory-confirmed influenza in older adults, 2010–2011 to 2015–2016 seasons in Ontario, Canada	Wrong comparator
Rao et al. (2021)	Evaluation of influenza vaccine effectiveness among young children receiving consecutive versus nonconsecutive vaccination during Influenza A(H3N2)-predominant seasons	Wrong timeline

Author (year of publication) with hyperlink	Title	Reason for exclusion
Gershon et al. (2020)	Influenza vaccine effectiveness in preventing hospitalizations in older patients with chronic obstructive pulmonary disease	Wrong timeline
Feng et al. (2018)	Effectiveness of influenza vaccination on influenza-associated hospitalisations over time among children in Hong Kong: A test-negative case-control study	Wrong timeline
Flannery et al. (2017)	Interim estimates of 2016–17 seasonal influenza vaccine effectiveness – United States, February 2017	Wrong timeline
Kurečič Filipović et al. (2015)	Influenza vaccine effectiveness estimates in Croatia in 2010-2011: A season with predominant circulation of A(H1N1)pdm09 influenza virus	Wrong timeline
Hélène et al. (2023)	The relative effectiveness of a high-dose quadrivalent influenza vaccine vs standard-dose quadrivalent influenza vaccines in older adults in France: A retrospective cohort study during the 2021-22 influenza season	Wrong timeline
Bi et al. (2024)	Evaluating reduced effectiveness after repeat influenza vaccination while accounting for confounding by recent infection and within-season waning	Wrong timeline
Bi et al. (2023)	Reduced effectiveness of repeat influenza vaccination: distinguishing among within-season waning, recent clinical infection, and subclinical infection	Wrong timeline
Graham et al. (2024)	Quantifying and adjusting for confounding from health-seeking behaviour and healthcare access in observational research	Wrong timeline
Nakafero et al. (2024)	Uptake, safety, and effectiveness of inactivated influenza vaccine in patients with inflammatory bowel disease: A nationwide study in the UK using data from the clinical practice research datalink	Wrong timeline
McGovern et al. (2024)	Relative vaccine effectiveness of MF59-adjuvanted vs high-dose trivalent inactivated influenza vaccines for prevention of test-confirmed influenza hospitalizations during the 2017–2020 influenza seasons	Wrong timeline
Nakayama et al. (2024)	The efficacy and safety of a quadrivalent live attenuated influenza nasal vaccine in Japanese children: A phase 3, randomized, placebo-controlled study	Wrong timeline
Prasert et al. (2024)	Influenza virus circulation and vaccine effectiveness during June 2021–May 2023 in Thailand	Wrong timeline
Chung et al. (2024)	Late-season influenza vaccine effectiveness against medically attended outpatient illness, United States, December 2022–April 2023	Wrong timeline
Chatzilena et al. (2024)	Winter 2022-23 influenza vaccine effectiveness against influenza-related hospitalised aLRTD: A test-negative, case-control study	Wrong timeline
Hughes Kramer et al. (2024)	Effectiveness of the influenza vaccine for preventing laboratory-confirmed influenza infections in outpatient immunocompromised adults, 2017–2018	Wrong timeline
Yang et al. (2024)	Repeated vaccination does not appear to significantly weaken the protective effect of influenza vaccine in the elderly: A test-negative case-control study in China	Wrong timeline
Whitaker et al. (2024)	End of 2022/23 season influenza vaccine effectiveness in primary care in Great Britain	Wrong timeline
Yang et al. (2024)	Effectiveness of inactivated influenza vaccine against laboratory-confirmed influenza among Chinese elderly: A test-negative design	Wrong timeline
Mangas-Moro et al. (2024)	Influenza vaccination mitigates severe complications in hospitalized patients: A ten-year observational study, Spain, 2009–2019	Wrong timeline
Tippett et al. (2024)	Influenza vaccine effectiveness pre-pandemic among adults hospitalized with congestive heart failure or chronic obstructive pulmonary disease and older adults	Wrong timeline
Lewis et al. (2024)	Vaccine effectiveness against Influenza A-associated hospitalization, organ failure, and death: United States, 2022–2023	Wrong timeline

