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Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

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Supplementary materials

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Contents

S1. Literature search strategy

PubMed:

("COVID-19"[tw] OR "COVID 19"[tw] OR "COVID19"[tw] OR "COVID2019"[tw] OR "COVID 2019"[tw] OR "COVID-2019"[tw] OR "novel coronavirus"[tw] OR "new coronavirus"[tw] OR "novel corona virus"[tw] OR "new corona virus"[tw] OR "SARS-CoV- 2"[tw] OR "SARSCoV2"[tw] OR "SARS-CoV2"[tw] OR "2019nCoV"[tw] OR "2019-nCoV"[tw] OR "2019 coronavirus"[tw] OR "2019 corona virus"[tw] OR "coronavirus disease 2019"[tw] OR "severe acute respiratory syndrome coronavirus 2"[nm] OR "severe acute respiratory syndrome coronavirus 2"[tw] OR "sars-coronavirus-2"[tw] OR "coronavirus disease 2019"[tw] OR "corona virus disease 2019"[tw])
AND
("COVID-19 Vaccines"[Mesh] OR "COVID-19 vaccine"[tiab] OR "mRNA-1273 vaccine" [Supplementary Concept] OR "mRNA-1273 vaccine"[tiab] OR "mRNA vaccine"[tiab] OR "mRNA COVID-19 vaccines"[tiab] OR "ChAdOx1 COVID-19 vaccine" [Supplementary Concept] OR "Ad5-nCoV vaccine" [Supplementary Concept] OR "Ad5-nCoV"[tiab] OR "Covid-19 aAPC vaccine" [Supplementary Concept] OR "Ad26.COV2.S vaccine" [Supplementary Concept] OR "Ad26.COV2.S vaccine"[tiab] OR "adenoviral vector vaccine"[tiab] OR "BNT162 vaccine" [Supplementary Concept] OR "BNT162b2"[tiab] OR "BNT162"[tiab] OR "CoronaVac" [tiab] OR "vaccin*"[tiab])
AND
("Clinical Trial, Phase IV" [Publication Type] OR "Controlled Clinical Trial" [Publication Type] OR "Randomized Controlled Trial" [Publication Type] OR "Case-Control Studies"[Mesh] OR "Retrospective Studies"[Mesh] OR "Retrospective"[tiab] OR "Cohort Studies"[Mesh] OR "Prospective Studies"[Mesh] OR "Prospective"[tiab] OR "Longitudinal Studies"[Mesh] OR "Follow-Up Studies"[Mesh] OR "Follow-up studies"[tiab] OR "cohort"[tiab] OR "test negative"[tiab] OR "Observational cohort"[tiab] OR "Test-negative design"[tiab] OR"RCT"[tiab] OR "randomized"[tiab] OR "randomised"[tiab] OR "randomly allocated"[tiab] OR "case-control"[tiab] OR "real-world effectiveness"[tiab] OR "effectiveness"[tiab] OR "association"[tiab] OR "impact"[tiab] OR "vaccine impact"[tiab]) NOT ("Clinical Trial, Phase I" [Publication Type] OR "Clinical Trial, Phase II" [Publication Type])
NOT ("animals"[mesh] NOT ("animals"[mesh] AND "humans"[mesh]))

Embase:

