Effectiveness of the XBB.1.5 and 2024/2025 COVID-19 Vaccines
Living Evidence Synthesis #21
(Version 21.5: 10 March 2025)

Appendix 1a: Summary of Included Studies (new studies or updated elements of studies in blue) presented in alphabetical order

Reference (author, year), with URL	Methods	Key findings	Implications	ROBINS-I
Andersen et al. (2025)[1]	Retrospective cohort study among immunocompetent non-pregnant adults ≥18 years of age who were residents of California or Louisiana and enrolled in health insurance plans reporting to HealthVerity. The study included 6,344,448 individuals between September 25, 2023, and March 31, 2024. Patients had to have at least one year of continuous California or Louisiana residency and at least one year of continuous pharmacy and medical enrollment before the study start date in a health insurance plan contributing to HealthVerity. Separate Cox proportional hazards models were used to estimate adjusted hazard ratios (HR) with 95% CI for the risk of outcomes of interest, using a time-varying exposure framework and time-fixed covariates. Models were adjusted for age, sex, State of residence, insurance payor, presence of any condition(s) indicating CDC-defined high risk for severe COVID-19, wellness visit in the	**Absolute VE (95% CI) against COVID-19 related ED or UC visits** *At least 14 days* • ≥18 years: 39 (27-49) **Incremental VE (95% CI) against COVID-19 related ED or UC visits** (compared to individuals who did not receive the XBB.1.5 variant adapted vaccines) *At least 14 days* • ≥18 years: 45 (34-54) • ≥65 years: 48 (33-60) **Incremental VE (95% CI) against COVID-19 related ED or UC visits** (compared to individuals who did not receive the XBB.1.5 variant adapted vaccines but received at least 1 BA.4/5 bivalent dose) *At least 14 days* • ≥18 years: 48 (38-57) **Incremental VE (95% CI) against COVID-19 related ED or UC visits** (compared to individuals	The Pfizer-BioNTech XBB1.5-adapted vaccine was associated with a reduced risk of hospitalisation and ED/UC visits due to COVID-19 among adults aged ≥18 years without immunocompromising conditions.	Serious

	year prior to index, influenza vaccination in the year prior to index, whether they had any outpatient visits 180 days prior to index, whether they had any emergency department visits 180 days prior to index, and whether they had medically attended COVID-19 in the 91 to 365 days prior to index. VE was calculated as 1 – adjusted HR multiplied by 100%. Time and setting: omicron sublineages (primarily XBB, EG.5.1 and JN)	who did not receive the XBB.1.5 variant adapted vaccines received at least 2 doses of wild-type vaccine only (no variant adapted vaccine of any kind)) *At least 14 days* • ≥18 years: 45 (35-54) **Absolute VE (95% CI) against COVID-19 related hospitalisation** *At least 14 days* • ≥18 years: 33 (13-48) **Incremental VE (95% CI) against COVID-19 related hospitalisation** (compared to individuals who did not receive the XBB.1.5 variant adapted vaccines) *At least 14 days* • ≥18 years: 36 (18-50) • ≥65 years: 47 (28-61) **Incremental VE (95% CI) against COVID-19 related hospitalisation** (compared to individuals who did not receive the XBB.1.5 variant adapted vaccines but received at least 1 BA.4/5 bivalent dose) *At least 14 days* • ≥18 years: 40 (23-54) **Incremental VE (95% CI) against COVID-19 related hospitalisation** (compared to individuals who did not receive the		

		XBB.1.5 variant adapted vaccines received at least 2 doses of wild-type vaccine only (no variant adapted vaccine of any kind)) *At least 14 days* • ≥18 years: 34 (16-49)		

Andersson et al. (2024)[2,3]	National cohort study using different nationwide registries, leading to a source population of 7,244,914 adults.
	
	The study included 3,752,564 adults aged ≥65 years living in Denmark, Sweden or Finland from 1 October 2023 to 21 April 2024.
	
	Included adults had no prior hospital admission related to covid-19 and received ≥4 prior COVID-19 vaccine doses (of AZD1222, BNT162b2, or mRNA-1273 vaccines only [AZD1222 as part of the primary vaccination course only]).
	
	Relative VE (1-risk ratio) was calculated using the cumulative incidences of covid-19 hospital admission and death for 24 weeks after immunisation among recipients of an XBB.1.5-containing covid-19 mRNA vaccine and matched non-recipients.
	
	Time and setting: XBB sublineages and BA.2.86 sublineages were the prevailing variants.
		Incremental VE (%) (95% CI) against COVID-19 related hospitalisations (compared to individuals who received at least 4 prior doses of COVID-19 vaccines)
		
		8 to 168 days since last dose:
		• As a 5th dose: 55.3 (43.2-67.4)
		• As a 6th dose: 56.7 (51.4 61.9)
		• As a 7th dose: 56.5 (47.3- 65.8)
		• ≥65 years: 57.9 (49.9-65.8)
		  ○ XBB: 75.1 (69.6-80.5)
		  ○ BA.2.26: 56.3 (48.5-64.0)
		• 65-74 years: 60.3 (51.9-68.7)
		• ≥75 years: 57.6 (47.8-67.5)
		
		8 to 27 days since last dose: 64.5 (49.0-80.0)
		
		28 to 48 days since last dose: 63.1 (54.9-71.3)
		
		49 to 69 days since last dose: 55.4 (35.6-75.1)
		
		70 to 90 days since last dose: 48.8 (33.1-64.4)
			The XBB.1.5 variant adapted vaccine was associated with a reduced risk of hospitalisation and death due to COVID-19 among adults ≥65 years of age who received at least 4 prior COVID-19 vaccine doses. These findings support XBB.1.5 recommendations for persons in this age group.	Serious

		91 to 111 days since last dose: 60.1 (38.4-81.8)
		
		112 to 132 days since last dose: 67.0 (41.3-92.8)
		
		133 to 153 days since last dose: 52.3 (9.5-95.0)
		
		154 to 174 days since last dose: 50.1 (-20.9-100.0)
		
		Incremental VE (%) (95% CI) against COVID-19 related death (compared to individuals who received at least 4 prior doses of COVID-19 vaccines)
		
		8 to 168 days since last dose:
		• As a 5th dose: 74.9 (67.4-82.3)
		• As a 6th dose: 75.6 (71.0-80.3)
		• As a 7th dose: 66.0 (54.4-77.5)
		• ≥65 years: 75.2 (70.6-79.9)
		  ○ XBB: 85.7 (80.6-90.8)
		  ○ BA.2.26: 78.0 (74.3-81.6)
		• 65-74 years: 71.7 (62.4-81.0)
		• ≥75 years: 76.0 (70.4-81.5)
		
		8 to 27 days since last dose: 82 (78.5-85.5)
		
		28 to 48 days since last dose: 79.3 (72.4-86.1)
		
		49 to 69 days since last dose: 74.6 (63.3-86.0)		

		70 to 90 days since last dose: 70.3 (53.6-87.0) *91 to 111 days since last dose:* 66.9 (35.3-98.4) *112 to 132 days since last dose:* 33.1 (-17.3-83.6) *133 to 153 days since last dose:* 69.4 (28.1-100.0) *154 to 174 days since last dose:* 73.4 (6.7-100.0)		
Appaneal et al. (2024)[4]	Nationwide test-negative case control study using the US Veterans Affairs Healthcare system. The study included 44,598 acute respiratory infection (ARI) episodes in adults aged ≥18 years diagnosed in the hospital, emergency department, urgent care or outpatient setting during the study period (September 5, 2024, and November 30, 2024). Patients had to be tested for SARS-CoV-2 via nucleic acid amplification test (NAAT) or rapid antigen test (RAT) within 14 days prior through 3 days after the ARI encounter. Patients could contribute more than one ARI episode to the study if the episodes were more than 30 days apart Adjusted odds ratios were calculated using a multivariate logistic regression model adjusting for (age, sex, race, ethnicity, body mass index (BMI) categories,	**Incremental VE (%) (95% CI) of the Pfizer-BioNTech KP.2-adapted vaccine against medically attended COVID-19 infections** (compared to individuals who did not receive any KP.2 variant adapted vaccine) *At least 14 days* • ≥18 years: 56 (36-69) • ≥65 years: 58 (36-73) **Incremental VE (%) (95% CI) of the Pfizer-BioNTech KP.2-adapted vaccine against COVID-19 related ED or UC visits** (compared to individuals who did not receive any KP.2 variant adapted vaccine) *At least 14 days* • ≥18 years: 57 (46-65)	The KP.2 variant adapted vaccine was associated with a reduced risk of medically attended COVID-19 infections, COVID-related ED or UC visits and COVID-related hospitalisation among adults **≥18** years of age. These findings support XBB.1.5 recommendations for persons in this age group.	Serious

	Charlson Comorbidity Index, smoking status, immunocompromised status, receipt of pneumococcal vaccine in the past 5 years, encounters with the VA healthcare system in the year prior, evidence of documents prior SARS-CoV-2 infection, US Census region. VE was calculated as 1 minus the corresponding adjusted OR (and 95% CI), multiplied by 100%. Time and setting: Omicron	**Incremental VE (%) (95% CI) of the Pfizer-BioNTech KP.2-adapted vaccine against COVID-19 related hospitalisations** (compared to individuals who did not receive any KP.2 variant adapted vaccine) *At least 14 days* • ≥18 years: 57 (46-65) • ≥65 years: 56 (44-66)		

Caffrey et al. (2024)[5,6]	Nationwide test-negative case control study using the US Veterans Affairs Healthcare system.
	
	The study included 113,174 acute respiratory infection (ARI) episodes in adults aged ≥18 years diagnosed in the hospital, emergency department, urgent care or outpatient setting during the study period (September 25, 2023, and January 31, 2024).
	
	Patients had to be tested for SARS-CoV-2 via nucleic acid amplification test (NAAT) or rapid antigen test (RAT) within 14 days prior through 3 days after the ARI encounter. Patients could contribute more than one ARI episode to the study if the episodes were more than 30 days apart and the encounter at the highest level of care (i.e., hospitalization > ED/UC visit > outpatient visit) was selected for inclusion.
		Incremental VE (95% CI) against COVID-19 related ED or UC visits (compared to individuals who did not receive the XBB.1.5 variant adapted vaccines)
		
		At least 14 days since last dose
		• ≥18 years: 39 (33-45)
		  ○ Immunocompromised: 34 (22-45)
		  ○ Immunocompetent: 42 (34-49)
		  ○ XBB and JN.1 sublineages: 43 (33-52)
		  ○ XBB sublineages: 50 (35-61)
		  ○ JN.1 sublineages: 33 (22-43)
		  ○ Individuals who received at least 1 BA.4/5 bivalent dose: 44 (37-51)
		  ○ Individuals who received 3 or more doses of original wild-type mRNA but no bivalent-adapted vaccines: 41 (25-53)
		• 18 to <65 years: 48 (37-57)
			The BNT162b2 XBB.1.5 variant adapted vaccine was associated with a reduced risk of hospitalisation, ED/UC visits and outpatient visits due to COVID-19 among adults aged ≥18 years. This protective effect seems less marked against the JN.1 sublineages than the XBB sublineages. The XBB.1.5 vaccine also provided some protection against hospitalisation, ED/UC visits and outpatient visits due to COVID-19 to immunocompromised individuals.	Moderate

	Adjusted odds ratios were calculated using a multivariate logistic regression model adjusting for (calendar week of ARI episode, age, sex, race, ethnicity, body mass index (BMI) categories, Charlson Comorbidity Index, receipt of influenza vaccine during the 2023-2024 season, receipt of pneumococcal vaccine in the past 5 years, encounters with the VA healthcare system in the year prior, smoking status, immunocompromised, and Census region, and prior documented SARS-CoV-2 infection. VE was calculated as 1 minus the corresponding adjusted OR (and 95% CI), multiplied by 100%. Time and setting: XBB sublineages and JN.1 sublineages were the prevailing variants.	• ≥65 years: 35 (27-43) *14 to 60 days since last dose* ○ XBB sublineages: 52 (37-63) ○ JN.1 sublineages: 41 (23-54) *61 to 133 days since last dose* ○ JN.1 sublineages: 30 (16-41) **Incremental VE (%) (95% CI) against COVID-19 related hospitalisations** (compared to individuals who did not receive the XBB.1.5 variant adapted vaccines) *At least 14 days since last dose* • ≥18 years: 43 (34-51) ○ Immunocompromised: 33 (16-47) ○ Immunocompetent: 49 (38-58) ○ XBB and JN.1 sublineages: 46 (32-58) ○ XBB sublineages: 61 (44-73) ○ JN.1 sublineages: 35 (20-48) ○ Individuals who received at least 1 BA.4/5 bivalent dose: 45 (34-54) ○ Individuals who received 3 or more doses of original wild-type mRNA but no bivalent-adapted vaccines: 56 (36-69) • 18 to <65 years: 58 (33-73) • ≥65 years: 41 (32-50) *14 to 60 days since last dose* ○ XBB sublineages: 62 (44-74) ○ JN.1 sublineages: 32 (3-52)		

		61 to 133 days since last dose ○ JN.1 sublineages: 37 (19-51) **Incremental VE (%) (95% CI) against COVID-19 related outpatient visits** (compared to individuals who did not receive the XBB.1.5 variant adapted vaccines) *At least 14 days since last dose* • ≥18 years: 27 (16-37) ○ Immunocompromised: 40 (19-55) ○ Immunocompetent: 22 (8-34) ○ XBB and JN.1 sublineages: 29 (9-44) ○ XBB sublineages: 51 (27-67) ○ JN.1 sublineages: 24 (5-39) ○ Individuals who received at least 1 BA.4/5 bivalent dose: 26 (11-39) ○ Individuals who received 3 or more doses of original wild-type mRNA but no bivalent-adapted vaccines: 38 (11-57) • 18 to <65 years: 34 (14-50) • ≥65 years: 24 (9-36) *14 to 60 days since last dose* • XBB sublineages: 50 (25-66) • JN.1 sublineages: 31 (1-52) *61 to 133 days since last dose* • JN.1 sublineages: 20 (-4-38)		
Carazo et al. (2024)[7]	A test-negative case-control study utilizing specimens tested for SARS-CoV-2 at any acute-care hospital in the province of	***Omicron (XBB, JN.1 or KP)***	The mRNA XBB.1.5 variant adapted vaccines were associated with a reduced risk	Serious

	Quebec from Quebec's provincial laboratory database. Overall, 114,005 test results from adults aged ≥60 years who presented with COVID-19 symptoms from October 29, 2023 (epi-week 2023-44) to August 17, 2024 (epi-week 2024-33) were included. Individuals could contribute multiple tests to the analysis. Logistic regression models to derive adjusted odds ratios (OR) and their 95% confidence intervals (95% CI) adjusted for sex, age group (60-69, 70-79 and ≥80 years), residence (home, private homes for older people), epi-week of specimen collection, chronic respiratory disease, chronic heart disease, cancer, obesity, neurological disease and multimorbidity (at least two chronic diseases). Estimated VE was calculated as (1 – adjusted OR)*100. Time and setting: omicron sublineages (primarily XBB, EG.5.1 and JN)	**Absolute VE (95% CI) against COVID-19 related hospitalisation** *At least 7 days* • ≥60 years: 29.6 (25.3-33.6) **Incremental VE (95% CI) against COVID-19 related hospitalisation** (compared to individuals who did not receive the XBB.1.5 variant adapted vaccines) *At least 7 days* • ≥60 years: 35.8 (26.3-44.1) **Incremental VE (95% CI) against COVID-19 related hospitalisation** (compared to individuals who did not receive the XBB.1.5 variant adapted vaccines but received an ancestral mRNA monovalent or bivalent vaccine dose during Quebec's prior vaccination campaign from July to December 2022) *At least 7 days* • ≥60 years: 29.9 (24.4-35.0) • 60-69 years: 3.9 (-17.7-21.5) • 70-79 years: 33.4 (24.1-41.5) • ≥ 80 years: 33.5 (26.2-40.0) • Prior infection: 43.4 (35.9-50.1) **Incremental VE (95% CI) against COVID-19 related hospitalisation** (compared to individuals who did not receive the	of COVID-19 related hospitalisations, especially during the period where the XBB variant was predominant. It still offered some protection against the JN.1 variant. The effectiveness waned over time.	