Author (year of publication) with hyperlink	Title	Reason for exclusion
Adams et al. (2024)	Vaccine effectiveness against pediatric Influenza-A-associated urgent care, emergency department, and hospital encounters during the 2022–2023 season: VISION network	Wrong timeline
Domnich et al. (2024)	Waning intra-season vaccine effectiveness against influenza A(H3N2) underlines the need for more durable protection	Wrong timeline
Whitaker et al. (2024)	Influenza vaccination during the 2021/22 season: A data-linkage test-negative case-control study of effectiveness against influenza requiring emergency care in England and serological analysis of primary care patients	Wrong timeline
Rose et al. (2024)	Vaccine effectiveness against influenza hospitalisation in adults during the 2022/2023 mixed season of influenza A(H1N1)pdm09, A(H3N2) and B circulation, Europe: VEBIS SARI VE hospital network	Wrong timeline
Al Kharusi et al. (2024)	Frequency of asthma exacerbations and upper respiratory tract infections among adults with asthma according to vaccination status: Does the annual influenza vaccine have a protective effect?	Wrong timeline
Pang et al. (2024)	Corrigendum to "Effectiveness of influenza vaccination on in-hospital death and recurrent hospitalization in older adults with cardiovascular diseases"	Wrong timeline
Olson et al. (2024)	Effectiveness of maternal influenza vaccination during pregnancy against influenza-associated emergency department visits and hospitalizations in infants <6 months of age	Wrong timeline
Glenn et al. (2024)	Influenza vaccine administration and effectiveness among children and adults with glomerular disease	Wrong timeline
Tsuzuki et al. (2023)	Association between seasonal influenza vaccination and antimicrobial use in Japan from the 2015–16 to 2020–21 seasons: From the VENUS study	Wrong timeline
Maurel et al. (2024)	Influenza vaccine effectiveness in Europe: Results from the 2022–2023 VEBIS (Vaccine Effectiveness, Burden and Impact Studies) primary care multicentre study	Wrong timeline
Kramer et al. (2023)	Effectiveness of the influenza vaccine for preventing laboratory-confirmed influenza infections in outpatient immunocompromised adults, 2017–2018	Wrong timeline
Hood et al. (2023)	Influenza vaccine effectiveness among children: 2011–2020	Wrong timeline
Hsiao et al. (2023)	Recombinant or standard-dose influenza vaccine in adults under 65 years of age	Wrong timeline
Wicke et al. (2023)	Schatzung der wirksamkeit der grippeimpfung anhand von sekundardaten: Eine kohortenstudie und propensity-score-matching-analyse von leistungsdaten aus Baden-Wurttemberg	Wrong timeline
Cowling et al. (2023)	Influenza vaccine effectiveness against influenza-associated hospitalization in Hong Kong children aged 9 months to 17 years, March–June 2023	Wrong timeline
Tenforde et al. (2023)	Influenza vaccine effectiveness against influenza-A-associated emergency department, urgent care, and hospitalization encounters among U.S. adults, 2022–2023	Wrong timeline
Fell et al. (2023)	Effectiveness of maternal influenza vaccination during pregnancy against laboratory-confirmed seasonal influenza among infants under 6 months of age in Ontario, Canada	Wrong timeline
Kildegaard et al. (2023)	Effectiveness of the quadrivalent live attenuated influenza vaccine against influenza-related hospitalisations and morbidity among children aged 2 to 6 years in Denmark: A nationwide cohort study emulating a target trial	Wrong timeline
Su et al. (2023)	Influenza vaccine effectiveness against influenza A during the delayed 2022/23 epidemic in Shihezi, China	Wrong timeline
Kislaya et al. (2023)	End of season 2022/2023 quadrivalent influenza vaccine effectiveness in preventing influenza in primary care in Portugal	Wrong timeline
Glenn et al. (2023)	Influenza vaccine administration and effectiveness among patients with glomerular disease	Wrong timeline