('COVID-19' OR 'COVID 19' OR 'COVID19' OR 'COVID2019' OR 'COVID 2019' OR 'COVID-2019' OR 'novel coronavirus' OR 'new coronavirus' OR 'novel corona virus' OR 'new corona virus' OR 'SARS-CoV-2' OR 'SARSCoV2' OR 'SARS-CoV2' OR '2019nCoV' OR '2019-nCoV' OR '2019 coronavirus' OR '2019 corona virus' OR 'coronavirus disease 2019' OR 'severe acute respiratory syndrome coronavirus 2'/exp OR 'severe acute respiratory syndrome coronavirus 2' OR 'sars-coronavirus-2' OR 'coronavirus disease 2019'/exp OR 'coronavirus disease 2019' OR 'corona virus disease 2019')
AND
('SARS-CoV-2 vaccine'/exp OR 'COVID-19 vaccine':ti,ab OR 'mRNA-1273 vaccine'/exp OR 'mRNA-1273 vaccine':ti,ab OR 'mRNA vaccine':ti,ab OR 'mRNA COVID-19 vaccines':ti,ab OR 'ChAdOx1 ncov 19'/exp OR 'Ad5 nCoV vaccine'/exp OR 'Ad5- nCoV':ti,ab OR 'Covid-19 aAPC vaccine':ti,ab OR 'Ad26.COV2.S vaccine'/exp OR 'Ad26.COV2.S vaccine':ti,ab OR 'adenoviral vector vaccine':ti,ab OR 'BNT 162 vaccine'/exp OR 'BNT162b2':ti,ab OR 'BNT162':ti,ab OR 'CoronaVac'/exp OR 'coronavac':ti,ab OR 'vaccin*':ti,ab)
AND
('phase 4 clinical trial'/exp OR 'Controlled Clinical Trial'/exp OR 'Randomized Controlled Trial'/exp OR 'Case Control Study'/exp OR 'Retrospective Study'/exp OR 'Retrospective':ti,ab OR 'Cohort analysis'/exp OR 'Prospective Study'/exp OR 'Prospective':ti,ab OR 'Longitudinal Study'/exp OR 'Follow Up'/exp OR 'Follow-up study':ti,ab OR 'cohort':ti,ab OR 'test negative':ti,ab OR 'Observational cohort':ti,ab OR 'postmarketing surveillance'/exp OR 'postmarketing surveillance':ti,ab OR 'Test-negative design':ti,ab

OR 'RCT':ti,ab OR 'randomized':ti,ab OR 'randomised':ti,ab OR 'randomly allocated':ti,ab OR 'case-control':ti,ab OR 'real-world effectiveness':ti,ab OR 'effectiveness':ti,ab OR 'association':ti,ab) NOT ('phase 1 clinical trial'/exp OR 'phase 2 clinical trial'/exp)
NOT ('animal'/exp NOT ('animal'/exp AND 'human'/exp))
NOT 'conference abstract'/it

WHO COVID Global Literature Database:

("COVID-19 Vaccines" OR "COVID-19 vaccine" OR "mRNA-1273 vaccine" OR "mRNA vaccine" OR "mRNA COVID-19 vaccines" OR "ChAdOx1 COVID-19 vaccine" OR "Ad5- nCoV" OR "Covid-19 aAPC vaccine" OR "Ad26.COV2.S vaccine" OR "adenoviral vector vaccine" OR "BNT162b2" OR "BNT162" OR "CoronaVac" OR vaccin*)
AND
("Phase IV" OR "Controlled Clinical Trial" OR "Randomized Controlled Trial" OR "Case- Control Studies" OR "Retrospective" OR "Cohort Studies" OR "Prospective" OR "Longitudinal Studies" OR "Follow-Up Studies" OR "Follow-up study" OR "cohort" OR "test negative" OR "Observational cohort" OR "Test-negative design" OR "RCT" OR "randomized" OR "randomised" OR "randomly allocated" OR "case-control" OR "real- world effectiveness" OR "effectiveness" OR "association") AND NOT ("Phase I" OR "Phase II")

SCOPUS:

TITLE-ABS-KEY(“novel coronavir*” OR “novel corona virus*” OR “2019 coronavirus” OR betacoronavir* OR covid19 OR "covid 19" OR ncov OR "CoV 2" OR cov2 OR sarscov2 OR sars-cov OR sarscov OR 2019ncov OR 2019-nCoV OR "novel CoV" OR “coronavirus infections”) AND TITLE-ABS-KEY(Vaccin* AND (effectiveness OR efficacy OR protection*) AND (postmarketing OR approved OR (post* W/5 approval) OR "real world" OR "phase IV" OR "phase 4" OR observational OR longitudinal OR spread OR transmission OR (rate* W/5 infection*) OR (reduc* W/5 infection*) OR "general population"))

Web of Science:

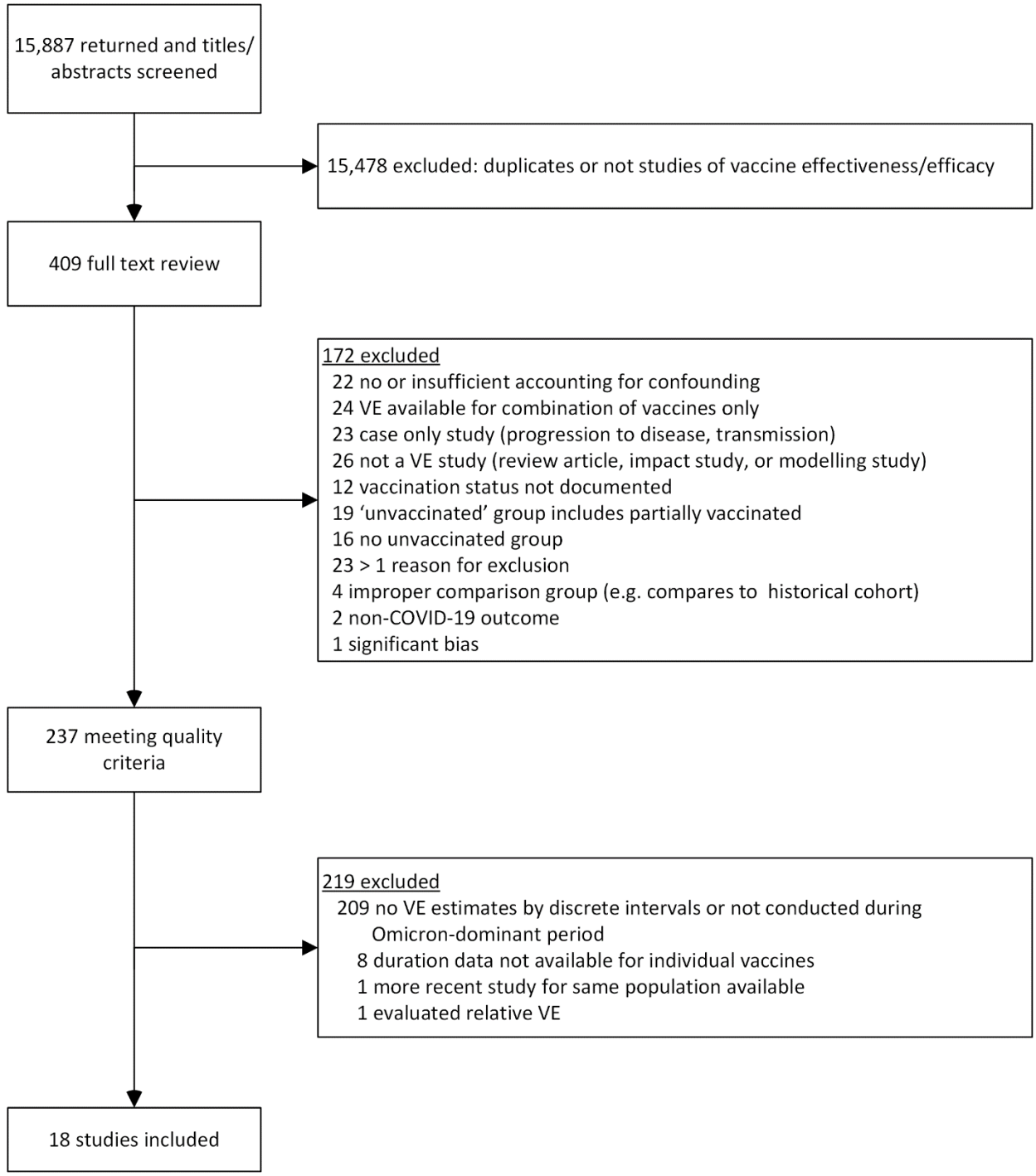
(TI=(covid-19 vaccine effectiveness)) OR AB=(covid-19 vaccine effectiveness)

medRxiv, bioRxiv, SSRN, Europe PMC, Research Square, Knowledge Hub:

“COVID-19 vaccine effectiveness” OR “COVID-19 vaccine efficacy”

In addition to the above databases, MMWR and Eurosurveillance are hand-searched weekly for new studies meeting eligibility criteria.