		XBB.1.5 variant adapted vaccines but received an ancestral mRNA monovalent or bivalent vaccine dose during Quebec's prior vaccination campaign from July to December 2022 **who had a prior COVDI-19 infection**) *At least 7 days* • Prior infection: 28.2 (13.6-40.3) ***XBB*** **Absolute VE (95% CI) against COVID-19 related hospitalisation** *At least 7 days* • ≥60 years: 54.0 (46.1-60.7) **Incremental VE (95% CI) against COVID-19 related hospitalisation** (compared to individuals who did not receive the XBB.1.5 variant adapted vaccines) *At least 7 days* • ≥60 years: 53.8 (37.3-66.0) **Incremental VE (95% CI) against COVID-19 related hospitalisation** (compared to individuals who did not receive the XBB.1.5 variant adapted vaccines but received an ancestral mRNA monovalent or bivalent vaccine dose during Quebec's prior vaccination campaign from July to December 2022) *At least 7 days*		

		• ≥60 years: 54.4 (45.9-61.6) • 60-69 years: 47.5 (10.5-69.2) • 70-79 years: 56.1 (40.6-67.6) • ≥ 80 years: 54.9 (43.3-64.1) • Prior infection: 73.6 (61.1-82.1) *7 to 60 days* • 60-69 years: 47.5 (10.5-68.2) • 70-79 years: 56.1 (40.6-67.6) • ≥ 80 years: 54.9 (43.3-64.1) *7 to 30 days* • ≥60 years: 53.2 (43.5-61.3) *31 to 60 days* • ≥60 years: 60.44 (46.0-70.9) **Incremental VE (95% CI) against COVID-19 related hospitalisation** (compared to individuals who did not receive the XBB.1.5 variant adapted vaccines but received an ancestral mRNA monovalent or bivalent vaccine dose during Quebec's prior vaccination campaign from July to December 2022 **who had a prior COVDI-19 infection**) *At least 7 days* • Prior infection: 65.5 (46.8-77.6) **JN.1**		

		Absolute VE (95% CI) against COVID-19 related hospitalisation *At least 7 days* • ≥60 years: 25.2 (17.5-32.1) **Incremental VE (95% CI) against COVID-19 related hospitalisation** (compared to individuals who did not receive the XBB.1.5 variant adapted vaccines) *At least 7 days* • ≥60 years: 30.8 (12.7-45.1) **Incremental VE (95% CI) against COVID-19 related hospitalisation** (compared to individuals who did not receive the XBB.1.5 variant adapted vaccines but received an ancestral mRNA monovalent or bivalent vaccine dose during Quebec's prior vaccination campaign from July to December 2022) *At least 7 days* • ≥60 years: 22.7 (12.1-32.0) • 60-69 years: -6.7 (-47.5-22.8) • 70-79 years: 25.5 (7.5-40.1) • ≥ 80 years: 28.8 (14.5-40.7) • Prior infection: 41.1 (27.5-52.1) *7 to 60 days* • 60-69 years: -23.7 (-91.7-20.2) • 70-79 years: 34.7 (11.1-52.0) • ≥ 80 years: 27.2 (6.2-43.6)		

		7 to 30 days • ≥60 years: 27.8 (3.4-46.0) *31 to 60 days* • ≥60 years: 22.5 (6.2-36.0 *61 to 91 days* • ≥60 years: 27.6 (14.5-38.8) *92 to 121 days* • ≥60 years: 19.8 (0.2-35.5) *122 to 152 days* • ≥60 years: 23.1 (-3.1-42.6) *153 to 182 days* • ≥60 years: 6.5 (-44.1-39.3) *183 to 213 days* • ≥60 years: -5.2 (-159.5-57.4) **Incremental VE (95% CI) against COVID-19 related hospitalisation** (compared to individuals who did not receive the XBB.1.5 variant adapted vaccines but received an ancestral mRNA monovalent or bivalent vaccine dose during Quebec's prior vaccination campaign from July to December 2022 **who had a prior COVDI-19 infection**) *At least 7 days* • Prior infection: 14.1 (-18.8-37.9)		

		KP **Absolute VE (95% CI) against COVID-19 related hospitalisation** *At least 7 days* • ≥60 years: -0.7 (-12.8-10.1) **Incremental VE (95% CI) against COVID-19 related hospitalisation** (compared to individuals who did not receive the XBB.1.5 variant adapted vaccines) *At least 7 days* • ≥60 years: 7.4 (-24.2-30.9) **Incremental VE (95% CI) against COVID-19 related hospitalisation** (compared to individuals who did not receive the XBB.1.5 variant adapted vaccines but received an ancestral mRNA monovalent or bivalent vaccine dose during Quebec's prior vaccination campaign from July to December 2022) **Received one dose of an mRNA XBB.1.5 variant adapted vaccine** *At least 7 days* • ≥60 years: -3.5 (-21.5-11.8) *7 to 60 days* • ≥60 years: 70.1 (31.4-86.9) *61 to 121 days*		

		• ≥60 years: 37.8 (-9.6-64.6) *122 to 182 days* • ≥60 years: 12.3 (-24.2-38.0) *183 to 243 days* • ≥60 years: 3.2 (-18.0-20.5) *244 to 304 days* • ≥60 years: -20.0 (-45.6- 1.0) **Received two doses of an mRNA XBB.1.5 variant adapted vaccine** *At least 7 days* • ≥60 years: 38.6 (13.6-56.4) *7 to 60 days* • ≥60 years: 57.1 (31.0-73.4) *61 to 121 days* • ≥60 years: 32 (-5.1-56.0) **Received one or two doses of an mRNA XBB.1.5 variant adapted vaccine** *At least 7 days* • ≥60 years: 0 (-16.7-15.2) • 60-69 years: -47.2 (-130.3-5.9) • 70-79 years: 10.3 (-18.5-32.0) • ≥ 80 years: 6.6 (-16.3-25.0) • Prior infection: 5.9 (-19.3-25.8)		

		7 to 60 days • ≥60 years: 60.2 (38.9-74.0) • 60-69 years: 53.2 (-136.2-90.7) • 70-79 years: 55.9 (-7.8-82.0) • ≥ 80 years: 63.0 (28.3-77.9) *61 to 121 days* • ≥60 years: 33.2 (3.6-53.7) *122 to 182 days* • ≥60 years: 13.6 (-22.1-38.9) *183 to 243 days* • ≥60 years: 3.2 (-18.0-20.5) *244 to 304 days* • ≥60 years: -20.0 (-45.6-1.0) **Incremental VE (95% CI) against COVID-19 related hospitalisation** (compared to individuals who did not receive the XBB.1.5 variant adapted vaccines but received an ancestral mRNA monovalent or bivalent vaccine dose during Quebec's prior vaccination campaign from July to December 2022 **who had a prior COVDI-19 infection**) *At least 7 days* • Prior infection: -24.9 (-97.3-21.0)		
Chong et al. (2024)[8]	A retrospective cohort study from Singapore	**aHR (95% CI) against positive COVID-19 test** (compared to	The mRNA XBB.1.5 variant adapted vaccines were	Moderate

	During the study period (6 November 2023 to 13 January 2024), 3,086,562 Singaporean citizens or permanent residents aged ≥18 years, who did not receive non-mRNA COVID-19 vaccines, and who were boosted (received ≥3 mRNA COVID-19 vaccine doses) before study start date were included.
	
	Individuals who received non-mRNA vaccines or received less than 3 mRNA vaccine doses were excluded.
	
	Cases had confirmed SARS-CoV-2 infection, defined as positive polymerase chain reaction (PCR) or positive rapid antigen test results.
	
	Cox regression was used to assess factors associated with SARS-CoV-2 infections and COVID-19–related ED visits or hospitalizations, adjusted for all available sociodemographic variables.
	
	Time and setting: JN.1
		individuals who did not receive the XBB.1.5 variant adapted vaccines but received at least 3 doses of COVID-19 vaccine)
		8-120 days since last dose
		• ≥18 years: 0.59 (0.52-0.66)
		  ○ Prior infection: 0.56 (0.47-0.67)
		
		aHR (95% CI) against COVID-19 related ED or UC visits (compared to individuals who did not receive the XBB.1.5 variant adapted vaccines but received at least 3 doses of COVID-19 vaccine)
		8-120 days since last dose
		• ≥18 years: 0.50 (0.34-0.73)
		  ○ Prior infection: 0.78 (0.43-1.43)
		
		aHR (95% CI) against COVID-19 related hospitalisations (compared to individuals who did not receive the XBB.1.5 variant adapted vaccines but received at least 3 doses of COVID-19 vaccine)
		8-120 days since last dose
		• ≥18 years: 0.58 (0.37-0.91)
		  ○ Prior infection: 0.57 (0.33-0.97)
			associated with a reduced risk of COVID-19 infections and ED/UC visits, hospitalisation due to COVID-19 among adults aged ≥18 years who received at least 3 prior mRNA COVID-19 vaccine doses. These findings support XBB.1.5 recommendations for individuals in this age group.	

DeCuir et al. (2024)[9]	A test-negative case-control study using VISION, a multisite, electronic health records (EHR)–based network including 369 EDs and UCs and 229 hospitals in eight states. During the study period (September 21,	**Incremental VE (%) (95% CI) against COVID-19 related ED or UC visits** (compared to individuals who have not received the XBB.1.5 variant adapted vaccines) *7 to 119 days since last dose*	The XBB.1.5 variant adapted vaccine provides considerable protection against COVID related ED or UC visits and hospitalisations in adults aged ≥18 years. There was no observed difference between	Serious*

	2023–January 9, 2024) 166,328 immunocompetent adults aged ≥18 years were included either from ED/UC encounters or hospital admissions and were tested for SARS-CoV-2 during the 10 days preceding or up to 72 hours after a COVID-19–associated ED/UC encounter or hospital admission. Case-patients were excluded if they had received a positive influenza or respiratory syncytial virus molecular test result at the time of their COVID-like illness encounter. The IVY network was also used in this study but outcomes from this network were excluded due to having a critical risk of bias. Time and setting: XBB sublineages and JN.1 sublineages were the prevailing variants.	• ≥18 years: 47 (44-50) • 18 to <65 years: 50 (44-55) • ≥65 years: 45 (41-49) *7 to 59 days since last dose* • ≥18 years: 51 (47-54) • 18 to <65 years: 52 (45-58) • ≥65 years: 49 (44-54) *60 to 119 days since last dose* • ≥18 years: 39 (33-45) • 18 to <65 years: 45 (34-55) • ≥65 years: 37 (29-44) **Incremental VE (%) (95% CI) against COVID-19 related hospitalisations** (compared to individuals who have not received the XBB.1.5 variant adapted vaccines) *7 to 119 days since last dose* • ≥18 years: 52 (47-57) • 18 to <65 years: 43 (20-59) • ≥65 years: 53 (47-58) *7 to 59 days since last dose* • ≥18 years: 53 (46-59) • 18 to <65 years: 42 (14-61) • ≥65 years: 54 (47-60) *60 to 119 days since last dose* • ≥18 years: 50 (40-59) • 18 to <65 years: 45 (-6-71) • ≥65 years: 50 (39-59)	age groups.	

Hansen et al. (2024)[10]	Cohort study using electronic health records and national administrative data. The study included 1,037,479 participants, individuals > 65 years old living in Denmark, capturing approximately 55% of all COVID-19 related hospitalisation during the study period (October 8 to October 26, 2023). All individuals included had received at least one booster. Hazard Ratio (HR) was estimated in a Cox proportional hazards regression model with calendar time as underlying time scale and adjustment for sex, 5-year age bands, residency region, and number of comorbidities (0, 1, 2, ≥3). Time and setting: Non-specific Omicron variant was the dominant variant (estimated 100%).	**HR against hospitalisation** Among adults aged > 65 years, those who have received the XBB.1.5 COVID-19 vaccine were much less likely to be hospitalised for COVID-19 compared with those who have not received the vaccine HR=0.239, 95% CI 0.152–0.377 after 7+ days since vaccination.	An XBB.1.5 vaccine was associated with a reduced risk of hospitalisation due to COVID-19 among adults > 65 years of age vaccinated with a booster dose. These findings support XBB.1.5 recommendations for individuals in this age group	Serious
Huiberts et al. (2024)[11]	Prospective cohort study using data from the VAccine Study COvid-19 (VASCO), Dutch. The study included 23,895 participants; individuals aged 18 -85 years old; XBB.1.5 vaccine-eligible adults who had previously received at least one booster, during the study period (9 October 2023 and 9 January 2024). Relative vaccine effectiveness (VE) was calculated using Cox proportional hazard models with calendar time as time scale, XBB.1.5-vaccination as time-varying exposure and adjustment for age	**Incremental VE (%) (95% CI) against positive test** (compared to individuals who have not received XBB.1.5 variant adapted vaccine, those who did) : *7 + days since last dose*: • 18-59 years: 41.3% (22.6-55.5) • 60-85 years: 50.3% (43.8-56.1) *1-6 weeks since last dose:* • 18-59 years: 40.2% (19.6-55.5) • 60-85 years: 52.1% (45.4-57.9) *7-12 weeks since last dose:* • 18-59 years: 46.7% (-5.7-73.1) • 60-85 years: 40.6% (25.7-52.4)	XBB.1.5 vaccination provides considerable protection against SARS-CoV-2 infection in the first 3 months after vaccination. Prior infection also provides some protection against new infection Recent prior infection also protects against new infection, but it should be kept in mind that experiencing a SARS-CoV-2 infection carries risks of severe illness, particularly among vulnerable groups, and post-COVID conditions.	Serious

	group, sex, education level, medical risk condition and infection history.	**Positive test with symptomatic infection:** *7+ days since last dose*: • 18-59 years; 34.7% (10.4-52.4) • 60-85 years; 55.0% (47.6-61.4) **Participants who received a bivalent mRNA booster in autumn 2022 COVID-19 vaccination campaign and XBB.1.5 variant adapted vaccine (compared to these without XBB.1.5 variant adapted vaccine)** *7+ days since last dose*: • 18-59 years; 44.6 (25.0-59.1) • 60-85 years; 51.4 (44.3-57.6) **Infection Status (compared to individuals who had no prior infection):** *No prior infection* *7+ days since last dose*: • 18-59 years; 11.7% (-60.9-51.6) • 60-85 years; 48.8% (36.4-58.8) *Infection ≥1 year ago* *7+ days since last dose*: • 18-59 years; 49.7% (22.8-67.2) • 60-85 years; 67.7% (61.2-73.1) *Infection <1 year ago* *7+ days since last dose*: • 18-59 years; 86.7% (68.9-94.3) • 60-85 years; 85.3% (80.6-88.9)	This underscores the importance of vaccination even for those who have previously been infected.	

Ioannou et al. (2025)[12]	Emulated target randomised controlled trial using the VHA's Corporate Data Warehouse and COVID-19 Shared Data Resource. Overall, 1,098,498 unique individuals were included for a total of 1,174,274 person-trial. Individuals had to be VHA enrollees aged 18 years or older, who were assigned to a VHA primary care team in the 18 months before the start of each 2-week trial, had a known residential address and VHA Integrated Service Network, and had received at least 1 earlier-formulation COVID-19 vaccine in the VHA health care system at any time in the past. Vaccine effectiveness was defined as 100 × (1 − risk ratio), where the risk ratio was calculated by dividing Aalen–Johansen estimates of period-specific cumulative incidences. Vaccine effectiveness 95% CIs were estimated by using a nonparametric percentile blocked bootstrap with 500 repetitions Time and setting: Omicron (primarily XBB, EG.5.1 and JN)	**Incremental VE (%) (95% CI) against positive NAAT or antigen test in individuals who received an mRNA XBB.1.5 variant-adapted vaccine and at least one prior dose of earlier-formulation COVID-19 vaccine** (compared to individuals who have not received any XBB.1.5 variant adapted vaccine but received at least one prior dose of earlier formulation COVID-19 vaccine) : *≥10 days* • 18 to 64 years: 8.56 (1.5-15.49) • 65 to 74 years: 0.22 (-6.49-7.32) • ≥75 years: -12.93 (-18.32--7.26) • Prior infection 90 to 365 days earlier: -11.82 (-29.01-0.32) • Prior infection over a year ago: 8.32 (0.55-15.97) • No prior infection: -5.97 (-10.36--1.26) *60 days follow up* • ≥18 years: 14.2 (10.17-17.74) *90 days follow-up* • ≥18 years: 7.3 (3.32-10.08) *120 days follow-up* • ≥18 years: 3.1 (-0.43-5.99) *End of the study* • ≥18 years: -3.3 (-6.78- -0.22) **Incremental VE (%) (95% CI) against COVID-19 related**	The XBB.1.5 variant adapted COVID-19 vaccine provided some protection against COVID related hospitalisations and deaths in adults aged ≥ 18 years. The effect was greater in younger individuals and was still present after 120 days.	Moderate

		hospitalisations in individuals who received an mRNA XBB.1.5 variant-adapted vaccine and at least one prior dose of earlier-formulation COVID-19 vaccine (compared to individuals who have not received any XBB.1.5 variant adapted vaccine but received at least one prior dose of earlier formulation COVID-19 vaccine) : *≥10 days* • 18 to 64 years: 29.7 (3.37-48.41) • 65 to 74 years: 15.65 (-5.44-34.15) • ≥75 years: 14.39 (0.71-26.52) • Prior infection 90 to 365 days earlier: 10.61 (-33.37-40.67) • Prior infection over a year ago: 9.26 (-15.13-30.24) • No prior infection: 18.99 (7.68-29.56) *60 days follow up* • ≥18 years: 37.6 (28.18-46.8) *90 days follow-up* • ≥18 years: 30.8 (21.89-38.53) *120 days follow-up* • ≥18 years: 25.2 (17.16-33.15) *End of the study* • ≥18 years: 16.6 (6.47-25.77)		

		Incremental VE (%) (95% CI) against COVID-19 related deaths in individuals who received an mRNA XBB.1.5 variant-adapted vaccine and at least one prior dose of earlier-formulation COVID-19 vaccine (compared to individuals who have not received any XBB.1.5 variant adapted vaccine but received at least one prior dose of earlier formulation COVID-19 vaccine) : *≥10 days* • 18 to 64 years: 83.62 (20.84-100) • 65 to 74 years: 27.2 (-21.05-58.62) • ≥75 years: 23.27 (-1.06-44.95) • Prior infection 90 to 365 days earlier: 8.27 (-153.94-65.64) • Prior infection over a year ago: 11.62 (-104.1-57.82) • No prior infection: 29.92 (6.27-48.53) *60 days follow up* • ≥18 years: 54.2 (28.26-72.57) *90 days follow-up* • ≥18 years: 44.3 (22.03-60.98) *120 days follow-up* • ≥18 years: 30.2 (6.96-47.7) *End of the study* • ≥18 years: 26.6 (5.53-42.32)		

Kirsebom et al. (2024)[13]	Test negative case-control study using England's national COVID-19 testing data, UKHSA IIS (a national vaccine) and the Register and Secondary Uses Service (the national electronic database of hospital admissions). This study included 28,916 hospitalised adults aged 65 years and older admitted for having an acute respiratory illness (positive PCR tests from hospitalised individuals are cases and negative PCR tests from hospitalised individuals are the controls) during the study period (4th September 2023 to 21st January 2024). Multivariable logistic regression was used with the test result as the outcome, vaccination status as the primary exposure variable of interest and adjusted for week of test date, gender, age (five-year age bands), NHS region, IMD quintile, ethnicity and clinical risk group status (encoded as a categorial variable with a level for all conditions other than severe immunosuppression and a level for severe immunosuppression as described above. VE was calculated as 1-odds ratio and given as a percentage. Time and setting: JN.1 sublineages were the prevailing variants.	**Incremental VE (%) (95% CI) against COVID-19 related hospitalisations** (compared to individuals who have not received the XBB.1.5 variant adapted vaccines) • 9 to 13 days since last dose: 37.4 (17.8-52.3) • 14 to 28 days since last dose: 54.8 (46.8-61.6) • 29 to 63 days since last dose: 48.3 (41.0-54.7) • 64 to 98 days since last dose: 42.2 (32.3-50.6)	The XBB.1.5 variant adapted COVID-19 vaccine provided a considerable level of protection against COVID related hospitalisations in adults aged ≥ 65 years. The effect was still present 98 days after the vaccination.	Moderate
Kirwan et al. (2024)[14]	Prospective cohort study part of the SIREN study. During the study period (1st October 2023 to 31st March 2024) 2,867 health care workers living in the UK, who are part of NHS, received their last COVID-	**Incremental VE (%) (95% CI) against positive PCR tests** (Compared to individuals who have not received the XBB.1.5 variant adapted vaccines but have received at least one booster)	The XBB.1.5 variant adapted vaccine was associated with a reduced risk of moderate COVID-19 infections among HCPs in the UK who received at least 1 prior COVID-19 vaccine booster	Serious