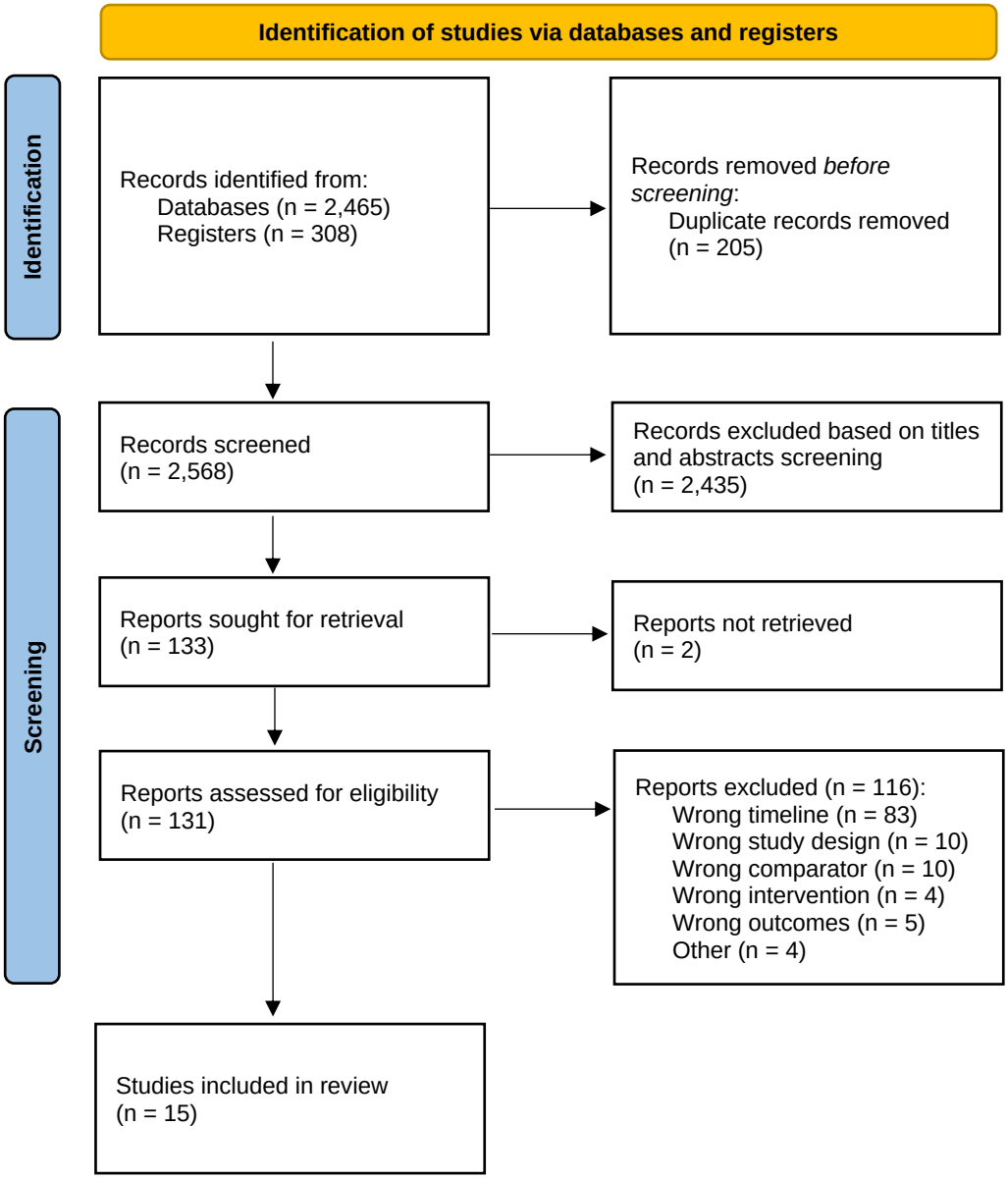
Author (year of publication) with hyperlink	Title	Reason for exclusion
Chaves et al. (2023)	High-dose influenza vaccine is associated with reduced mortality among older adults with breakthrough influenza even when there is poor vaccine-strain match	Wrong timeline
Pott et al. (2023)	Vaccine effectiveness of non-adjuvanted and adjuvanted trivalent inactivated influenza vaccines in the prevention of influenza-related hospitalization in older adults: A pooled analysis from the Serious Outcomes Surveillance (SOS) Network of the Canadian Immunization Research Network (CIRN)	Wrong timeline
Fornaguera et al. (2023)	Influenza vaccine effectiveness against hospitalization, season 2021/22: A test-negative design study in Barcelona	Wrong timeline
Martínez-Baz et al. (2023)	Influenza vaccine effectiveness in preventing laboratory-confirmed influenza cases and hospitalizations in Navarre, Spain, 2022–2023	Wrong timeline
Li et al. (2023)	Effect of influenza vaccination on rate of influenza virus infection in Chinese military personnel, 2015–2016: A cluster randomized trial	Wrong timeline
Zimmerman et al. (2023)	Vaccine effectiveness of recombinant and standard dose influenza vaccines against influenza related hospitalization using a retrospective test-negative design	Wrong timeline
Fowlkes et al. (2023)	Interim effectiveness estimates of 2023 Southern Hemisphere influenza vaccines in preventing influenza-associated hospitalizations – REVELAC-i Network, March–July 2023	Wrong timeline
Domnich et al. (2023)	Influenza vaccine effectiveness in preventing hospital encounters for laboratory-confirmed infection among Italian adults, 2022/23 season	Wrong timeline
Sominina et al. (2023)	Assessing the intense Influenza A(H1N1)pdm09 epidemic and vaccine effectiveness in the post-COVID season in the Russian Federation	Wrong timeline
Saadatian-Elahi et al. (2023)	Patient influenza vaccination reduces the risk of hospital-acquired influenza: An incident test negative-case control study in Lyon university hospital, France (2004–2020)	Wrong timeline
Chung et al. (2023)	Evaluating the impact of statin use on influenza vaccine effectiveness and influenza infection in older adults	Wrong timeline
Tenforde et al. (2023)	Vaccine effectiveness against influenza-associated urgent care, emergency department, and hospital encounters during the 2021–2022 season, VISION network	Wrong timeline
Stuurman et al. (2023)	Brand-specific estimates of influenza vaccine effectiveness for the 2021-2022 season in Europe: Results from the DRIVE multi-stakeholder study platform	Wrong timeline
Wagner et al. (2023)	Single-dose vaccination among infants and toddlers provides modest protection against influenza illness, which wanes after 5 months	Wrong timeline
Hood et al. (2023)	Influenza vaccine effectiveness among children: 2011–2020	Wrong timeline
Yokomichi et al. (2023)	Association of influenza vaccination or influenza virus infection history with subsequent infection risk among children: The Japan Environment and Children's Study (JECS)	Wrong timeline
Uemura et al. (2023)	Duration of influenza vaccine effectiveness in the elderly in Japan: A retrospective cohort study using large-scale population-based registry data	Wrong timeline
Chard et al. (2023)	End-of-season influenza vaccine effectiveness during the Southern Hemisphere 2022 influenza season – Chile, Paraguay, and Uruguay	Wrong timeline
Awadalla et al. (2023)	Moderately low effectiveness of the influenza quadrivalent vaccine: Potential mismatch between circulating strains and vaccine strains	Wrong timeline
Tenforde et al. (2023)	Vaccine effectiveness against Influenza A(H3N2)-associated hospitalized illness: United States, 2022	Wrong timeline
Price et al. (2023)	Influenza vaccine effectiveness against Influenza A(H3N2)-related illness in the United States during the 2021–2022 influenza season	Wrong timeline
Owusu et al. (2023)	Effectiveness of maternal influenza vaccination in Peru PRIME cohort	Wrong timeline