S2. Study Selection



S3. Inclusion and exclusion criteria for search for VE studies

Identification of eligible vaccine effectiveness studies was a two-step process. First, as part of a larger effort, all studies that estimate VE of COVID-19 vaccines are identified. Second, studies meeting criteria for estimating waning VE against Omicron were selected among these.

Step 1. Identifying vaccine effectiveness studies

All primary research studies of vaccine effectiveness underwent initial full-text review by 2 independent reviewers (AB and KKW) with additional review by 2 senior team members (MMH and MKP). During full-text review, a vaccine effectiveness study was initially excluded if it did not contain at least one vaccine effectiveness estimate that met all the following quality criteria. This was done to ensure a baseline level of quality and/or comparability of estimates for real-world studies.

Inclusion criteria

- Published or preprint studies or reports with adequate scientific details.
- VE estimates must have confidence intervals around the estimate (except in those cases where it is unable to be calculated) and values of estimates must be presented clearly.
- All studies must include persons with and without the clinical outcome under investigation.
- All studies of primary series vaccine effectiveness must compare persons with and without vaccination; studies of booster dose vaccine effectiveness must compare persons with and without a booster dose (either unvaccinated or persons having completed primary series vaccination without a booster).
- Due to the effect of confounders, the study design must account for confounding either by matching or by adjusting for confounders in the analysis. At a minimum, the study must adjust for or match by age and calendar time. Studies that report only unmatched and unadjusted VE estimates may be included if the authors report that adjustment was performed and no difference in results was observed.
- All outcomes must be laboratory confirmed (by PCR, genomic sequencing or rapid antigen testing).
- At least 90% of participants must have a confirmed vaccination status, rather than relying on recall.
- Study must assess vaccine effectiveness of a COVID-19 vaccine on SARS-COV-2/COVID-19-specific outcomes (i.e., infection, symptomatic disease, severe disease/death)

Exclusion criteria

- Press releases, presentations, or media reports
- Review articles, modelling studies, impact studies
- Estimates only available from a low-resolution chart will be excluded
- Case only studies, such as progression to disease and transmission studies
- The study uses a modelled comparison group or compares to a historical cohort
- Studies with syndromic outcomes without laboratory confirmation
- Study includes days 0-12 post-vaccination in unvaccinated definition
- Presence of significant bias as determined by expert consensus
- Unvaccinated group is restricted to persons previously infected with SARS-CoV-2
- Effectiveness estimates provided for a combination of vaccines rather than individual vaccines (exception is for mRNA vaccines)

Step 2. Identifying studies of vaccine effectiveness over time against Omicron

After application of the above initial quality criteria, a second set of criteria were applied to determine inclusion for this specific analysis.

Inclusion criteria

- Study presented vaccine effectiveness estimates during a period when Omicron was the dominant circulating variant as noted by the authors or presented vaccine effectiveness estimates specifically against Omicron (i.e. Omicron cases were confirmed by genomic sequencing).
- Study presented vaccine effectiveness estimates for at least two discrete time intervals after receipt of the final dose in the primary series or of a booster dose.

Exclusion criteria

- Effectiveness estimates provided for the mRNA vaccines combined. While initial inclusion criteria allowed for studies reporting a combined VE estimate for the mRNA vaccines, differences between the mRNA vaccines have now been reported, particularly for Omicron (see summary of vaccine effectiveness studies on www.VIEW-hub.org). Of note, for all evaluations combining vaccines, an unbiased estimate of the rate of decline in VE could only be obtained if overall VE does not differ between the evaluated vaccines and if the proportion of the study population receiving each vaccine is constant over time. Because both of these conditions could be verified in such evaluations, this exclusion criterion was added.
- A more recent study provides more up-to-date or more appropriate vaccine effectiveness estimates for the same population (e.g. a study that only provides estimates for a sub-population of previously infected persons would be excluded if another study provided estimates for the entire population regardless of prior infection)
- Study evaluated relative vaccine effectiveness (i.e. for booster studies the reference group was persons having completed a primary series rather than unvaccinated persons)

S4. Characteristics and Results of Included Vaccine Effectiveness Studies against Omicron