	19 booster more than 6 months ago, contributed at least 2 PCR tests to the study (SIREN) and did not receive more than 5 COVID-19 doses were included. Individuals who received more than 5 COVID-19 vaccine doses before October 2023 were excluded. Cases were defined as having a positive PCR test, they were further divided in two categories using a questionnaire: *Mild/asymptomatic cases*: Episodes without symptoms, or with acute respiratory symptoms lasting <5 days, or with non-acute respiratory symptoms *Moderate cases*: Moderate symptoms were defined as influenza-like illness (ILI), or acute respiratory illness (ARI) lasting 5 or more days, or any sick leave. Vaccine effectiveness (VE) and acquired protection were estimated from the multi-state model as: 1 – adjusted hazard ratio. Time and setting: Omicron sublineages were the prevailing variants.	*61-122 days since last dose*: • All infections: 24.1 (-0.7-42.9) • Moderate infections: 36.8 (6.3-57.4) • Mild/asymptomatic infections: 12 (-26.4-38.8) *123-183 days since last dose*: • All infections: 26.7 (-27.5-57.9) • Moderate infections: 64.8 (8.5-86.5) • Mild/asymptomatic infections: 17.8 (-122.1-37.5)	doses. This effect was more pronounced 123-183 days after the administration of the XBB.1.5 vaccine than after 61-122 days. These findings support XBB.1.5 recommendations for individuals in this group.	
Kopel et al. (2024)[15, 16]	Retrospective cohort study of adult aged ≥18 years from the Veradigm Network (EHR linked to healthcare claims sourced from Komodo Health). During the study period (September 12 to December 15, 2023), 1,718,670 adults living in the US were included in the study, of these, 859,335 received the Moderna mRNA XBB.1.5 variant adapted vaccine and were matched with	**Incremental VE (%) (95% CI) against any COVID-19 infections** (Compared to individuals who have not received the XBB.1.5 variant adapted vaccines) *7+ days since last dose* • ≥18 years: 33.1 (30.2-35.9) • ≥18 years with at least one medical condition: 34.5 (31.2-37.6)	The Moderna mRNA XBB.1.5 variant adapted vaccine offered some protections against COVID-19 infections and a moderate protection against COVID-19 related hospitalisations. The protection offered remained mostly the same for all age groups.	Serious

	individuals who did not receive any 2023/2024 vaccines. All individuals were required to have continuous enrollment in medical and pharmacy claims from September 12, 2022, through 7 days after the index date. Authors reported two outcomes, COVID-19-related hospitalization and medically attended COVID-19 (e.g., emergency department visits, urgent care visits, office visits, telemedicine visits, laboratory results), which could include asymptomatic infections. Vaccine effectiveness (VE) was estimated from cox regression models to calculate hazard ratios (HR), and 95% confidence intervals (95% CI) were then converted to VE estimates. Time and setting: Omicron sublineages were the prevailing variants.	• ≥50 years: 35.3 (32.2-38.2) • ≥65 years: 38.7 (35.4-41.9) **Incremental VE (%) (95% CI) against COVID-19 related hospitalisations** (Compared to individuals who have not received the XBB.1.5 variant adapted vaccines) *7+ days since last dose* • ≥18 years: 60.2 (53.4-66.0) • ≥18 years with at least one medical condition: 58.7 (51.3-65.0) • ≥50 years: 61.1 (54.3-66.9) • ≥65 years: 60.5 (53.3-66.6)		
Lanièce Delaunay et al. (2024) [17,18]	Test negative case-control study from multiple European countries part of the VEBIS primary care study. During the study period (September 2023 and January 2024), 5,454 individuals were recruited from primary care physicians or paediatricians who swab all or a systematic sample of patients consulting with acute respiratory infection (ARI). Logistic regression was used to estimate the odds ratio (OR) of vaccination among cases and controls, adjusting for study site, age, sex, presence of four commonly collected chronic conditions (diabetes,	**Incremental VE (%) (95% CI) of the mRNA XBB.1.5 variant-adapted vaccines against medically attended COVID-19 infections** (compared to individuals who did not receive the XBB.1.5 variant-adapted vaccine) *≥7 days* • ≥ 5 years: 40 (26-53) • <50-65 years: 59 (18-82) • >50-65 years: 37 (19-51) *7 to 41 days*	The mRNA XBB.1.5 variant adapted vaccine offered some protections against COVID-19 medically attended infections. The protection waned over time and was greater against the XBB variants.	Serious

	heart disease, lung disease and immuno-deficiency) and onset date. VE was estimated as (1-OR), expressed as a percentage. Time and setting: Omicron	• ≥ 5 years: 48 (31-61) • <50-65 years: 69 (28-90) • >50-65 years: 45 (26-60) *42 to 119 days* • ≥ 5 years: 29 (3-49) • <50-65 years: 28 (-128-84) • >50-65 years: 26 (-3-48) *≥14 days* • ≥ 5 years: 40 (24-54) • <50-65 years: 70 (30-90) • >50-65 years: 36 (16-51) *14 to 41 days* • ≥ 5 years: 51 (33-66) • >50-65 years: 45 (22-62) *42 to 119 (when considering at least 14 days post vaccination)* • ≥ 5 years: 26 (-2-47) • <50-65 years: 21 (-150-82) • >50-65 years: 24 (-6-47) XBB variant *≥7 days* • ≥ 5 years: 50 (-17-82) • >50-65 years: 63 (6-88) *7 to 41 days* • ≥ 5 years: 46 (-32-82) • >50-65 years: 63 (-2-90)		

Lee et al. (2024)[19]	Test negative case-control study using linked databases in Ontario This study included 24,498 community-dwelling adults aged ≥50 years who underwent ≥1 polymerase chain reaction (PCR) test for SARS-CoV-2 from September 24, 2023, to June 1, 2024. They used a multivariable logistic regression to estimate the relative change in the odds of severe outcomes (defined as the proportionate reduction in the odds of hospitalization/death). Relative vaccine effectiveness (rVE) was calculated using the formula (1−adjusted odds ratio)*100%. Models were adjusted for age, sex, public health unit region, neighborhood-level socio-demographic variables, influenza vaccination status (proxy for health behaviors), comorbidities, receipt of home care services, and week of test (modeled using restricted cubic splines) Time and setting: XBB (24 September 2023−23 December 2023) and JN/KP (24 December 2023−1 June 2024)	**Incremental VE (%) (95% CI) against COVID-19 related hospitalisations of mRNA XBB.1.5 variant-adapted vaccine and at least 2 doses of a non XBB.1.5 mRNA vaccine** (Compared to individuals who have not received the XBB.1.5 variant adapted vaccines but received at least 2 doses of a non XBB.1.5 mRNA vaccine) *91 to 182 days* • ≥50 years: 44 (32-54) *183 to 274 days* • ≥50 years: 21 (-15-46) **Incremental VE (%) (95% CI) against COVID-19 related hospitalisations of mRNA XBB.1.5 variant-adapted vaccine and at least 2 doses of a non XBB.1.5 mRNA vaccine** (Compared to individuals who have not received the XBB.1.5 variant adapted vaccines but received the original monovalent mRNA vaccine) *91 to 182 days* • ≥50 years: 53 (42-62) **Incremental VE (%) (95% CI) against COVID-19 related hospitalisations of mRNA XBB.1.5 variant-adapted vaccine**	The mRNA XBB.1.5 variant adapted vaccines were associated with a reduced risk of hospitalisation due to COVID-19 among adults aged ≥50 years who did not receive the XBB.1.5 variant adapted vaccine but received at least two doses of a non XBB.1.5 mRNA vaccine. The effect waned over time.	Serious

		and at least 2 doses of a non XBB.1.5 mRNA vaccine (Compared to individuals who have not received the XBB.1.5 variant adapted vaccines but received a bivalent mRNA vaccine) *91 to 182 days* • ≥50 years: 43 (28-55)		
Lee et al. (2024)[20, 21]	Test negative case-control study from 6 university hospitals across South Korea. During the study period (October 26 to December 31, 2023), 5,516 symptomatic adults aged ≥18 year who underwent PCR testing or rapid antigen testing in the emergency department, outpatient clinics, general wards, or intensive care units of each hospital were included in the study. Only PCR tests conducted within 14 days before presentation at the emergency department, outpatient clinics, or screening centers and within 72 h thereafter were considered. In inpatient cases, only tests conducted within 14 days before admission and within 72 h thereafter were considered. In intensive care unit cases, only tests conducted within 14 days before admission and within 72 h thereafter were considered. All XBB.1.5 variant adapted vaccine administered were mRNA vaccines. The incremental and absolute VE, odds ratios (ORs) and 95% confidence intervals (CIs) were estimated using multivariable logistic regression. The VE	**Absolute VE (%) (95% CI) against medically attended infections** *7-59 days since last dose* • ≥18 years: 65.2 (36.1-81.0) • ≥ 65 years: 67.2 (34.3-83.6) *Median of 25.5 days since last dose* • ≥18 years: 71.0 (44.6-84.8) **Incremental VE (%) (95% CI) against medically attended infections** (Compared to individuals who have not received the XBB.1.5 variant adapted vaccines) *7-59 days since last dose* • ≥18 years: 57.7 (34.7-72.6) • ≥ 65 years: 60.2 (35.6-75.4) **Incremental VE (%) (95% CI) against medically attended infections** (Compared to individuals who have not received the XBB.1.5 variant adapted vaccines but have received at least one dose of COVID-19 vaccine)	The XBB.1.5 variant adapted vaccine was associated with a reduced risk of medically attended COVID-19 infections and hospitalisation due to COVID-19 among adults aged ≥18 years who did not receive the XBB.1.5 variant adapted vaccine. This effect was slightly greater in older individuals ≥65 years. The effect was also greater when compared to individuals who were never vaccinated against COVID-19. These findings support XBB.1.5 recommendations for individuals in this age group.	Serious

	(%) was calculated as (1 − adjusted OR) × 100.
	
	Time and setting: Omicron sublineages were the prevailing variants.
		7-59 days since last dose
		• ≥18 years: 55.6 (31.2-71.3)
		  o Immunocompromised: 47.6 (-43.6-80.9)
		  o Immunocompetent: 57.7 (31.0-74.1)
		• ≥ 65 years: 57.6 (30.9-74.0)
		
		Absolute VE (%) (95% CI) against COVID-19 related hospitalisation
		7-59 days since last dose
		• ≥18 years: 77.3 (51.1-89.5)
		• ≥ 65 years: 72.8 (37.3-88.2)
		
		Incremental VE (%) (95% CI) against COVID-19 related hospitalisation
		(Compared to individuals who have not received the XBB.1.5 variant adapted vaccines)
		7-59 days since last dose
		• ≥18 years: 64.3 (35.9-80.2)
		• ≥ 65 years: 66.5 (38.1-81.8)
		Incremental VE (%) (95% CI) against COVID-19 related hospitalisation
		(Compared to individuals who have not received the XBB.1.5 variant adapted vaccines but have received at least on dose of COVID-19 vaccine)
		7-59 days since last dose
		• ≥18 years: 61.2 (29.7-78.6)
		  o Immunocompromised: 79.4 (7.4-95.4)		

		○ Immunocompetent: 56.4 (16.2-77.3) • ≥ 65 years: 64.1 (33.2-80.7)		
Lin et al. (2024)[22]	Retrospective cohort study from the US. During the study period (September 11, 2023, and February 21, 2024), 1,830,088 individuals of all ages whose information is available in the Nebraska Electronic Disease Surveillance System and the Nebraska State Immunization Information System (NESIIS) were included Cases were considered as positive COVID-19 tests, at home tests were generally not included and individuals were generally symptomatic. Time and setting: XBB.1.5 and JN.1	**Incremental VE (%) (95% CI) against COVID-19 infections** (compared to individuals who have not received the XBB.1.5 variant adapted vaccines) *During XBB.1.5 and JN.1 (by number of days since vaccination)* • 7 to 13: 16.8 (13.7-19.8) • 14 to 20: 30.8 (25.6-35.7) • 21 to 27: 42.5 (35.8-48.5) • 28 to 34: 52.2 (44.6-58.7) • 35 to 41: 45.0 (40.2-49.5) • 42 to 48: 36.9 (30.2-42.9) • 49 to 55: 35.8 (29.9-41.3) • 56 to 62: 34.7 (29.5-39.6) • 63 to 69: 33.7 (28.9-38.1) • 70 to 76: 32.6 (28.1-36.8) • 77 to 83: 31.4 (27.0-35.6) • 84 to 90: 30.3 (25.5-34.8) • 91 to 97: 29.1 (23.8-34.1) • 98 to 104: 28.0 (21.8-33.7) • 105 to 111: 26.8 (19.5-33.3) • 112 to 118: 25.5 (17.1-33.1) • 119 to 125: 24.3 (14.6-32.9) • 126 to 132: 23.0 (11.9-32.7) • 133 to 139: 21.8 (9.1-32.6) • 140 to 146: 20.4 (6.2-32.5) • 147 to 153: 19.1 (3.2-32.4) • 154 to 160: 17.8 (0.1-32.4) • 161 to 167: 16.4 (-3.2-32.3)	The XBB.1.5 variant adapted vaccine was associated with a reduced risk of COVID-19 infections among individuals of all ages who did not receive the XBB.1.5 variant adapted vaccine. This effect was slightly greater against the XBB.1.5 subvariant than the JN.1 subvariant. The effect waned over time after reaching a peak.	Moderate

		During XBB.1.5 (by number of days since vaccination) • *7 to* 13: 22.7 (17.6-27.5) • 14 to 20: 40.3 (32.2-47.5) • 21 to 27: 53.9 (44.1-61.9) • 28 to 34: 64.4 (54.0-72.4) • 35 to 41: 57.1 (50.7-62.7) • 42 to 48: 48.5 (40.7-55.2) • 49 to 55: 46.7 (39.6-52.9) • 56 to 62: 44.8 (38.5-50.5) • 63 to 69: 42.9 (37.1-48.2) • 70 to 76: 40.9 (35.6-45.8) • 77 to 83: 38.9 (33.8-43.6) • 84 to 90: 36.8 (31.6-41.6) • 91 to 97: 34.6 (29.0-39.8) • 98 to 104: 32.3 (25.9-38.2) • 105 to 111: 30.0 (22.5-36.7) • 112 to 118: 27.6 (18.7-35.4) • 119 to 125: 25.0 (14.6-34.2) • 126 to *132*: *22.4 (10.2-33.1)* *During JN.1 (by number of days since vaccination)* • 7 to 13: 13.6 (9.7- 17.4) • 14 to 20: 25.4 (18.4-31.7) • 21 to 27: 35.5 (26.3-43.6) • 28 to 34: 44.3 (33.5-53.4) • 35 to 41: 34.8 (27.3-41.6) • 42 to 48: 23.8 (11.4-34.4) • 49 to 55: 22.2 (11.8-31.4) • 56 to 62: 20.6 (11.6-28.7) • 63 to 69: 19.0 (10.6-26.6) • 70 to 76: 17.4 (8.5-25.4) • 77 to 83: 15.7 (5.3-24.9) • 84 to 90: 13.9 (1.3-25.0)		

		Incremental VE (%) (95% CI) against COVID-19 related hospitalisation (compared to individuals who have not received the XBB.1.5 variant adapted vaccines) *During XBB.1.5 and JN.1 (by number of days since vaccination)* • 7 to 13: 24.1 (16.7-30.9) • 14 to 20: 42.4 (30.5-52.2) • 21 to 27: 56.3 (42.1-66.9) • 28 to 34: 66.8 (51.7-77.1) • 35 to 41: 65.3 (52.5-74.7) • 42 to 48: 63.8 (52.6-72.4) • 49 to 55: 62.3 (51.7-70.6) • 56 to 62: 60.6 (49.4-69.4) • 63 to 69: 58.9 (45.6-69.0) • 70 to 76: 57.1 (40.4-69.2) • 77 to 83: 55.3 (34.0-69.7) • 84 to 90: 53.3 (26.3-70.5) • 91 to 97: 51.3 (17.3-71.3) • 98 to 104: 49.2 (7.0-72,2) • 105 to 111: 47.0 (-4.8-73.2) • 112 to 118: 44.7 (-18.3-74.1) • 119 to 125: 42.3 (-33.6-75.1) • 126 to 132: 39.8 (-51.0-76.0) • 133 *to 139*: *37.1 (-70.8-76.9)* *During XBB.1.5 (by number of days since vaccination)* • *7 to* 13: 28.4 (18.3-37.3) • 14 to 20: 48.7 (33.2-60.7) • 21 to 27: 63.3 (45.4-75.3)		

		• 28 to 34: 73.7 (55.4-84.5) • 35 to 41: 71.7 (55.7-81.9) • 42 to 48: 69.6 (55.5-79.2) • 49 to 55: 67.2 (54.6-76.3) • 56 to 62: 64.7 (52.4-73.8) • 63 to 69: 62.0 (48.5-72.0) • 70 to 76: 59.1 (42.4-71.0) • 77 to 83: 56.0 (34.2-70.6) • 84 to 90: 52.7 (23.7-70.6) • 91 to 97: 49.0 (10.7-70.9) • 98 to 104: 45.1 (-5.0-71.3) • 105 to 111: *40.9 (-23.8-71.8)* *During JN.1 (by number of days since vaccination)* • *7* to 13: 20.5 (8.8-30.7) • 14 to 20: 36.9 (16.9-52.0) • 21 to 27: 49.8 (24.2-66.8) • 28 to 34: 60.1 (30.9-77.0) • 35 to 41: 56.8 (33.5-71.9) • 42 to 48: 53.1 (28.6-69.2) • 49 to 55: 49.2 (14.0-70.0) • 56 to 62: 44.9 (-10.4-72.5) • 63 to 69: *40.3 (-45.9-75.6)* **Incremental VE (%) (95% CI) against COVID-19 related death** (compared to individuals who have not received the XBB.1.5 variant adapted vaccines) *During XBB.1.5 and JN.1 (by number of days since vaccination)* • **7** to 13: 27.2 (9.9-41.3) • 14 to 20: 47.1 (18.8-65.5)		

		• 21 to 27: 61.5 (26.8-79.7) • 28 to 34: 72.0 (34.0-88.1) • 35 to 41: 70.5 (36.2-86.3) • 42 to 48: 68.8 (37.9-84.4) • 49 to 55: 67.1 (39.0-82.3) • 56 to 62: 65.3 (39.5-80.1) • 63 to 69: 63.4 (38.9-78.1) • 70 to 76: 61.4 (37.1-76.4) • 77 to 83: 59.3 (33.7-75.1) • 84 to 90: 57.1 (28.5-74.3) • 91 to 97: 54.8 (21.2-74.0) • 98 to 104: 52.3 (11.8-74.2) • 105 to 111: 49.7 (0.1-74.7) • 112 to 118: 46.9 (-14.2-75.3) • 119 to 125: 44.0 (-31.3-76.1) • 126 to 132: 41.0 (-51.6-77.0) • 133 to 139: 37.7 (-75.7-77.9) *During XBB.1.5 (by number of days since vaccination)* • 7 to 13: 39.0 (11.6-57.9) • 14 to 20: 62.8 (21.9-82.3) • 21 to 27: 77.3 (31.0-92.6) • 28 to 34: 86.2 (39.0-96.9) • 35 to 41: 84.6 (40.4-96.0) • 42 to 48: 82.7 (41.6-94.9) • 49 to 55: 80.7 (42.4-93.5) • 56 to 62: 78.4 (42.7-91.8) • 63 to 69: 75.8 (42.5-89.8) • 70 to 76: 72.9 (41.3-87.5) • 77 to 83: 69.7 (38.8-85.0) • 84 to 90: 66.1 (34.4-82.5) • 91 to 97: 62.1 (27.2-80.3) • 98 to 104: 57.6 (16.4-78.5) • 105 to 111: 52.6 (0.9-77.3)		