Author (year of publication) with hyperlink	Title	Reason for exclusion
Vaikutyte et al. (2023)	Influenza vaccine effectiveness in patients hospitalized with severe acute respiratory infection in Lithuania during the 2019–2020 influenza season: A test negative case – control study	Wrong timeline
Aso et al. (2023)	Effectiveness of vaccination on influenza-related critical illnesses in the elderly population	Wrong timeline
Sahni et al. (2023)	Sustained within-season vaccine effectiveness against influenza-associated hospitalization in children: Evidence from the new vaccine surveillance network, 2015–2016 through 2019–2020	Wrong timeline
Zimmerman et al. (2023)	Vaccine effectiveness of recombinant and standard dose influenza vaccines against outpatient illness during 2018–2019 and 2019–2020 calculated using a retrospective test-negative design	Wrong timeline
Regan et al. (2023)	Severity of influenza illness by seasonal influenza vaccination status among hospitalised patients in four South American countries, 2013–19: A surveillance-based cohort study	Wrong timeline
Panatto et al. (2023)	Surveillance of severe acute respiratory infection and influenza vaccine effectiveness among hospitalized Italian adults, 2021/22 season	Wrong timeline
Skowronski et al. (2023)	Vaccine effectiveness estimates from an early-season influenza A(H3N2) epidemic, including unique genetic diversity with reassortment, Canada, 2022/23	Wrong timeline
Kissling et al. (2023)	Influenza vaccine effectiveness against influenza A subtypes in Europe: Results from the 2021–2022 I-MOVE primary care multicentre study	Wrong timeline
Acevedo-Rodriguez et al. (2024)	Influenza incidence, lineages, and vaccine effectiveness estimates in Lima, Peru, 2023	Wrong timeline

Appendix 4: The ROBINS-I assessment included in the synthesis

First author, published year	Confounding	Selection of participants	Classification of interventions	Deviations from intended interventions	Missing data	Measurement of outcomes	Selection of reported result	Overall bias
Choi 2024	Moderate	Low	Low	Low	Moderate	Moderate	Low	Moderate
Costantino 2024	Moderate	Low	Low	Low	Moderate	Low	Low	Moderate
Domnich 2024	Low	Low	Low	Low	Low	Moderate	Moderate	Moderate
Frutos 2024	Low	Low	Low	Low	Low	Low	Low	Low
Gào 2024	Moderate	Low	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate
Lei 2024	Moderate	Low	Moderate	Low	low	Moderate	Low	Moderate
Maurel 2024	Low	Low	Moderate	Moderate	Moderate	Low	Low	Moderate
Mi 2024	Moderate	Low	Low	Moderate	Low	Moderate	Moderate	Moderate
Pérez-Gimeno 2024	Low	Low	Low	Low	Low	Low	Low	Low
Shinjoh 2024	Moderate	Low	Low	Moderate	Moderate	Moderate	low	Moderate
Smolarchuk 2024	Low	Low	Low	Low	Low	Low	Low	Low
Whitaker 2024	Low	Low	Low	Low	Low	Low	Low	Low
Zeno 2024	Low	Low	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate
Zhu 2024	Low	Low	Low	Low	Low	Low	Low	Low
Skowronski 2024	Moderate	Low	Low	Low	Low	Low	Low	Moderate

Appendix 5: PRISMA flow diagram



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