Study First Author (Country)	Study Design (Variables controlled for in vaccine effectiveness estimates)	Testing Period	Study population (years)	PRIMARY SERIES				BOOSTER			
				Vaccine	Disease Outcome*	Time interval since final dose (days)	Vaccine effectiveness (95% CI)	Vaccine	Disease Outcome*	Time interval since booster dose (days)	Vaccine effectiveness (95% CI)
Baum [1] (Finland)	Retrospective cohort (age, sex, region of residence, residence in a long-term care facility, influenza vaccination in 2019–2020, number of nights hospitalized between 2015 and 2019 and presence of predisposing comorbidities)	Dec 27, 2020 - Feb 19, 2022	≥70 years	Pfizer BioNTech - Comirnaty	Severe Disease	14-90	91 (79-96)	Pfizer BioNTech - Comirnaty	Severe Disease	14-60	95 (94-97)
										>60	90 (97-93)
						91-180	76 (56-86)	Moderna – mRNA-1273		14-60	94 (89-97)
										>60	48 (-13-76)
						>180	61 (48-71)				
				Moderna - mRNA-1273		14-90	92 (43-99)	Pfizer BioNTech - Comirnaty		14-60	96 (82-99)
										>60	100 (46.5-100)
						91-180	90 (28-99)	Moderna - mRNA-1273		14-60	97 (92-99)
						>180	72 (43-86)			>60	92 (79-97)
				AstraZeneca - Vaxzevria		91-180	41 (-140-86)	Pfizer BioNTech - Comirnaty		14-60	98 (89-100)
										>60	90 (27-99)
						>180	43 (-10-70)	Moderna - mRNA-1273		14-60	100 (73.7-100)
										>60	40 (-336-92)
Buchan[2] (Canada)	Test-negative case control (age, sex, region of residence, comorbidities, influenza vaccination, prior infection, week of testing, and neighbourhood-level information on median household income, proportion of the working population employed as non-health essential workers, mean number of persons per dwelling, and	Nov 22, 2021 - Mar 6, 2022	12-17 years	Pfizer BioNTech - Comirnaty	Symptomatic disease	7-59	51 (38-61)				
						60-119	31 (20-41)				
						120-179	29 (19-38)				
						>180	29 (17-38)				
					Severe disease	7-59	76 (-10-95)				
						60-119	83 (55-93)				
						120-179	82 (64-91)				
						>180	88 (77-94)				

	proportion of the population who self-identify as a visible minority)										
Cerqueira-Silva[3] (Brazil)	Test-negative case control (race, state of residence, region, comorbidities)	Jan 01, 2022 - Mar 22, 2022	18+	Pfizer BioNTech - Comirnaty	Symptomatic disease	14-69	36·9 (36·2-37·6)	Pfizer BioNTech - Comirnaty	Symptomatic disease	14-34	35·2 (33·7-36·7)
						70-139	10·8 (10·1-11·6)			35-62	28·4 (26·0-30·8)
						>139	6·9 (5·6-8·2)			63-90	36·3 (29·9-42·2)
					Severe disease	14-69	74·5 (71·4-77·2)		Severe disease	14-34	88·3 (85·1-90·7)
						70-139	75·3 (73·8-78·3)			35-62	90·0 (86·0-92·9)
						>139	71·5 (68·5-74·2)			63-90	82·5 (64·0-91·5)
				AstraZeneca - Vaxzevria	Symptomatic disease	14-69	15·9 (14·3-17·4)	Pfizer BioNTech - Comirnaty	Symptomatic disease	14-34	42·8 (42·1-43·5)
						70-139	-8·8 (-9·7- -7·9)			35-62	26·1 (25·1-27·0)
						>139	-1·4 (-2·2- -0·6)			63-90	11·2 (9·9-12·6)
										91-173	4·9 (2·7-7·0)
					Severe disease	14-69	66·7 (61·0-71·6)		Severe disease	14-34	89·9 (88·9-90·7)
						70-139	63·8 (62·0-65·6)			35-62	87·1 (86·1-87·9)
						>139	57·4 (55·8-58·9)			63-90	82·0 (80·6-83·3)
										91-173	80·2 (77·9-82·2)
Cerqueira-Silva (Scotland)[3]	Test-negative case control (sex, age, socioeconomic status, smoking, BMI, blood pressure, immune-compromised status)			Pfizer BioNTech - Comirnaty	Symptomatic disease	14-69	43·7 (37·3-49·5)	Pfizer BioNTech - Comirnaty	Symptomatic disease	14-34	52·9 (49·3-56·3)
						70-139	9 (3·6-14·2)			35-62	46·1 (42·2-49·7)
						>139	-5.7 (-11·3- -0·4)			63-90	35·9 (30·8-40·7)
										91-173	30·1 (23·5-36·1)
								Moderna - mRNA-1273		14-34	60·1 (55·3-64·3)
										35-62	50·8 (45·6-55·6)
										63-90	38·8 (29·5-46·9)
										91-173	23·4 (3·4-39·3)
					Severe disease	14-69	68.8 (-87·0-94·8)	Pfizer BioNTech - Comirnaty	Severe disease	14-34	81·6 (29·9-95·2)
						70-139	42.4 (-35·0-75·4)			35-62	73·0 (35·7-88·7)
						>139	38.8 (-20·0-68·8)			63-90	59·2 (9·7-81·6)
										91-174	75·7 (33·9-91·0)
								Moderna - mRNA-1273		14-34	32·7 (-184·5-84·1)
										35-62	86·9 (27·2-97·6)
										63-90	70·7 (-23·9-93·1)
										91-174	93·7 (31·6-99·4)
				AstraZeneca - Vaxzevria	Symptomatic disease	14-69	18·1 (-6·7- 37·2)	Pfizer BioNTech - Comirnaty	Symptomatic disease	14-34	49·0 (45·3-52·4)
						70-139	-29·6 (-53·7- -9·3)			35-62	41·5 (37·4-45·4)
						>139	-31·6 (-40·2- -23·6)			63-90	29·7 (23·6-35·3)
										91-174	18·2 (7·2-28·0)
								Moderna - mRNA-1273		14-34	55·3 (50·9-59·3)
										35-62	45·9 (40·8-50·7)
										63-90	23·9 (14·3-32·4)
										91-174	26·2 (10·3-39·2)