		• 112 to 118: 46.9 (-20.4-76.6) • 119 to 125: 40.6 (-49.0-76.3) • 126 to 132: 33.6 (-86.7-76.4) *During JN.1 (by number of days since vaccination)* • 7 to 13: 20.4 (-4.6-39.4) • 14 to 20: 36.6 (-9.5-63.3) • 21 to 27: 49.6 (-14.5-77.8) • 28 to 34: 59.8 (-19.8-86.5) • 35 to 41: 58.0 (-7.7-83.6) • 42 to 48: 56.0 (0.8-80.5) • 49 to 55: 54.0 (5.0-77.7) • 56 to 62: 51.9 (4.1-75.9) • 63 to 69: 49.7 (-2.9-75.4) • 70 to 76: 47.3 (-16.8-76.2) • 77 to 83: 44.9 (-37.9-78.0) • 84 to 90: 42.3 (-67.4-80.1)		
Link-Gelles (2025)[23]	Retrospective cohort study in the Virtual SARS-CoV-2, Influenza, and Other respiratory viruses Network (VISION) and Investigating Respiratory Viruses in the Acutely Ill (IVY) network. 173,883 adults aged ≥18 years with COVID-19-like illness who visited emergency departments (EDs), urgent care (UC) facilities, or were hospitalized in the U.S. were included during the study period (September 2024–January 2025). Eligible patients had a molecular (e.g., real-time reverse transcription–polymerase chain reaction [RT-PCR]) or antigen testing for SARS-CoV-2 during the 10 days preceding or ≤72 hours after an eligible ED/UC encounter or hospital	**Incremental VE (%) (95% CI) of the 2024/2025 variant-adapted vaccine against COVID-19 related ED or UC visits** (compared to individuals who did not receive any 2024-2025 variant adapted vaccine) *7 to 199 days* • ≥18 years: 33 (28-38) • 18 to 64 years: 30 (20-39) • ≥65 years: 35 (29-41) *7 to 59 days* • ≥18 years: 36 (29-42)	The 2024-2025 variant adapted vaccine was associated with a reduced risk of COVID-19 related ED or UC visits among individuals of all ages who did not receive the 2024-2025 variant adapted vaccine.	Serious

	admission. Odds ratios (OR) and 95% CIs were estimated using multivariable logistic regression. VE models were adjusted a priori for age, sex, race and ethnicity, calendar time, and geographic region. VE was calculated as (1 − adjusted OR) x 100%. Time and setting: JN or KP	• 18 to 64 years: 36 (23-46) • ≥65 years: 36 (28-44) *60 to 199 days* • ≥18 years: 30 (22-37) • 18 to 64 years: 21 (5-35) • ≥65 years: 34 (25-42)		
Link-Gelles (2024)[24]	Test-negative case-control study using VISION, a multisite, electronic health records (EHR). For this study, only these sites contributed: HealthPartners (Minnesota and Wisconsin), Intermountain Health (Utah), Kaiser Permanente Northern California (California), Kaiser Permanente Northwest (Oregon and Washington), Regenstrief Institute (Indiana), and University of Colorado (Colorado). Throughout the study period (September 2023 to February 2024) the study included 14,586 hospitalizations among adults aged ≥18 years with immunocompromising conditions and who had COVID-19–like illness with SARS-CoV-2 molecular testing during the 10 days preceding admission or up to 72 hours after admission. Case-patients were persons who received a positive SARS-CoV-2 test result using a molecular test and received a negative or indeterminate or had an unknown test	**Incremental VE (%) (95% CI) against COVID-19 related hospitalisations** (compared to individuals who have not received the XBB.1.5 variant adapted vaccines) • ≥7 days since last dose: 36 (25-46) • 7 to 59 days since last dose: 38 (23-50) • 60 to 119 days since last dose: 34 (16-47)	The XBB.1.5 variant adapted COVID-19 vaccine provided a considerable level of protection against COVID related hospitalisations in immunocompromised adults aged ≥ 18 years. The effect was still present 119 days after the vaccination.	Serious

	result for both respiratory syncytial virus and influenza. Control patients were those who received a negative SARS-CoV-2 test result using a molecular test and received a negative influenza test result or had an unknown influenza test result. Odds ratios (ORs) and 95% CIs were estimated using multivariable logistic regression comparing persons who received an updated COVID-19 vaccine dose with those who did not, VE was calculated as (1 − adjusted OR) × 100%. Time and setting: Omicron sublineages were the prevailing variants.			
Link-Gelles (2024)[25]	A test-negative case-control study design was used to recruit all adults (18+) who had a test conducted at a participating CVS pharmacy or Walgreen between 21st of September 2023 and 14th of January 2024. Individuals were excluded if: 1) they had a self-reported immunocompromising condition; 2) received Novavax as the most recent dose and received <2 total COVID-19 vaccine doses; 3) received the Janssen COVID-19 vaccine after May 12, 2023; 4) received their most recent dose <7 days before testing or between September 1st and 12th (for those who received the XBB vaccine); 5) received their most recent dose <2 months before testing (for those who did not receive the XBB vaccine); 6) only reported month	**Incremental VE (%) (95% CI) against medically attended symptomatic COVID-19 infections compared to individuals who have not received XBB.1.5** *7+ days since receiving the XBB.1.5 variant adapted vaccine:* • ≥18 years: 54% (46-60) • 18-49 years: 57% (48-65) • ≥50 years: 46% (31-58) *7-59 days since receiving the XBB.1.5 variant adapted vaccine:* • ≥18 years: 58% (48-65) • 18-49 years: 64% (53-73) • ≥50 years: 45% (26-60)	Updated monovalent COVID-19 XBB.1.5 vaccines provided 54% (95% CI = 46–60%) protection against SARS-CoV-2 infection caused by JN.1 and XBB-related lineages in persons recently vaccinated compared with those who did not receive the XBB.1.5 vaccine. The effectiveness of vaccination may decrease over time, especially against less severe disease.	Serious

	and year of the most recent vaccine dose rather than calendar date; 7) received a positive SARS-CoV-2 test result during the preceding 90 days. A total of 9,222 nucleic acid amplification test results were included in the study. The incremental vaccine VE against symptomatic disease was calculated by comparing odds of receipt versus nonreceipt of the updated COVID-19 vaccine among case- and control patients. Time and setting: XBB subvariants and the JN.1 variant were dominant.	*59-119 days since receiving the XBB.1.5 variant adapted vaccine:* • ≥18 years: 49% (36-58) • 18-49 years: 48% (31-60) • ≥50 years: 47% (24-62)		
Liu et al. (2024)[26]	Retrospective cohort study from Australia. During the study period (August 2023 to February 2024), 4,119,000 individuals aged ≥65 years recorded in the Census who had not migrated or died by study commencement on the 1 August 2023 were included. All XBB.1.5 variant adapted vaccine administered were mRNA vaccines. COVID-19 mortality was defined as a death registration where the underlying cause of death was recorded as ICD-10 code U07.1 or U07.2. Vaccine effectiveness was calculated using the formula (1-aHR) * 100%. Time and setting: Omicron subvariants were dominant, including the JN.1	**Incremental VE (%) (95% CI) against COVID-19 related death** (compared to individuals who have not received the XBB.1.5 variant adapted vaccines but have received a booster at least 1 year earlier) *During Omicron (August 2023 to February 2024) – 8-90 days since last dose* • ≥65 years: 74.7 (59.9-84.1) • ≥75 years: 76.7 (61.4-85.9) *During JN.1 (1 December 2023-29 February 2024) – 8-90 days since last dose* • ≥65 years:74.6 (59.4-84.0)	The mRNA XBB.1.5 variant adapted vaccines were associated with a reduced risk of death due to COVID-19 among adults ≥65 years of age did not receive the XBB.1.5 variant adapted vaccine but received booster at least a year prior. This effect was slightly greater in older individuals ≥75 years. And did not differ when focusing on the JN.1 dominance period. These findings support XBB.1.5 recommendations for individuals in this age group.	Serious

	subvariant (1 December 2023-29 February 2024).			
Monge et al. (2024)[27]	Retrospective cohort study under the Vaccine Effectiveness Burden and Impact Studies (VEBIS) project, funded by the European Centre of Disease Prevention and Control. The VEBIS-EHR network includes Belgium, Denmark, Italy, Spain (Navarra), Norway, Portugal and the Netherlands. Overall, during the study period (October–November 2023), 22,110,131 individuals eligible to receive the autumnal booster vaccination at the beginning of the campaign, specifically, those 65 years or older, with at least complete primary vaccination and who, in the last 90 days, had no vaccine dose administered and no documented SARS-CoV-2 infection, were included. A cox regression with calendar time as the underlying scale was used to estimate vaccine hazard ratios and derived VE [HR;VE=(1−HR)×100] and 95% confidence intervals (95%CI), the model was adjusted by 5-year age-groups, sex, region in the country, comorbidities and previous number of vaccine booster doses. Time and setting: Omicron (primarily XBB, EG.5.1 and JN.1)	**Incremental VE (%) (95% CI) against COVID-19 related hospitalisations** of the mRNA XBB.1.5 variant adapted vaccine in individuals who received at least a complete primary series (compared to individuals who have not received the XBB.1.5 variant adapted vaccines but received at least a complete primary series) *≥14 days* • 65-79 years: 66.8 (58.1-73.7) • ≥80 years: 65.9 (56.9-73.1) **Incremental VE (%) (95% CI) against COVID-19 related death** of the mRNA XBB.1.5 variant adapted vaccine in individuals who received at least a complete primary series (compared to individuals who have not received the XBB.1.5 variant adapted vaccines but received at least a complete primary series) *≥14 days* • 65-79 years: 66.9 (42.2-81.0) • ≥80 years: 72.3 (50.5-84.5)	The mRNA XBB.1.5 variant adapted vaccines were associated with a reduced risk of hospitalisation and death due to COVID-19 among adults ≥65 years of age did not receive the XBB.1.5 variant adapted vaccine but received at least a complete primary series.	Serious
Nguyen et al. (2024)[28,29]	Test negative case-control study part of the id.Drive study in Belgium, Germany, Italy, Spain	**Absolute VE (%) (95% CI) against COVID-19 related hospitalisation**	The Pfizer-BioNTech XBB1.5-adapted vaccine was associated with a reduced risk	Serious

	During the study period (2 October 2023 to 2 April 2024), 1,425 individuals aged ≥18 years, eligible for COVID-19 vaccination and admitted at one of the study centers (23 centers) of the id.Drive study for at least one overnight stay with a severe acute respiratory infection (SARI) were included. Symptom onset must have occurred within 1 days prior to admission. Patients who were infected with the JN.1 variant or experienced symptom onset during the JN.1 prevalent period. All XBB.1.5 variant adapted vaccine administered were Pfizer-BioNTech XBB1.5-adapted vaccine.
	
	Cases were defined as a positive test on at least one of the following: RT-PCR, multiplex PCR, transcripted mediated assay.
	
	Odds ratios and 95% confidence intervals (CI) that compared the odds of vaccination among test-positive cases to the odds of vaccination among test negative controls were estimated from multivariable generalized estimating equation (GEE) logistic regression models that accounted for heterogeneity among study sites and adjusted for date of symptom onset, age, sex, and number of chronic conditions.
	
	Time and setting: JN.1
		≥14 days since last dose:
		• ≥18 years: 52.1 (9.8-74.5)
		
		Incremental VE (%) (95% CI) against COVID-19 related hospitalisation
		(compared to individuals who have not received the XBB.1.5 variant adapted vaccines)
		≥14 days since last dose
		• ≥18 years: 53.8 (38.4-65.4)
		  ○ Immunocompromised or cancer: 56.0 (22.4-75.0)
		  ○ Prior infection: 58.2 (34.0-73.5)
		  ○ No prior infection: 53.9 (27.5-70.7)
		• 18 to <65 years: 56.5 (18.6-76.8)
		• ≥65 years: 53.9 (40.4-64.3)
		• 65 to 79 years: 62.5 (40.0-76.6)
		• ≥80 years: 48.8 (36.9-58.5)
		
		14-27 days since last dose
		• ≥18 years: 52.2 (41.3-61.1)
		• ≥65 years: 61.6 (34.2-77.6)
		
		28-55 days since last dose
		• ≥18 years: 48.9 (17.9-68.2)
		• ≥65 years: 44.4 (11.7-65.0)
		
		56-83 days since last dose
		• ≥18 years: 56.9 (39.5-69.2)
		• ≥65 years: 57.4 (43.7-67.7)
		
		84-111 days since last dose
		• ≥18 years: 54.6 (50.2-58.5)
			of hospitalisation due to COVID-19 among adults ≥18 years of age did not receive the XBB.1.5 variant adapted vaccine but received at least a year prior. This effect was slightly greater in older individuals (65 to 79 years) than younger individuals (18 to <65 years), however it was not the case in individuals aged ≥80 years. These findings support XBB.1.5 recommendations for individuals in this age group.	

		• ≥65 years: 60.5 (57.7-63.3) *112-153days since last dose* • ≥18 years: 59.5 (21.4-79.1) • ≥65 years: 51.2 (16.1-71.6) **Incremental VE (%) (95% CI) against COVID-19 related hospitalisation** (compared to individuals who have not received the XBB.1.5 variant adapted vaccines but received at least 1 BA.4/5 bivalent dose) *≥14 days since last dose* • ≥18 years: 61.0 (35.1-76.6) **Relative VE (%) (95% CI) against COVID-19 related hospitalisation** (Compared to individuals who have not received the XBB.1.5 variant adapted vaccines but received 2 mRNA wild type doses only *≥14 days since last dose* • ≥18 years: 48.8 (44.2-53.0)		
Nunes et al. (2024)[30, 31]	Retrospective cohort study from Belgium, Denmark, Italy, Navarre (Spain), Norway, Portugal and Sweden part of the VEBIS-EHR study. During the study period (December 2023/January 2024 - depending on the country - until 25 February 2024), 20,183,622 individuals aged ≥65 years residing in one of the regions, included in and eligible to receive the autumnal 2023 vaccine dose at the start of the country-	**Incremental VE (%) (95% CI) against COVID-19 related hospitalisation** (compared to individuals who have not received the XBB.1.5 variant adapted vaccines but received at least 2 COVID-19 vaccine doses) *≥14 days since last dose* • 65-79 years: 50.2 (44.6-55.2) • ≥80 years: 40.7 (35.1-45.9)	The XBB.1.5 variant adapted vaccine was associated with a reduced risk of COVID-19 related hospitalisation and death among individuals aged ≥65 years who did not receive the XBB.1.5 variant adapted vaccine but received at least 2 COVID-19 vaccine doses. The effect was lesser in older individuals (≥80 years) than in younger individuals (65-79 years) and	Serious

	specific vaccination campaign were included. Study site-specific aHR estimates and standard errors were pooled using a random-effects meta-analysis using Paule-Mantel method. Pooled VE was estimated as (1-pooled aHR)x100. A fixed-effects model was used as a secondary analysis. Time and setting: BA.2.86 and JN.1	*14-89 days since last dose* • 65-79 years: 50.9 (45.1-56.0) • ≥80 years: 42.1 (36.4-47.2) *90-179 days since last dose* • 65-79 years: 47.3 (32.0-59.1) • ≥80 years: 38.6 (17.4-54.3) **Incremental VE (%) (95% CI) against COVID-19 related death** (compared to individuals who have not received the XBB.1.5 variant adapted vaccines but received at least 2 COVID-19 vaccine doses) *≥14 days since last dose* • 65-79 years: 57.5 (41.5-69.1) • ≥80 years: 48.4 (38.2-56.9) *14-89 days since last dose* • 65-79 years: 59.2 (41.3-71.7) • ≥80 years: 51.2 (41.9-59.0) *90-179 days since last dose* • 65-79 years: 54.0 (-16.3-81.8) • ≥80 years: 9.4 (-85.5-55.8)	waned over time. The effect waned over time after reaching a peak.	
Rudolph et al. (2025) [32]	Test-negative case control study in the US. 22,884 CVS MinuteClinic patients aged 18+ years who tested for SARS-CoV-2 between September 5, 2024 (≥14 days after approval of KP.2 vaccines) and December 8, 2024, were included. Patients had to be symptomatic to be	**OR (95% CI) of the Pfizer-BioNTech KP.2-adapted vaccine against medically attended COVID-19 infections** (compared to individuals who did not receive any KP.2 variant adapted vaccine)	The KP.2 variant adapted vaccine was associated with a reduced risk of COVID-related ED or UC visits among adults **≥18** years of age. The iVE decreased slightly with age but still provided some protection. These findings support XBB.1.5 recommendations	Serious

	included and could not have been tested more than once during the study period. Adjusted odds ratios (ORs) and 95% Confidence Intervals (CIs) were calculated from generalized estimating equations logistic regression models that clustered on patient's State of residence and adjusted for calendar month of testing and other potentially confounding demographic and clinical characteristics. Time and setting: Omicron	*At least 14 days* • ≥18 years: 0.52 (0.41-0.65) • 18-64 years: 0.43 (0.32-0.59) • 18-49 years: 0.41 (0.28-0.59) • 50-64 years: 0.45 (0.25-0.80) • ≥50 years: 0.61 (0.47-0.80) • ≥65 years: 0.76 (0.58-0.98)	for persons in this age group.	
Shresta et al. (2024)[33]	Prospective cohort study in Ohio, USA. During the study period (10 October 2023 until 5 February 2024), 48,210 Cleveland Clinic Health System (CCHS) employees in employment at any Cleveland Clinic location in Ohio on 10 October 2023, the day the 2023–2024 formulation of the COVID-19 vaccine was available to employees at Cleveland Clinic, were included in the study. All XBB.1.5 variant adapted vaccine administered were mRNA vaccines. Cases were defined as a positive NAAT for SARS-CoV-2 any time after the study start date. A positive test more than 90 days following the date of a previous infection was considered a new episode of infection. Vaccine effectiveness (VE) was calculated from the hazard ratios (HRs) for 2023–2024 formula COVID-19 vaccination in	**Incremental VE (%) (95% CI) against Positive NAAT for SARS-CoV-2** (compared to individuals who have not received the XBB.1.5 variant adapted vaccines) *≥7 days since last dose* • Before JN.1 became pre-dominant: 42 (32-51) • After JN.1 became pre-dominant: 19 (-1-35)	The mRNA XBB.1.5 variant adapted vaccines were associated with a reduced risk of COVID-19 infections among HCP who did not receive the XBB.1.5 variant adapted vaccine. The effect was lesser once the JN.1 subvariant became dominant.	Serious

	the multivariable model using the formula VE = 1 – HR. Time and setting: Omicron			
Skowronski (2024)[34]	A test-negative case-control study using the Canadian Sentinel Surveillance Network. A total of 2,176 individuals aged 12+ were recruited from community-based sentinel practitioners in British Columbia, Ontario and Quebec. All individuals presented with an acute respiratory illness within 7 days of onset. The analysis included specimens collected between 29 October 2023 (week 44) and 13 January 2024 (week 2). VE was calculated as 1−OR × 100%. ORs compared test positivity between vaccinated and unvaccinated participants by logistic regression with covariate adjustment as specified. Time and setting: Most samples whose genetic lineage was tested belonged the JN.1 variant, followed by the HV.1, XBB subline ages and EG.5.1 variant.	**Incremental VE (%) (95% CI) >14 days after receiving the XBB.1.5 vaccine against medically attended symptomatic laboratory confirmed COVID-19 infection compared to individuals who have not received the XBB.1.5 variant adapted vaccine** • ≥12 years: 44 (14-63) • 12-64 years: 46 (2-70) • ≥65 years: 46 (-3-72) *Received their previous (non XBB vaccine) more than 12 weeks ago* • ≥12 years: 41 (13-60) *Received their previous (non XBB vaccine) more than 12 weeks ago* • ≥12 years: 47 (21-65) *Had a previous COVID-19 infection* • ≥12 years: 67 (28-85) *Excluding individuals who tested positive for influenza from the COVID-19 control group* • ≥12 years: 54 (31-70) *Had a previous COVID-19 infection and excluding individuals who tested*	Monovalent XBB.1.5 vaccine provides comparable protection, reducing the risk of medically attended COVID-19 cases by about half overall. Notably, its effectiveness was even higher, reducing the risk by about two-thirds among individuals who were previously infected with COVID-19. This indicates that the vaccine may offer enhanced protection for individuals who have already had COVID-19.	Serious

		positive for influenza from the COVID-19 control group • ≥12 years: 72 (39-87)		
Tartof et al. (2024)[35]	A test-negative case-control study using the Kaiser Permanente Southern California records. 15,233 children ages 5 to 17 years during the 2023-2024 respiratory virus season (study period: October 10, 2023, through April 30, 2024). Participants were required to have ≥1 year of health plan membership (allowing for a 31-day gap in membership to account for delays in membership renewal) to determine comorbidities and medical history. For patients that had multiple encounters, only the first encounter was included to maintain independence of outcome events. SARS-CoV-2 tests among cases and controls were restricted to those administered ≤14 days prior to the initial ARI encounter through ≤3 days after the encounter. Odds ratios (ORs) and 95% CIs were calculated from multivariable logistic regression models. Vaccine effectiveness was calculated as 1 − OR multiplied by 100%. Significance was determined with 95% CIs. Time and setting: Omicron (primarily XBB, EG.5.1, JN and KP.3)	**Incremental VE (%) (95% CI) of the Pfizer-BioNTech XBB1.5-adapted vaccine against COVID-19 related ED or UC visits** (compared to individuals who did not receive any XBB.1.5 variant adapted vaccine) *14 days* • 5-17 years: 65 (36-81) • 5-11 years: 68 (11-88) • 12-17 years: 63 (20-83)	The Pfizer-BioNTech XBB1.5-adapted vaccine provides considerable protection against COVID related ED or UC visits in children <18 years. There was no observed difference between age groups.	Moderate
Tartof et al. (2024)[36] Earlier version of the study (pre-print)[37]	A test-negative case-control study using the Kaiser Permanente Southern California records. 53,036 individuals aged 18+ included	**Incremental VE (%) (95% CI) against COVID-19 related ED/UC visits:**	XBB1.5-adapted vaccines provided significant additional protection against COVID-19 related hospitalization, ED or UC,	Moderate

	(Preprint, n=24,007) have been diagnosed with an acute respiratory infection (ARI) and tested for COVID-19 while being admitted to the hospital, visited the emergency department, visited the urgent care or had an in-person outpatient encounter (only in the preprint) during the study period (11 October 2023 through 29 February 2024) For the preprint the study period extended from October 10, 2023, through December 10, 2023. SARS-CoV-2 PCR tests among cases and controls were restricted to those administered ≤14 days prior to the initial ARI encounter through ≤3 days after the encounter. Patients could contribute ≥1 event to the study if events were >30 days apart. Adjusted odds ratios (OR) and 95% CI were estimated from multivariable logistic regression models that were adjusted for patient demographic and clinical characteristics. Time and setting: XBB sub lineages were the dominant variants.	(compared to individuals who have not received the XBB.1.5 variant adapted vaccine) *Median of 59 days since last dose* • ≥18 years (Omicron): 40 (34-45) • ≥18 years (JN.1): 41 (32-49) *14 to <60 days since last dose* • ≥18 years (JN.1): 52 (39-61) *60 to 156 days since last dose* • ≥18 years (JN.1): 34 (22-44) *Median of 52 days since last dose* • ≥18 years (XBB): 55 (45-64) *14 to <60 days since last dose* • ≥18 years (XBB): 59 (48-68) *60 to 128 days since last dose* • ≥18 years (XBB): 39 (10-59) **Incremental VE (%) (95% CI) against COVID-19 related hospitalisation:** (compared to individuals who have not received the XBB.1.5 variant adapted vaccine) *Median of 57 days since last dose* • ≥18 years (Omicron): 57 (45-66) • ≥18 years (JN.1): 54 (33-69) *14 to <60 days since last dose*	and outpatient visits. These findings support XBB.1.5 recommendations for broad age-based use of annually updated COVID-19 vaccines.	

		• ≥18 years (JN.1): 50 (15-71) *60 to 156 days since last dose* • ≥18 years (JN.1): 57 (30-73) *Median of 52 days since last dose* • ≥18 years (XBB): 65 (41-79) *14 to <60 days since last dose* • ≥18 years (XBB): 74 (49-87) **OR (95% CI) against hospitalisation – Data from pre-print (XBB sublineage):** After a median of 30 days (range: 14 - 73), individuals who received BNT162b2 XBB.1.5- adapted vaccine *compared to individuals who did not receive the XBB.1.5 vaccine* ● 18+ years: 0.37 (0.2 to 0.67) ● 18 - 64 years: 0.32 (0.04 to 2.48) ● 65+ years: 0.37 (0.2 to 0.69) *Compared to individuals who received the BA.4/5-adapted bivalent vaccine but no, XBB.1.5-adapted vaccine.* ● 18+ years: 0.4 (0.21 to 0.75) ● 18 - 64 years: 0.35 (0.04 to 2.99) ● 65+ years: 0.39 (0.2 to 0.76) *Compared to individuals who received ≥3 doses of wild-type vaccine but no variant-adapted vaccines of any kind.*		

		• 18+ years: 0.36 (0.2 to 0.65) • 18 - 64 years: 0.27 (0.03 to 2.14) • 65+ years: 0.36 (0.19 to 0.68) *Compared to individuals who received ≥2 doses of wild-type vaccine but no variant-adapted vaccines of any kind.* • 18+ years: 0.37 (0.2 to 0.67) • 18 - 64 years: 0.3 (0.04 to 2.32) • 65+ years: 0.37 (0.2 to 0.7) *Compared to individuals who were unvaccinated.* • 18+ years: 0.32 (0.16 to 0.64) • 18 - 64 years: 0.37 (0.04 to 3.22) • 65+ years: 0.29 (0.14 to 0.61) **OR (95% CI) against COVID related emergency department/urgent care (ED or UC) visits – Data from preprint (XBB sublineage)** After a median of 30 days (range: 14 - 73), individuals who received BNT162b2 XBB.1.5- adapted vaccine *compared to individuals who did not receive the XBB.1.5 vaccine* • 18+ years: 0.42 (0.34 to 0. 53) • 18 - 64 years: 0.36 (0.24 to 0.54) • 65+ years: 0.45 (0.34 to 0.59) *Compared to individuals who received the BA.4/5-adapted bivalent vaccine but no*		

		XBB.1.5-adapted vaccine. ● 18+ years: 0.43 (0.34 to 0.55) ● 18 - 64 years: 0.40 (0.26 to 0.62) ● 65+ years: 0.43 (0.31 to 0.58) *Compared to individuals who received ≥3 doses of wild-type vaccine but no variant-adapted vaccines of any kind.* ● 18+ years: 0.41(0.33 to 0.51) ● 18 - 64 years: 0.34 (0.23 to 0.51) ● 65+ years: 0.45 (0.34 to 0.6) *Compared to individuals who received ≥2 doses of wild-type vaccine but no variant-adapted vaccines of any kind.* ● 18+ years: 0.42 (0.33 to 0.52) ● 18 - 64 years: 0.35 (0.23 to 0.52) ● 65+ years: 0.46 (0.35 to 0.61) *Compared to individuals who were unvaccinated.* ● 18+ years: 0.4 (0.31 to 0.52) ● 18 - 64 years: 0.37 (0.24 to 0.56) ● 65+ years: 0.33 (0.22 to 0.49) **OR (95% CI) against medically attended COVID infections – Data from preprint (XBB sublineage)** After a median of 30 days (range: 14 - 73), individuals who received BNT162b2 XBB.1.5- adapted		

		vaccine *compared to individuals who did not receive the XBB.1.5 vaccine* ● 18+ years: 0.42 (0.27 - 0.66) ● 18 - 64 years: 0.68 (0.46 - 1.01) ● 65+ years: 0.32 (0.21 - 0.51) *Compared to individuals who received the BA.4/5-adapted bivalent vaccine but no XBB.1.5-adapted vaccine* ● 18+ years: 0.49 (0.35 to 0.68) ● 18 - 64 years: 0.78 (0.5 to 1.21) ● 65+ years: 0.29 (0.18 to 0.47) *Compared to individuals who received ≥3 doses of wild-type vaccine but no variant-adapted vaccines of any kind.* ● 18+ years: 0.44 (0.33 to 0.6) ● 18 - 64 years: 0.6 (0.4 to 0.9) ● 65+ years: 0.35 (0.22 to 0.55) *Compared to individuals who received ≥2 doses of wild-type vaccine but no variant-adapted vaccines of any kind.* ● 18+ years: 0.46 (0.34 to 0.62) ● 18 - 64 years: 0.65 (0.43 to 0.97) ● 65+ years: 0.33 (0.21 to 0.53) *Compared to those who were unvaccinated.* ● 18+ years: 0.57 (0.39 to 0.84) ● 18 - 64 years: 0.83 (0.52 to 1.33) 65+ years: 0.4 (0.18 to 0.87)		
UK Health Security Agency (2024)[38]	A test-negative case-control study design was used to recruit all individuals aged 65+ years in England from the national database who have had at least 2 days stay	**Incremental VE (%) (95% CI) against hospitalisation**	Incremental effectiveness against hospitalisation for XBB.1.5 vaccines peaked at 55.4% after 2-4 weeks since	Moderate

	in the hospital and a respiratory code in the primary diagnostic field during the study period (4th September 2023 to 17th December 2023) All individuals included (n = 16,549) had previously received at least one booster. The incremental VE of receiving a bivalent BA.1 booster vaccine in addition to at least 2 doses of a prior monovalent vaccine was used in the calculation Time and setting: Non-specific Omicron variant was the dominant variant (estimated 96%)	Compared to those who did not receive the BNT162b2 XBB.1.5 vaccine, those who received BNT162b2 XBB.1.5. • 9 to 13 days: 42.3% (95% CI, 20.5 to 58.2), • 2 to 4 weeks: 55.4% (95% CI, 45 to 63.8), and • 5 to 9 weeks: 50.9% (95% CI, 37.5 to 61.5)	vaccination. These findings show that VE against hospitalisation of XBB.1.5 did not meet WHO recommendations of VE against severe disease (≥ 90%, with the lower 95% CI ≥ 70%)	
Wilson et al. (2024)[39]	Matched cohort in the US using medical and pharmacy claims data from HealthVerity. Overall, 2,544,322 adults aged ≥ 18 years, who were vaccinated from 12 September 2023 through 31 December 2023 were included and followed through 26 January 2024. Individuals had to have continuous medical and pharmacy enrollment (with 45-day allowable gaps) from 365 days prior to index date through CED and at least one medical or pharmacy claim in baseline 365 days to be included. The hazard ratio (HR) of COVID-19 hospitalization versus unexposed individuals over the study period was estimated using Cox proportional hazards regression. VE was calculated as (1-HR) * 100%.	**Incremental VE (%) (95% CI) of the Moderna mRNA XBB.1.5 variant-adapted vaccine against medically attended COVID-19 infections** (compared to individuals who did not receive any XBB.1.5 variant adapted vaccine) *At least 8 days* • ≥18 years: 25 (24-27) • Immunocompromised: 28 (25-30) • 18-49 years: 25 (23-27) • 50 to 64 years: 19 (16-22) • ≥65 years: 21 (18-24) **Incremental VE (%) (95% CI) of the Moderna mRNA**	The Moderna mRNA XBB.1.5 variant adapted vaccine offered some protections against medically attended COVID-19 infections and COVID-19 related hospitalisations. The protection offered was similar for all age groups.	Serious

	Time and setting: Omicron (primarily XBB, EG.5.1 and JN)	**XBB.1.5 variant-adapted vaccine against COVID-19 related hospitalisations** (compared to individuals who did not receive any XBB.1.5 variant adapted vaccine) *At least 8 days* • ≥18 years: 51 (48-54) • Immunocompromised: 46 (39-52) • 18-49 years: 51 (45-57) • 50 to 64 years: 47 (42-52) • ≥65 years: 56 (51-61)		

*Hospitalisation data from the IVY database had a critical risk of bias and were excluded
ED: emergency department, HCP: health care professionals, HR: hazard ratio, OR: odds ratio, UC: urgent care, UK: United Kingdom, US: United States

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Appendix 1b: Summary of studies excluded for critical risk of bias

Study ID	First author	Title	Reason for critical bias decision
09A-4	Antunes[1, 2]	Early COVID-19 XBB.1.5 vaccine effectiveness against hospitalisation among adults targeted for vaccination, VEBIS hospital network, Europe, October 2023–January 2024	• Meeting serious risk of bias in 3 of 4 domains ○ Method for confirming vaccination - No data is provided on how vaccination information was captured, expect that the information needed to be collected from patient and entered into study database. ○ Accounting for prior infection – Not reported or analysed ○ Adjustments - Did not adjust for SES, ethnicity, race, occupation
15M-4	Ma[3,4]	Effectiveness of Updated 2023–2024 (Monovalent XBB.1.5) COVID-19 Vaccination Against SARS-CoV-2 Omicron XBB and BA.2.86/JN.1 Lineage Hospitalization and a Comparison of Clinical Severity — IVY Network, 26 Hospitals, October 18, 2023– March 9, 2024	• Meeting serious risk of bias in 3 of 4 domains ○ Method for confirming vaccination - state registry data, hospital EMR, or self-report ○ Accounting for prior infection – Not reported or analysed ○ Adjustments - Did not adjust for SES or occupation
31M-5	Merdrignac[5]	Effectiveness of XBB.1.5 Vaccines Against Symptomatic SARS-CoV-2 Infection in Older Adults During the JN.1 Lineage-Predominant Period, European VEBIS Primary Care Multicentre Study, 20 November 2023-1 March 2024	• Down-graded for lack of adjustment for calendar time
17N-3	Nham[6]	Effectiveness of COVID-19 XBB.1.5 monovalent mRNA vaccine in Korea: interim analysis	Downgraded for not adjusting or accounting for calendar time
02V-1	van Werkhoven[7]	Early COVID-19 vaccine effectiveness of XBB.1.5 vaccine against hospitalisation and admission to intensive care, the Netherlands, 9 October to 5 December 2023	• Meeting serious risk of bias in 3 of 4 domains. ○ Study design – serious bias in missing data ○ Assignment of COVID outcome – serious bias in missing data ○ Accounting for prior infection – not reported ○ Adjustments – Did not adjust for comorbidities, race/ethnicity, or SES

SES: socio-economic status

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3. Ma KC, Surie D, Lauring AS, Martin ET, Leis AM, Papalambros L, et al. Effectiveness of Updated 2023-2024 (Monovalent XBB.1.5) COVID-19 Vaccination Against SARS-CoV-2 Omicron XBB and BA.2.86/JN.1 Lineage Hospitalization and a Comparison of Clinical Severity-IVY Network, 26 Hospitals, October 18, 2023-March 9, 2024. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America [Internet]. 2024; Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emexb&NEWS=N&AN=644960526

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Appendix 2: VE against other COVID-19-related outcomes (e.g., outpatient visits) of the XBB.1.5 adapted COVID-19 vaccine compared to those who have not received the XBB.1.5 adapted COVID-19 vaccine

None

Appendix 3: Search strategy

Rounds 1 to 3

Medline and Embase

Row #	Syntax
1	vaccination/ or vaccine/
2	"Vaccin*".mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kf, fx, dq, bt, nm, ox, px, rx, ui, sy, ux, mx]
3	1 or 2
4	("XBB.1.5" OR "XBB1.5").mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kf, fx, dq, bt, nm, ox, px, rx, ui, sy, ux, mx]
5	(effectiveness or efficacy or protection).mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kf, fx, dq, bt, nm, ox, px, rx, ui, sy, ux, mx]
6	4 AND 5
7	3 AND 6
8	remove duplicates from 7

NIH/iCite (except PubMed)

Syntax	Filters
vaccin* AND (effectiveness OR efficacy OR protection) AND ("XBB.1.5" OR "XBB1.5")	Look up in title and abstract

Round 4 and forward

Medline and Embase

Row #	Syntax
1	vaccination/ or vaccine/
2	"Vaccin*".mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kf, fx, dq, bt, nm, ox, px, rx, ui, sy, ux, mx]
3	1 or 2
4	("XBB.1.5" OR "XBB1.5" OR "2024-2025" OR "2024/2025" OR "KP.2" OR "KP2" OR "JN.1" OR "JN1").).mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kf, fx, dq, bt, nm, ox, px, rx, ui, sy, ux, mx]
5	(effectiveness or efficacy or protection).mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kf, fx, dq, bt, nm, ox, px, rx, ui, sy, ux, mx]
6	4 AND 5
7	3 AND 6
12	remove duplicates from 11

NIH/iCite (except PubMed)

Syntax	Filters
vaccin* AND (effectiveness OR efficacy OR protection) AND ("XBB.1.5" OR "XBB1.5" OR "2024-2025" or "2024/2025" or "KP.2" or "KP2" or "JN.1" or "JN1")	Look up in title and abstract

Appendix 4: Definitions and glossary

Full vaccine series: Receipt of one of the following COVID-19 vaccines authorised by Health Canada:
- Two doses of AstraZeneca/COVISHIELD (AZD1222/ChAdOx1, Vaxzevria), Moderna (mRNA-1273, Spikevax), Novavax, or Pfizer-BioNTech (BNT162b2, Comirnaty);
- One dose of Janssen (Johnson & Johnson: Ad26.COV2.S, Jcovden); or
- A combination of the above

Fully vaccinated: A person who is at least 14 days post having received one of the following vaccine schedules:
- the full series of a COVID-19 vaccine authorized by Health Canada (see above); or
- the full series of the above vaccines plus an additional dose in immunocompromised individuals

Additional dose: A person who has received:
- a full series of a COVID-19 vaccine authorised by Health Canada (see above) plus an additional dose of a COVID-19 vaccine authorised by Health Canada; or
- the full series of the above vaccines plus two additional doses in immunocompromised individuals

Confirmed infection: A person with confirmation of infection with SARS-CoV-2 documented by the detection of at least 1 specific gene target by a validated laboratory-based nucleic acid amplification test (NAAT) assay (e.g. real-time PCR or nucleic acid sequencing) performed at a community, hospital, or reference laboratory (the National Microbiology Laboratory or a provincial public health laboratory) (2).

Hospitalisation due to COVID-19: Inpatient admission to a hospital and/or ICU unit, associated with laboratory-confirmed SARS-CoV-2 infection.

ICU admission due to COVID-19: Inpatient admission to the ICU unit, associated with laboratory-confirmed SARS-CoV-2 infection.

Death due to COVID-19: Death resulting from a clinically compatible illness in a probable or confirmed COVID-19 case, with no presence of clear alternative causes unrelated to COVID-19 (e.g., trauma, poisoning, drug overdose).

Post-COVID-19 conditions: Occurs in individuals with a history of probable or confirmed SARS-CoV-2 infection, usually 3 months from the onset of COVID-19 with symptoms that last for at least 2 months and cannot be explained by an alternative diagnosis. Common symptoms include fatigue, shortness of breath, cognitive dysfunction but also others and generally have an impact on everyday functioning. Symptoms may be new onset following initial recovery from an acute COVID-19 episode or persist from the initial illness. Symptoms may also fluctuate or relapse over time.

Medically attended infection: medical care for lab-confirmed symptomatic infection but no admission to hospital (medically diagnosed COVID-19); medical care could be sought in any community service setting, such as inpatient care, outpatient care, an emergency room, or urgent care.

MIS-C: Multisystem inflammatory syndrome in children is a post-viral inflammatory syndrome that temporally follows coronavirus disease 2019 (COVID-19). Symptoms may include fever, abdominal pain, vomiting, diarrhea, skin rash and other signs of inflammation. MIS-C occurs in children and adolescent 0-19 years of age with fever for three or more days AND two of the following:

1. Rash or bilateral non-purulent conjunctivitis or mucocutaneous inflammation signs (oral, hands or feet),
2. Hypotension or shock,
3. Features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including ECHO findings or elevated troponin/N-terminal pro-brain natriuretic peptide (NT-proBNP),
4. Evidence of coagulopathy (by prothrombin time, partial thromboplastin time, elevated D-dimer),
5. Acute gastrointestinal problems (diarrhea, vomiting or abdominal pain) AND Elevated markers of inflammation such as C-reactive protein, erythrocyte sedimentation rate or procalcitonin AND no other obvious microbial cause of inflammation, including bacterial sepsis, staphylococcal or streptococcal shock syndromes AND Evidence of COVID-19

Variants of concern (VOC): A SARS-CoV-2 variant is considered a VOC in Canada based on a set of criteria including increased transmissibility or detrimental change in COVID-19 epidemiology, increased virulence, decreased effectiveness of vaccines, and so on. As of January 17, 2022, there is currently no VOCs.

Vaccine effectiveness (VE): A measure of how well a vaccine protects people from getting the outcome of interest in real-world practice (For example: VE of 92% against infection means that 92% of people will be protected from becoming infected with COVID and 8% of people will still be at risk of becoming infected with COVID). In the context of the current report, we have utilised the term vaccine effectiveness to cover all studies. However, we are aware that the studies that have been included range from efficacy through to effectiveness studies. We decided to use this terminology as it is consistent with how most evidence synthesis products describe these studies. To be consistent with this, in the French summary we have utilised the term efficacité, and it is noted that in French there is no distinction between the translations of efficacy and effectiveness.

Absolute vaccine effectiveness (aVE): Refers to vaccine protection that is estimated by comparing vaccinated individuals with unvaccinated individuals.

Relative vaccine effectiveness: The term used to refer to the effectiveness of a vaccine when it is measured by comparing people who have received one vaccine type or regimen to those who received a different vaccine type or regimen.

Incremental vaccine effectiveness (iVE): Measure of VE that compares the frequency of health outcomes in people who received one type of vaccine to people who received different, multiple vaccines or no vaccines at all. iVE is the measure used when there is a combination of previous vaccination exposures in the comparator group (i.e., there is a "not up to date" comparator group); combines absolute and relative VE as a measure the added benefit of COVID-19 vaccines.

AZ: AstraZeneca

CIs: Confidence Intervals

ED: emergency department

HCW: Healthcare workers

ICU: Intensive care unit

LTC: Long-term care

LTCF: Long-term care facility

MOD: Moderna

Obs: observational study

Omicron: variant of interest (XBB.1.5, EG.5, BA.2.86, JN.1)

OR: odds ratio

PF: Pfizer

RCT: Randomized controlled trial

RoB: Risk of Bias

UC: Urgent care

UK: United Kingdom

USA: United States of America

VOI: variant of interest

WHO: World Health Organization

Appendix 5: Critical appraisal process

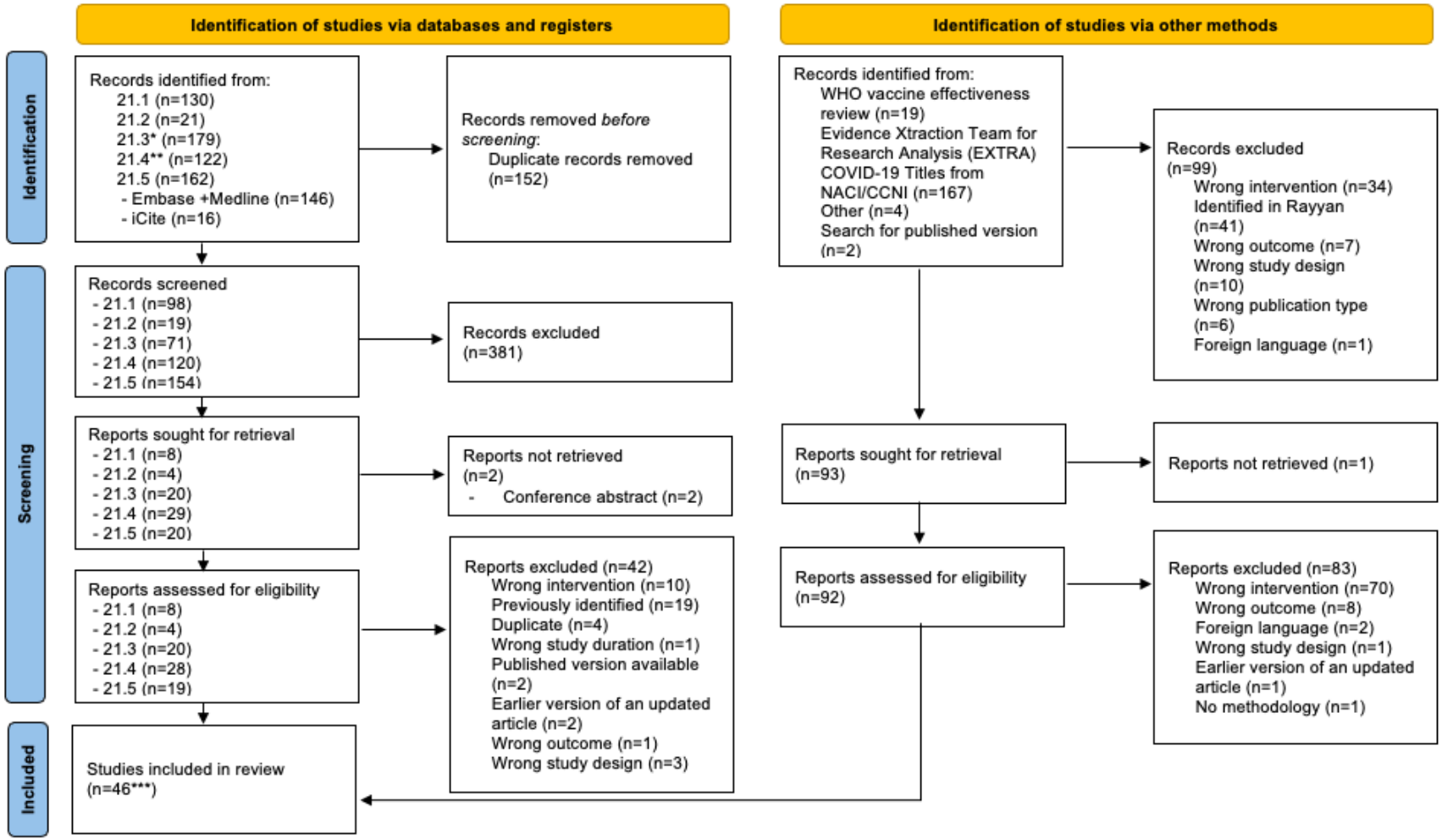
We appraised the quality of the individual studies using an adapted version of ROBINS-I. This tool classifies the Risk of Bias of a study as **Low, Moderate, Serious, Critical, or No Information**. *Low Risk of Bias indicates High Quality, and Critical Risk of Bias indicates Very Low (insufficient) Quality*. ROBINS-I appraises 7 bias domains and judges each study against an ideal reference randomised controlled trial. To improve the utility of ROBINS-I for assessing studies reporting vaccine effectiveness, we have focused on study characteristics that introduce bias as reported in the vaccine literature (see WHO. Evaluation of COVID-19 vaccine effectiveness. Interim Guidance. 17 March 2021). An overall judgement of "critical" is given when the study is judged to be at critical risk of bias in at least one domain or if three or more domains are judged to be "serious".

Appendix 6: Data-extraction template

Study details	
Source	First author of study and year of publication
Location	Country data was collected in
COI	If conflicts of interest were reported
Funding	public or industry
Study design	RCT/cohort/data-linkage/test-negative/case-control/other
Publication format	Peer-reviewed / pre-print / report
Population(s)	general public/HCW
Total (N)	Total study sample
Age	Description of age of the population
Female	number or %
Race/ethnicity	Description of the race/ethnicity of the population
Population (primary serie)	Details on primary serie received previously
Population (boosters)	Details on boosters received previously
Population (COVID-19 history)	Details on the COVID-19 history of the population
Definition of infections	How were COVID-19 infections defined
Definition of COVID hospitalisations	How were COVID-19 hospitalisations defined
Definition of COVID outpatient visits	How were COVID-19 outpatient visits defined
Definition of COVID emergency department visits	How were COVID-19 emergency department visits defined
Definition of COVID ICU admission	How were COVID-19 ICU admissions defined
Definition of post-COVID conditions	How were post-COVID-19 conditions defined
Definition of MIS-C	How was MIS-C defined
Definition of COVID deaths	How were COVID-19 deaths defined
Vaccines	Details of what vaccines were included in the study
Comparator	What comparison group was used to generate VE
Study calendar time	When was the study conducted

Outcomes	
Variant sub-group	Was a specific variant being studied (any, delta, or omicron)
Was VOC or VOI sequenced	Yes or no, only applicable if looking at a variant
Outcome	Cases, hospitalisations, ICU, deaths, post-COVID-conditions, or MIS-C
Specific vaccine	If individual vaccine data is reported
Vaccine class	mRNA, adenovirus, protein subunit, or mixed (reporting mRNA, adenovirus, and/or mixed doses)
Effect measure used	VE, RR, or other
Level of CIs	95% or 99%
Time window	Time since second dose administered
VE outcome	Reported point estimate
Lower CI	Reported lower CI
Upper CI	Reported upper CI
Adjustments	What variables were used to adjust for in analyses
Comments	

Appendix 7a: Flow chart of studies included in the current update:



*Includes a search strategy adjustment

**Included a search strategy adjustment to include the 2024-2025 vaccine

***Seven of these were excluded for having a critical risk of bias, 2 of these are published version of a pre-print that was excluded for having a critical risk of bias and 8 of these are updates or published versions of previously included articles

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71. For more information, visit: http://www.prisma-statement.org/

Appendix 7b. Summary of excluded studies during full text screening (new studies are in blue)

Author (year of publication)	Title	Reason for exclusion
Andersson et al. (2024) – Round 4 with search strategy adjustments	Comparative effectiveness of the monovalent XBB.1.5-containing covid-19 mRNA vaccine across three Nordic countries	Previously identified
Caffrey et al. (2024) – Round 4 with search strategy adjustments	Effectiveness of BNT162b2 XBB vaccine in the US Veterans Affairs Healthcare System	Previously identified
Chong et al.(2024)	Risks of SARS-CoV-2 JN.1 Infection and COVID-19-Associated Emergency Department Visits/Hospitalizations Following Updated Boosters and Prior Infection: A Population-Based Cohort Study	Previously identified
DeCuir et al. (2024) – Round 4 with search strategy adjustments	Interim Effectiveness of Updated 2023-2024 (Monovalent XBB.1.5) COVID-19 Vaccines Against COVID-19-Associated Emergency Department and Urgent Care Encounters and Hospitalization Among Immunocompetent Adults Aged >=18 Years - VISION and IVY Networks, September 2023-January 2024	Previously identified
Hansen et al. (2024)	Short-term effectiveness of the XBB.1.5 updated COVID-19 vaccine against hospitalisation in Denmark: a national cohort study	Previously identified
Huiberts et al. (2024)	Effectiveness of Omicron XBB.1.5 vaccine against SARS-CoV-2 Omicron XBB and JN.1 infection in a prospective cohort study in the Netherlands, October 2023 to January 2024	Duplicate
Huiberts et al. (2024)	Effectiveness of Omicron XBB.1.5 vaccine against SARS-CoV-2 Omicron XBB and JN.1 infection in a prospective cohort study in the Netherlands, October 2023 to January 2024	Previously identified
Huiberts et al. (2024) – Round 4 with search strategy adjustments	Effectiveness of Omicron XBB.1.5 vaccine against SARS-CoV-2 Omicron XBB and JN.1 infection in a prospective cohort study in the Netherlands, October 2023 to January 2024	Duplicate
Huiberts et al. (2024) – Round 5	Effectiveness of Omicron XBB.1.5 vaccine against infection with SARS-CoV-2 Omicron XBB and JN.1 variants, prospective cohort study, the Netherlands, October 2023 to January 2024	Previously identified
Huiberts et al. (2024) – Round 4 with search strategy adjustments	Effectiveness of Omicron XBB.1.5 vaccine against infection with SARS-CoV-2 Omicron XBB and JN.1 variants, prospective cohort study, the Netherlands, October 2023 to January 2024	Previously identified
Huiberts et al. (2024)	Effectiveness of Omicron XBB.1.5 vaccine against infection with SARS-CoV-2 Omicron XBB and JN.1 variants, prospective cohort study, the Netherlands, October 2023 to January 2024	Previously identified

Kirsebom et al. (2023)	Long-term duration of protection of ancestral-strain monovalent vaccines and effectiveness of the bivalent BA.1 boosters against COVID-19 hospitalisation during a period of BA.5, BQ.1, CH.1.1. and XBB.1.5 circulation in England	Wrong intervention
Kirsebom et al. (2024) – Round 4 with search strategy adjustments	Effectiveness of Autumn 2023 COVID-19 vaccination and residual protection of prior doses against hospitalisation in England, estimated using a test-negative case-control study	Duplicate
Kirsebom et al. (2024)	Effectiveness of Autumn 2023 COVID-19 vaccination and residual protection of prior doses against hospitalisation in England, estimated using a test-negative case-control study	Duplicate
Kirsebom et al. (2024) – Round 4 with search strategy adjustments	Effectiveness of autumn 2023 COVID-19 vaccination and residual protection of prior doses against hospitalisation in England, estimated using a test-negative case-control study	Previously identified
Kirwan et al. (2024) – Round 5	Protection of vaccine boosters and prior infection against mild/asymptomatic and moderate COVID-19 infection in the UK SIREN healthcare worker cohort: October 2023 to March 2024	Previously identified
Kirwan et al. (2024) – Round 4 with search strategy adjustments	Protection of vaccine boosters and prior infection against mild/asymptomatic and moderate COVID-19 infection in the UK SIREN healthcare worker cohort: October 2023 to March 2024	Duplicate
Laniece Delaunay et al. (2024) – Round 4 with search strategy adjustments	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	Previously identified
Lasrado et al. (2024)	Waning immunity and IgG4 responses following bivalent mRNA boosting	Wrong intervention
Levy et al. (2024)	XBB.1.5 mRNA COVID-19 Vaccination and Inpatient or Emergency Department Visits Among Adults Infected with SARS-CoV-2 JN.1 and XBB-Lineage Variants	Previously identified
Levy et al. (2024) – Round 4 with search strategy adjustments	XBB.1.5 mRNA COVID-19 Vaccination and Inpatient or Emergency Department Visits Among Adults Infected with SARS-CoV-2 JN.1 and XBB-Lineage Variants	Previously identified
Levy et al. (2024)	XBB.1.5 mRNA COVID-19 Vaccination and Inpatient or Emergency Department Visits Among Adults Infected with SARS-CoV-2 JN.1 and XBB-Lineage Variants	Wrong comparison
Lewnard et al (2023)	Increased vaccine sensitivity of an emerging SARS-CoV-2 variant	Wrong intervention

Lin et al. (2024)	Effectiveness of XBB.1.5 vaccines and antiviral drugs against severe outcomes of omicron infection in the USA	Wrong study duration
Lin et al. (2024)	Effectiveness of XBB.1.5 vaccines and antiviral drugs against severe outcomes of omicron infection in the USA	Previously identified
Lin et al. (2024) – Round 4 with search strategy adjustments	Effectiveness of XBB.1.5 vaccines and antiviral drugs against severe outcomes of omicron infection in the USA	Previously identified
Lin et al (2023)	Effects of COVID-19 vaccination and previous SARS-CoV-2 infection on omicron infection and severe outcomes in children under 12 years of age in the USA:an observational cohort study	Wrong intervention
Link-Gelles et al (2023)	Early Estimates of Bivalent mRNA Booster Dose Vaccine Effectiveness in Preventing Symptomatic SARS-CoV-2 Infection Attributable to Omicron BA.5- and XBB/XBB.1.5-Related Sublineages Among Immunocompetent Adults - Increasing Community Access to Testing Program, United States, December 2022-January 2023	Wrong intervention
Link-Gelles et al. (2024) – Round 4 with search strategy adjustments	Early Estimates of Updated 2023-2024 (Monovalent XBB.1.5) COVID-19 Vaccine Effectiveness Against Symptomatic SARS-CoV-2 Infection Attributable to Co-Circulating Omicron Variants Among Immunocompetent Adults - Increasing Community Access to Testing Program, United States, September 2023-January 2024	Previously identified
Machado et al. (2024)	Immune Evasion of SARS-CoV-2 Omicron Subvariants XBB.1.5, XBB.1.16 and EG.5.1 in a Cohort of Older Adults after ChAdOx1-S Vaccination and BA.4/5 Bivalent Booster	Wrong intervention
Mousten-Helms et al. (2024)	Relative vaccine protection, disease severity, and symptoms associated with the SARS-CoV-2 omicron subvariant BA.2.86 and descendant JN.1 in Denmark: a nationwide observational study	Wrong study design
Moustsen-Helms et al. (2024) – Round 4 with search strategy adjustments	Relative vaccine protection, disease severity, and symptoms associated with the SARS-CoV-2 omicron subvariant BA.2.86 and descendant JN.1 in Denmark: a nationwide observational study	Previously identified
Pather et al. (2024) – Round 4 with search strategy adjustments	A Brighton Collaboration standardized template with key considerations for a benefit-risk assessment for the Comirnaty COVID-19 mRNA vaccine	Wrong study design
Tartof et al. (2024) – Round 4 with search strategy adjustments	Effectiveness of BNT162b2 XBB Vaccine against XBB and JN.1 Sub-lineages	Duplicate

Roa et al. (2024)	SCB-2019 protein vaccine as heterologous booster of neutralizing activity against SARS-CoV-2 Omicron variants after immunization with other COVID-19 vaccines	Wrong intervention
Salvulescu et al. (2024)	Effectiveness of the autumn 2023 COVID-19 vaccine dose in hospital-based healthcare workers: results of the VEBIS healthcare worker vaccine effectiveness cohort study, seven European countries, season 2023/24	Wrong intervention
Salvulescu et al. (2024)	Relative effectiveness of the second booster COVID-19 vaccines against laboratory confirmed SARS-CoV-2 infection in healthcare workers: VEBIS HCW VE cohort study (1 October 2022-2 May 2023)	Wrong intervention
Sakr et al. (2024)	Booster doses of COVID-19 vaccine enhance neutralization efficiency against XBB.1.5	Wrong intervention
Skowronski et al. (2024)	2023/24 mid-season influenza and Omicron XBB.1.5 vaccine effectiveness estimates from the Canadian Sentinel Practitioner Surveillance Network (SPSN)	Previously identified
Zaeck et al. (2024) – Round 4 with search strategy adjustments	Original COVID-19 priming regimen impacts the immunogenicity of bivalent BA.1 and BA.5 boosters	Wrong intervention

Appendix 7b. Summary of excluded studies during hand search (new studies are in blue)

Author (year of publication)	Title	Reason for exclusion
Abukhalil et al. (2024)	COVID-19 Vaccines Breakthrough Infections and Adverse Effects Reported by the Birzeit University Community in Palestine.	Wrong intervention
Alberto et al. (2024)	Real-world effectiveness of the CoronaVac vaccine in a retrospective population-based cohort in four Colombian Cities 2021-2022	Wrong intervention
Allahgholipour et al. (2024)	COVID-19 vaccines breakthrough infection and adverse reactions in medical students: a nationwide survey in Iran	Wrong intervention
Al-Rousan et al. (2024)	Evaluation of the effects of MERCK, MODERNA, PFIZER/BioNTech, and JANSSEN COVID-19 vaccines on vaccinated people: A metadata analysis	Wrong study design
Altas et al. (2024)	Frequency of SARS-COV-2 infection and COVID-19 vaccine uptake and protection among Syrian refugees: COVID-19 Vaccine among Syrian Refugees	Wrong intervention
Althaus et al. (2024)	How effective is the BNT162b2 mRNA vaccine against SARS-CoV-2 transmission and infection? A national programme analysis in Monaco, July 2021 to September 2022	Wrong intervention
Álvarez-Sánchez et al. (2024)	Effect of vaccination on COVID-19 mortality during omicron wave among highly marginalized mexican population	Wrong intervention
Alzubaidi et al. (2024)	Protective effect of COVID-19 vaccination against a SARS-CoV-2 reinfection in the Babil Province	Wrong outcome
Andersen et al. (2025)	Effectiveness of BNT162b2 XBB.1.5 vaccine in immunocompetent adults using tokenization in two U.S. states	Previously identified
Andersson et al. (2024)	Adverse Events After XBB.1.5-Containing COVID-19 mRNA Vaccines	Wrong outcome
Andersson et al. (2024)	Comparative effectiveness of the monovalent XBB.1.5-containing covid-19 mRNA vaccine across three Nordic countries	Previously identified
Andrews et al. (2024)	OpenSAFELY: Effectiveness of COVID-19 vaccination in children and adolescents	Wrong intervention
Ann Costa Clemens et al. (2024)	Interchangeability of different COVID-19 vaccine platforms as booster doses: A phase 3 study mimicking real-world practice	Wrong intervention
Antonacci et al. (2024)	SC-31 SARS-CoV-2 vaccination influence in development of Long-COVID clinical phenotypes	Wrong publication type

Antunes et al. (2024)	Early COVID-19 XBB.1.5 Vaccine Effectiveness Against Hospitalisation Among Adults Targeted for Vaccination, VEBIS Hospital Network, Europe, October 2023–January 2024	Previously identified
Appaneal et al. (2024)	Early effectiveness of the BNT162b2 KP.2 vaccine against COVID-19 in the US Veterans Affairs Healthcare System. medRxiv. Published online December 29	Previously identified
Baltu et al. (2024)	COVID-19 vaccination among adolescents and young adults with chronic kidney conditions: a single-center experience	Wrong outcome
Bejko et al. (2024)	High Vaccine Effectiveness Against Severe Covid-19 Outcomes During the Omicron Era in Luxembourg: A Nationwide Retrospective Cohort Study (December 2021-March 2023)	Wrong intervention
Bejko et al. (2024)	High vaccine effectiveness against severe COVID-19 outcomes and population preventable fraction during the Omicron era in Luxembourg: A nationwide retrospective risk factor analysis	Wrong intervention
Bytyci et al. (2024)	Immunocompromised individuals are at increased risk of COVID-19 breakthrough infection, hospitalization, and death in the post-vaccination era: A systematic review	Wrong study design
Caffrey et al. (2024)	Effectiveness of BNT162b2 XBB vaccine in the US Veterans Affairs Healthcare System	Previously identified
Cai et al. (2024)	Impact of COVID-19 vaccination status on hospitalization and disease severity: A descriptive study in Nagasaki Prefecture, Japan	Wrong intervention
Camacho et al. (2024)	The impact of comorbidity status in COVID-19 vaccines effectiveness before and after SARS-CoV-2 omicron variant in northeastern Mexico: a retrospective multi-hospital study	Wrong intervention
Canaan et al. (2024)	Efficacy and safety of SARS-COV-2 vaccines in breast cancer patients : Egyptian experience	Wrong outcome
Carazo et al. (2024)	Monovalent mRNA XBB.1.5 vaccine effectiveness against COVID-19 hospitalization in Quebec, Canada: impact of variant replacement and waning protection during 10-month follow-up	Previously identified
Cardemil et al. (2024)	Maternal COVID-19 Vaccination and Prevention of Symptomatic Infection in Infants	Wrong outcome
Caron et al. (2024)	A Comparison of COVID-19 Associated Hospitalization Rates Among Unvaccinated Versus Vaccinated Residents in Rhode Island, September 2022 to March 2024.	Wrong outcome

Chalkias et al. (2024)	Interim Report of the Reactogenicity and Immunogenicity of Severe Acute Respiratory Syndrome Coronavirus 2 XBB–Containing Vaccines	Wrong outcome
Chanchlani et al. (2024)	COVID-19 vaccine effectiveness among South Asians in Canada	Wrong intervention
Chaudhary et al. (2024)	Breakthrough COVID-19 Infection Among the General Community, Frontline Workers, and Healthcare Workers During the Second and Third Wave in North India: A Longitudinal Study.	Wrong intervention
Chen et al. (2024)	Safety and effectiveness of COVID-19 vaccines among the elderly in the real world	Foreign language
Chen et al. (2024)	Uptake, effectiveness and safety of COVID-19 vaccines in individuals at clinical risk due to immunosuppressive drug therapy or transplantation procedures: a population-based cohort study in England	Previously identified
Chen et al. (2024)	Uptake, effectiveness and safety of COVID-19 vaccines in individuals at clinical risk due to immunosuppressive drug therapy or transplantation procedures: a population-based cohort study in England	Wrong intervention
Chirasuthat et al. (2024)	Immunogenicity, Effectiveness, and Safety of COVID-19 Vaccines among Patients with Immune-Mediated Dermatological Diseases: A Systematic Review and Meta-analysis	Wrong study design
Chivu et al. (2024)	Hybrid Immunity and the Incidence of SARS-CoV-2 Reinfections during the Omicron Era in Frontline Healthcare Workers	Wrong intervention
Chong et al. (2024) – pre published	Risks of SARS-CoV-2 JN.1 infection and COVID-19 associated emergency-department (ED) visits/hospitalizations following updated boosters and prior infection: a population-based cohort study	Previously identified
Chong et al. (2024) - published	Risks of SARS-CoV-2 JN.1 infection and COVID-19 associated emergency-department (ED) visits/hospitalizations following updated boosters and prior infection: a population-based cohort study	Previously identified
Cortés et al. (2024)	Effectiveness of COVID-19 Vaccines in Colombia: Findings from Two Highly Specialized Healthcare Centers	Wrong publication type
Costiniuk et al. (2024)	Correlates of Breakthrough SARS-CoV-2 Infections in People with HIV: Results from the CIHR CTN 328 Study	Wrong intervention
Cotton et al. (2024)	The effect of SARS-COV-2 variant on non-respiratory features and mortality among vaccinated and non-fully vaccinated patients	Wrong intervention

Dal Negro et al. (2024)	mRNA vaccines protect from the lung microvasculature injury and the capillary blood volume loss occurring in SARS-CoV-2 paucisymptomatic infections	Wrong intervention
Dam et al. (2024)	COVID-19 outcome trends by vaccination status in Canada, December 2020–January 2022	Wrong intervention
De troyer et al. (2024)	Clinical effectiveness of coronavirus disease 2019 vaccination in patients with multiple sclerosis stratified by disease-modifying treatment	Wrong intervention
Deutschl et al. (2024)	Impact of Vaccination Status on Outcome of Patients With COVID-19 and Acute Ischemic Stroke Undergoing Mechanical Thrombectomy	Wrong intervention
Devendra et al. (2024)	The Relationship of COVID-19 Vaccination With Mechanical Ventilation and Mortality Among 7,365 Hospitalized Patients in Hawai'i	Wrong publication type
Di et al. (2024)	Impact of COVID-19 Vaccination with BNT162b2 on the Frequency of Acute Symptoms Among Symptomatic US Adults Testing Positive for SARS-CoV-2 at a National Retail Pharmacy	Wrong publication type
Dimitrov et al. (2024)	Assessment of COVID-19 vaccine effectiveness in a nation with a low vaccination coverage: insights from real-world data and propensity score matched analyses	Wrong intervention
Dimitrova et al. (2024)	VACCINE BREAKTHROUGH CASES AMONG HOSPITALISED PATIENTS IN THE INTENSIVE CARE UNIT FOR COVID-19 IN NORTH-EASTERN BULGARIA	Wrong intervention
Durier et al. (2024)	Incidence of COVID-19 mRNA vaccine symptomatic breakthrough infections during Omicron circulation in adults with or without infection prior to vaccination	Wrong intervention
Ehsan et al. (2024)	Prevalence of covid-19 breakthrough after vaccination and adverse effects of vaccines	Wrong intervention
Falsaperla et al. (2024)	SARS-CoV-2 parental vaccination and risk of multisystem inflammatory syndrome in children: a single-center retrospective study	Wrong intervention
Favà et al. (2024)	Hybrid immunity protection against SARS-CoV-2 and severe COVID-19 in kidney transplantation: a retrospective, comparative cohort study	Wrong intervention
Feldstein et al. (2025)	Effectiveness of mRNA COVID-19 vaccines and hybrid immunity in preventing SARS-CoV-2 infection and symptomatic COVID-19 among adults in the United States	Previously identified

Fernandez-Garcia et al. (2024)	Effectiveness and safety of COVID-19 vaccines on maternal and perinatal outcomes: a systematic review and meta-analysis	Wrong study design
Franklin et al. (2024)	COVID-19 Vaccination Coverage, and Rates of SARS-CoV-2 Infection and COVID-19–Associated Hospitalization Among Residents in Nursing Homes — National Healthcare Safety Network, United States, October 2023–February 2024	Wrong outcome
Galgut et al. (2024)	COVID-19 vaccines are effective at preventing symptomatic and severe infection among healthcare workers: A clinical review	Wrong study design
Gallardo-Nelson et al. (2024)	4th booster-dose SARS-CoV-2 heterologous and homologous vaccination in rheumatological patients	Wrong intervention
Gao et al. (2024)	COVID-19 vaccination and long COVID among 50 years older and above European: The role of chronic multimorbidity	Wrong intervention
Garrett et al. (2024)	Safety, Effectiveness and Immunogenicity of heterologous mRNA-1273 Boost after Prime with Ad26.COV2.S among Healthcare Workers in South Africa: the single-arm, open-label, Phase 3 SHERPA Study	Wrong intervention
Garza-Silva et al. (2024)	Effectiveness of different booster vaccine combinations against SARS-CoV-2 during a six-month follow-up in Mexico and Argentina	Wrong intervention
Gayed et al. (2024)	Safety and Immunogenicity of the Monovalent Omicron XBB.1.5-Adapted BNT162b2 COVID-19 Vaccine in Individuals ≥12 Years Old: A Phase 2/3 Trial	Wrong outcome
Gazitt et al. (2024)	COVID-19 Vaccine Effectiveness among Patients with Psoriatic Disease: A Population-Based Study	Wrong intervention
Gim et al. (2024)	Vaccine Effectiveness Against Severe Acute Respiratory Syndrome Coronavirus 2 Reinfection by Type and Frequency of Vaccine: A Community-Based Case-Control Study	Wrong intervention
Guedalia et al. (2024)	Maternal hybrid immunity and risk of infant COVID-19 hospitalizations: national case-control study in Israel	Wrong intervention
Gutfreund et al. (2024)	The effectiveness of the COVID-19 vaccines in the prevention of post-COVID conditions in children and adolescents: a systematic literature review and meta-analysis	Wrong study design
Gwak et al. (2024)	Short-Term Relative Effectiveness of Homologous NVX-CoV2373 and BNT162b2 COVID-19 Vaccinations in South Korea	Wrong intervention

Hamid Reza Shamsollahi, Younesian (2024)	Effectiveness of Mass Vaccination for Prevention of Hospitalization, Severe Disease and Death Due to Sars-Cov-2 Omicron Ba.2 Variant; a Case- Population Study	Wrong intervention
Hannawi et al. (2024)	Efficacy, immunogenicity, and safety of a monovalent mRNA vaccine, ABO1020, in adults: A randomized, double-blind, placebo-controlled, phase 3 trial	Previously identified
Horvath et al. (2024)	Vaccine Effectiveness against GP-Attended Symptomatic COVID-19 and Hybrid Immunity among Adults in Hungary during the 2022–2023 Respiratory Season Dominated by Different SARS-CoV-2 Omicron Subvariants	Wrong intervention
Hu et al. (2024)	Evaluation of vaccine effectiveness of mRNA COVID-19 vaccines in children: a systematic review and meta-analysis	Wrong study design
Huang et al. (2024)	The Effectiveness of Vaccination on the COVID-19 Epidemic in California	Wrong intervention
Huang et al. (2024)	The Effectiveness of Vaccination on the COVID-19 Epidemic in California	Duplicate
Huiberts et al. (2024)	Effectiveness of Omicron XBB.1.5 vaccine against SARS-CoV-2 Omicron XBB and JN.1 infection in a prospective cohort study in the Netherlands, October 2023 to January 2024	Previously identified
Huiberts et al. (2024)	Vaccine effectiveness of primary and booster COVID-19 vaccinations against SARS-CoV-2 infection: repeat analyses with updated data for the prospective cohort study in the Netherlands from July 2021 to June 2022	Wrong intervention
Ioannou et al. (2025)	Effectiveness of the 2023-to-2024 XBB.1.5 COVID-19 Vaccines Over Long-Term Follow-up: A Target Trial Emulation	Previously identified
Jangiam et al. (2024)	Relative vaccine effectiveness of ChAdOx1/AZD1222 vaccines as booster dose via intradermal injection with a one-fifth dose compared with the intramuscular injection in the prevention of SAR-CoV-2 infections in Phuket – A Retrospective Cohort Study	Wrong intervention
Janzic et al. (2024)	Prospective Observational Study of COVID-19 Vaccination in Patients with Thoracic Malignancies: Adverse Events, Breakthrough Infections and Survival Outcomes	Wrong intervention
Jimenez-Sepulveda et al. (2024)	Effectiveness of mRNA booster doses in preventing infections and hospitalizations due to SARS-CoV-2 and its dominant variant over time in Valencian healthcare workers, Spain	Wrong intervention

Kassanjee et al. (2024)	COVID-19 Vaccine Uptake and Effectiveness by Time since Vaccination in the Western Cape Province, South Africa: An Observational Cohort Study during 2020–2022	Wrong intervention
Kastelewicz et al. (2024)	Incidence of SARS-CoV-2 infection among healthcare workers before and after COVID-19 vaccination in a tertiary paediatric hospital in Warsaw: A retrospective cohort study	Wrong intervention
Kavikondala et al. (2024)	Comparative Effectiveness of mRNA-1273 and BNT162b2 COVID-19 Vaccines Among Older Adults: Systematic Literature Review and Meta-Analysis Using the GRADE Framework	Wrong study design
Keane et al. (2024)	Effectiveness of BNT162b2 Vaccine for Preventing COVID-19-Related Hospitalizations: A Test-Negative Case–Control Study	Wrong intervention
Khater et al. (2024)	Effectiveness of COVID-19 vaccination among patients hospitalized from April 2020 to March 2021: A Retrospective cohort study	Wrong intervention
Kirk et al. (2024)	Real-world comparative effectiveness of a third dose of mRNA-1273 versus BNT162b2 among adults aged ≥ 65 years in the United States	Wrong intervention
Kopel et al. (2024)	Effectiveness of the 2023-2024 Omicron XBB.1.5-containing mRNA COVID-19 vaccine (mRNA-1273.815) in preventing COVID-19-related hospitalizations and medical encounters among adults in the United States: An interim analysis	Previously identified
Kopel et al. (2024)	Effectiveness of the 2023–2024 Omicron XBB.1.5-containing mRNA COVID-19 Vaccine (mRNA-1273.815) in Preventing COVID-19–related Hospitalizations and Medical Encounters Among Adults in the United States	Previously identified
Kostinov et al. (2024)	Effect of influenza, pneumococcal and SARS-CoV-2 vaccination on the incidence and severity of COVID-19 in health care workers at a single institution (epidemiologic study)	Wrong intervention
Lang et al. (2024)	COVID-19 Vaccine Effectiveness and Digital Pandemic Surveillance in Germany (eCOV Study): Web Application–Based Prospective Observational Cohort Study	Wrong intervention
Lanièce Delaunay et al. (2024)	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	Previously identified
Lanièce Delaunay et al. (2024)	COVID-19 Vaccine Effectiveness in Autumn and Winter 2022 to 2023 Among Older Europeans	Wrong intervention

Lanièce Delaunay et al. (2024)	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	Duplicate
Lanièce Delaunay et al. (2024)	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	Previously identified
Lazar Neto et al. (2024)	Effectiveness of COVID-19 vaccines against severe COVID-19 among patients with cancer in Catalonia, Spain	Wrong intervention
Lee et al. (2023)	Clinical and Economic impact of updated Fall 2023 COVID-19 vaccines in the Immunocompromised Population in Canada	Wrong study design (modelling study)
Lee et al. (2024)	Limited durability of protection conferred by XBB.1.5 vaccines against Omicron-associated severe outcomes among community-dwelling adults aged ≥50 years, Ontario, Canada, September 2023 to June 2024	Previously identified
Lee et al. (2024)	Estimates of vaccine effectiveness of the updated monovalent XBB.1.5 COVID-19 vaccine against symptomatic SARS-CoV-2 infection, hospitalization, and receipt of oxygen therapy in South Korea - October 26 to December 31, 2023	Previously identified
Levy et al. (2024)	XBB.1.5 mRNA COVID-19 Vaccination and Inpatient or Emergency Department Visits Among Adults Infected with SARS-CoV-2 JN.1 and XBB-Lineage Variants	Previously identified
Li et al. (2024)	Effectiveness and safety of immune response to SARS-CoV-2 vaccine in patients with chronic kidney disease and dialysis: A systematic review and meta-analysis	Wrong study design
Lin et al. (2024)	Impact of Booster Vaccination Interval on SARS-CoV-2 Infection, Hospitalization, and Death	Wrong intervention
Lin et all. (2024)	Effectiveness of XBB.1.5 Vaccines Against Omicron Subvariants	Previously identified
Link-Gelles et al. (2024)	Interim Effectiveness of Updated 2023-2024 (Monovalent XBB.1.5) COVID-19 Vaccines Against COVID-19-Associated Hospitalization Among Adults Aged ≥18 Years with Immunocompromising Conditions - VISION Network, September 2023-February 2024	Previously identified
Liu et al. (2024)	Effectiveness of XBB.1.5 monovalent COVID-19 vaccine against COVID-19 mortality in Australians aged 65 years and older during August 2023 to February 2024	Previously identified
Lu et al. (2024)	Preliminary Report of Nationwide COVID-19 Vaccine Compensation in Taiwan	Wrong intervention

Lu et al. (2024)	The effect of COVID-19 vaccine to the Omicron variant in children and adolescents: a systematic review and meta-analysis	Wrong study design
Lu et al. (2024)	Real-world Effectiveness of mRNA COVID-19 Vaccines Among US Nursing Home Residents Aged ≥65 Years in the Pre-Delta and High Delta Periods	Wrong intervention
Ma et al. (2024)	Effectiveness of Updated 2023–2024 (Monovalent XBB.1.5) COVID-19 Vaccination Against SARS-CoV-2 Omicron XBB and BA.2.86/JN.1 Lineage Hospitalization and a Comparison of Clinical Severity — IVY Network, 26 Hospitals, October 18, 2023–March 9, 2024	Previously identified
Ma et al. (2024)	Effectiveness of Updated 2023–2024 (Monovalent XBB.1.5) COVID-19 Vaccination Against SARS-CoV-2 Omicron XBB and BA.2.86/JN.1 Lineage Hospitalization and a Comparison of Clinical Severity IVY Network, 26 Hospitals, October 18, 2023–March 9, 2024	Duplicate
Ma et al. (2024)	Effectiveness of Updated 2023–2024 (Monovalent XBB.1.5) COVID-19 Vaccination Against SARS-CoV-2 Omicron XBB and BA.2.86/JN.1 Lineage Hospitalization and a Comparison of Clinical Severity — IVY Network, 26 Hospitals, October 18, 2023–March 9, 2024	Duplicate
Malden et al. (2024)	Post-COVID conditions following COVID-19 vaccination: a retrospective matched cohort study of patients with SARS-CoV-2 infection	Wrong intervention
Marron et al. (2024)	The impact of the COVID-19 vaccination programme on symptomatic and severe SARS-CoV-2 infection during a period of Omicron variant dominance in Ireland, December 2021 to March 2023	Wrong intervention
Marziali et al. (2024)	Efficacy and safety of BNT162b2 mRNA vaccine in a cohort of 90 transfusion dependent thalassemia patients	Wrong intervention
McDonnell et al. (2024)	COVID-19 Vaccination in Patients with Inborn Errors of Immunity Reduces Hospitalization and Critical Care Needs Related to COVID-19: a USIDNET Report	Wrong intervention
Melo et al. (2024)	Epidemiological Monitoring of Covid-19 in Healthcare Professionals: Effects of Vaccination in the Hospital Setting	Wrong intervention
Merdrignac et al. (2024)	Effectiveness of XBB.1.5 Vaccines Against Symptomatic SARS-CoV-2 Infection in Older Adults During the JN.1 Lineage-Predominant	Previously identified

	Period, European VEBIS Primary Care Multicentre Study, 20 November 2023–1 March 2024	
Mesle et al. (2024)	Estimated number of lives directly saved by COVID-19 vaccination programmes in the WHO European Region from December, 2020, to March, 2023: a retrospective surveillance study	Wrong intervention
Mielke et al. (2024)	Updated Bivalent COVID-19 Vaccines Reduce Risk of Hospitalization and Severe Outcomes in Adults: An Observational Cohort Study	Wrong intervention
Mimura et al. (2024)	Association between mRNA COVID-19 vaccine boosters and mortality in Japan: The VENUS study	Wrong intervention
Mirofsky et al. (2024)	Vaccination impact: mortality and time shift to Covid-19 maximum severity in hospitalized patients - An Argentine multicenter registry	Wrong intervention
Moller et al. (2024)	Effectiveness of Autumn 2023 COVID-19 vaccination and residual protection of prior doses against hospitalisation in England, estimated using a test-negative case-control study	Previously identified
Moor et al. (2024)	Sex differences in symptoms following the administration of BNT162b2 mRNA Covid-19 Vaccine in Children below 5 Years of age in Germany (CoVacU5): a retrospective cohort study	Wrong intervention
Moreno-Echevarria et al. (2024)	Incidence and risk factors of omicron variant SARS-CoV-2 breakthrough infection among vaccinated and boosted individuals	Wrong intervention
Moreno et al. (2024)	Incidence and risk factors of SARS-CoV-2 breakthrough infection in the early Omicron variant era among vaccinated and boosted individuals in Chicago	Wrong intervention
Morlacchi et al. (2024)	COVID-19 Vaccine in Lung and Liver Transplant Recipients Exceeds Expectations: An Italian Real-Life Experience on Immunogenicity and Clinical Efficacy of BNT162b2 Vaccine	Wrong intervention
Mousten-Helms et al. (2024)	Relative vaccine protection, disease severity, and symptoms associated with the SARS-CoV-2 omicron subvariant BA.2.86 and descendant JN.1 in Denmark: a nationwide observational study	Previously identified
Nguyen et al. (2025)	Effectiveness of the BNT162b2 XBB.1.5-adapted vaccine against COVID-19 hospitalization related to the JN.1 variant in Europe: a test-negative case-control study using the id.DRIVE platform	Previously identified
Nham et al. (2024)	Effectiveness of COVID-19 XBB.1.5 monovalent mRNA vaccine in Korea: interim analysis	Previously identified
Nham et al. (2024)	Effectiveness of COVID-19 XBB.1.5 monovalent mRNA vaccine in Korea: interim analysis	Duplicate

Niessen et al. (2024)	Vaccine effectiveness against COVID-19 related hospital admission in the Netherlands by medical risk condition: A test-negative case-control study	Wrong intervention
Nunes et al. (2024) - preprint	Monovalent XBB.1.5 COVID-19 vaccine effectiveness against hospitalisations and deaths during the Omicron BA.2.86/JN.1 period among older adults in seven European countries: A VEBIS-EHR Network Study	Previously identified
Nunes et al. (2024) – published version	Monovalent XBB.1.5 COVID-19 vaccine effectiveness against hospitalisations and deaths during the Omicron BA.2.86/JN.1 period among older adults in seven European countries: A VEBIS-EHR Network Study	Previously identified
Obel et al. (2024)	Confounding and Negative Control Methods in Observational Study of SARS-CoV-2 Vaccine Effectiveness: A Nationwide, Population-Based Danish Health Registry Study	Wrong intervention
Ogata et al. (2024)	Vaccine Effectiveness against SARS-CoV-2 among Household Contacts during Omicron BA.2–Dominant Period, Japan	Wrong intervention
Ogilvie et al. (2024)	Effectiveness of BNT162b2 COVID-19 primary series vaccination in children aged 5–17 years in the United States: a cohort study	Wrong intervention
Palazzo et al. (2024)	Breakthrough SARS-CoV-2 infection in fully vaccinated patients with systemic lupus erythematosus: results from the COVID-19 Vaccination in Autoimmune Disease (COVAD) study	Wrong intervention
Pallet et al. (2024)	Reduced risk for Omicron SARS-CoV-2 infection observed in older adults with hybrid immunity	Wrong intervention
Pandey et al. (2024)	Effectiveness of Vaccine on Outcome in SARS-COV-2 Hospitalised Patients	Wrong intervention
Pastore et al. (2024)	Homologous or heterologous administration of mRNA or adenovirus-vectored vaccines show comparable immunogenicity and effectiveness against the SARS-CoV-2 omicron variant	Wrong intervention
Petrakis et al. (2024)	The prevalence of long COVID-19 syndrome in hospitalized patients with COVID-19 pneumonia.	Wrong outcome
Poh et al. (2024)	First SARS-CoV-2 Omicron infection as an effective immune booster among mRNA vaccinated individuals: final results from the first phase of the PRIBIVAC randomised clinical trial	Wrong intervention

Pool et al. (2024)	Effectiveness of ChAdOx1 nCoV-19 and BBIBP-CorV vaccines against COVID-19-associated hospitalisation and death in the Seychelles infected adult population	Wrong intervention
Prathapasinghe et al. (2024)	A prospective study to explore the impact of the vaccination status on disease severity and mortality in Covid-19	Wrong publication type
Protopapas et al. (2024)	Breakthrough COVID-19 Infections after Booster SARS-CoV-2 Vaccination in a Greek Cohort of People Living with HIV during the Delta and Omicron Waves	Wrong intervention
Quek et al. (2024)	Hybrid immunity augments cross-variant protection against COVID-19 among immunocompromised individual	Wrong intervention
Rebertson et al. (2024)	Risk Factors for Long Covid in a United States Prospective Longitudinal Community-Based Cohort	Wrong intervention
Rodrigues et al. (2024)	Real-world Effectiveness of original BNT162b2 mRNA COVID-19 against symptomatic Omicron infection among Children 5-11 years of age in Brazil: a prospective test-negative design study	Wrong intervention
Romeiser et al. (2024)	COVID-19 Booster Vaccination Status and Long COVID in the United States: A Nationally Representative Cross-Sectional Study	Wrong intervention
Rover et al. (2024)	Association between Vaccination and Persistent Covid-19-Related Symptoms Among Patients with Mild Omicron Infection: A Prospective Cohort Study	Wrong intervention
Sadat et al. (2024)	Determination of COVID-19 Late Disorders as Possible Long-COVID and/or Vaccination Consequences	Wrong intervention
Salvulescu et al. (2024)	Effectiveness of the autumn 2023 COVID-19 vaccine dose in hospital-based healthcare workers: results of the VEBIS healthcare worker vaccine effectiveness cohort study, seven European countries, season 2023/24.	Previously identified
Sezerol et al. (2024)	Relative effectiveness of COVID-19 vaccine booster doses in people aged 65 and older-a retrospective cohort study in Türkiye	Previously identified
Sharma et al. (2023)	Comparative Analysis Of Covid-19 Vaccine Efficacy In Heart Transplant Recipients On Standardized Immunotherapy Regimens	Wrong publication type
Shen et al. (2024)	Influence of vaccination on critical COVID-19 patients with acute respiratory failure: a retrospective cohort study	Wrong intervention
Shikami et al. (2024)	Effect of mRNA vaccines on preventing hospitalization in patients with new coronavirus infection during the predominance of the Alpha/Delta variant	Foreign language

Shimada et al. (2024)	Effectiveness and duration of additional immune defense provided by SARS-CoV-2 infection before and after receiving the mRNA COVID-19 vaccine BNT162b2	Wrong outcome
Soyer et al. (2024)	COVID-19 Breakthrough Infection after Vaccination and Substance Use Disorders: A Longitudinal Cohort of People with and without HIV Receiving Care in the United States Veterans Health Administration	Wrong intervention
Stalman et al. (2024)	Clinical and humoral responses after SARS-CoV-2 breakthrough infections in patients with immunosuppressants	Wrong intervention
Stankov et al. (2024)	Humoral and cellular immune responses following BNT162b2 XBB.1.5 vaccination	Previously identified
Su et al. (2024)	Safety and immunogenicity of heterologous boosting with a bivalent SARS-CoV-2 mRNA vaccine (XBB.1.5/BQ.1) in Chinese participants aged 18 years or more: A randomised, double-blinded, active-controlled phase 1 trial	Wrong outcome
Sun et al. (2024)	Real-World Effectiveness of a Third Dose of mRNA-1273 Versus BNT162b2 on Inpatient and Medically Attended COVID-19 Among Immunocompromised US Adults	Wrong intervention
Takahashi et al. (2024)	Efficiency of indirect protection of COVID-19 vaccination and interactions between indirect and direct protection on household transmission	Wrong intervention
Tartof et al. (2024)	Estimated Effectiveness of the BNT162b2 XBB Vaccine Against COVID-19	Earlier version of an updated article
Tartof et al. (2024)	Effectiveness of BNT162b2 XBB Vaccine Against XBB and JN.1 Sublineages	Previously identified
Tartof et al. (2024)	Effectiveness of BNT162b2 XBB Vaccine Against XBB and JN.1 Sublineages	Previously identified
Tem-eiam (2024)	The impact of COVID-19 booster vaccination on reducing mortality in patients hospitalized with COVID-19 at Sisaket Hospital	Wrong intervention
Torgauten et al. (2024)	Hospitalisations and humoral COVID-19 vaccine response in vaccinated rituximab-treated multiple sclerosis patients	Wrong intervention
Torres-Rufas et al. (2024)	Effectiveness and Safety of the COVID-19 Vaccine in Patients with Rheumatoid Arthritis in a Real-World Setting	Wrong outcome

Townsend et al. (2024)	Investigating incidence of and factors associated with SARS-CoV-2 infection over a nine-month period in a highly-vaccinated healthcare worker cohort	Wrong intervention
Turpin et al. (2024)	Risk factors for COVID-19 hospitalisation after booster vaccination during the Omicron period: A French nationwide cohort study	Wrong outcome
Uemura et al. (2024)	Duration of effectiveness of the COVID-19 vaccine in Japan: A retrospective cohort study using large- scale population-based registry data	Wrong intervention
Uemura et al. (2024)	Duration of effectiveness of the COVID-19 vaccine in Japan: a retrospective cohort study using large-scale population-based registry data	Wrong intervention (published version)
UKHSA et al. (2024)	COVID-19 vaccine surveillance report November 2024	No methodology
Urquidi et al. (2024)	Vaccine effectiveness in reducing COVID-19-related hospitalization after a risk-age-based mass vaccination program in a Chilean municipality: A comparison of observational study designs	Wrong intervention
Van Werkhoven et al. (2023)	Early COVID-19 vaccine effectiveness of XBB.1.5 vaccine against hospitalization and ICU admission, the Netherlands, 9 October - 5 December 2023	Previously identified
Vásquez-Velásquez et al. (2024)	Death Risk Response of High-Altitude Resident Populations to COVID-19 Vaccine: A Retrospective Cohort Study	No access to full text
Vivaldi et al. (2024)	COVID-19 severity and risk of SARS-CoV-2-associated asthma exacerbation by time since booster vaccination: a longitudinal analysis of data from the COVIDENCE UK study	Wrong intervention
Wilson et al. (2024)	Evaluating the Effectiveness of mRNA-1273.815 Against COVID-19 Hospitalization Among Adults Aged ≥ 18 Years in the United States	Previously identified
Wu et al. (2024)	Protection of prior SARS-CoV-2 infection, COVID-19 boosters, and hybrid immunity against Omicron severe illness: A population-based cohort study of five million residents in Canada	Wrong intervention
Yamamoto et al. (2024)	Protection of Omicron bivalent vaccine, previous infection, and their induced neutralizing antibodies against symptomatic infection with Omicron XBB.1.16 and EG.5.1	Wrong outcome
Yang et al. (2024)	The impact of COVID vaccination on incidence of long COVID and healthcare resource utilisation in a primary care cohort in England, 2021-2022	Wrong intervention

Yildirim et al. (2024)	Impact of vaccination on ICU admissions of hospitalized COVID-19 patients in a country with a heterologous vaccine policy	Wrong intervention
Yumiya et al. (2024)	Effectiveness of COVID-19 mRNA vaccine in preventing infection against Omicron strain: Findings from the Hiroshima Prefecture COVID-19 version J-SPEED for PCR center	Wrong intervention
Zhang et al. (2024)	Analysis of cases of reinfection of past SARS-CoV-2 patients in Pudong New Area of Shanghai	Foreign language
Zhao et al. (2024)	Efficacy and prognostic factors of COVID-19 vaccine in patients with hepatocellular carcinoma: Analysis of data from a prospective cohort study	Wrong intervention