					Severe disease	70-139	68·9 (-254·3-97·3)	Pfizer BioNTech - Comirnaty	Severe disease	14-34	81·8 (55·0-92·6)
						>139	48·4 (-20·1-77. ·8)			35-62	87·3 (69·0-94·8)
										63-90	84·2 (59·8-93·8)
										91-174	93·4 (69·4-98·6)
								Moderna - mRNA-1273		35-62	95·4 (80·9-98·9)
										63-90	96·0 (77·6-99·3)
										91-174	90·2 (-88·4-99·5)
Chemaitelly[4] (Qatar)	Test-negative case control (sex, 10-year age group, nationality, and calendar week of PCR test)	Dec 23, 2021 - Feb 2, 2022	All ages	Pfizer BioNTech - Comirnaty	Symptomatic disease	0-29	61·9 (49·9-71·1)	Pfizer BioNTech - Comirnaty	Symptomatic disease	7-20	53·6 (47·4 to 59·1)
						30-59	45·9 (33·8-55·8)			21-34	56·6 (50·8 to 61·7)
						60-89	36·3 (25·1-45·8)			35-48	46·2 (39·7 to 52·0)
						90-119	28·5 (18·0-37·8)			49-62	38·0 (28·1 to 46·5)
						120-149	10·6 (-2·3-21·9)			63-76	43·7 (32·9 to 52·7)
						150-179	14·3 (6·2-21·8)			≥77	37·6 (28·8 to 45·4)
						180-209	9·6 (2·4-16·3)				
						210-239	-7·5 (-15·3 to -0·2)				
						240-269	1·5 (-6·2-8.7)				
						270-299	-17·7 (-25·6 to -10·3)				
						300-329	-0·3 (-10·2-8·6)				
						≥330	16·5 (3·1-28·1)				
					Severe disease	0-179	73·7 (46·8-87·0)		Severe disease	1-41	90·6 (77·8 to 96·0)
						≥180	80·7 (71·3-87·0)			≥42	90·8 (81·5 to 95·5)
				Moderna - mRNA-1273	Symptomatic disease	0-89	44·8 (16·0-63·8)	Moderna - mRNA-1273	Symptomatic disease	7-20	53·1 (40·7 to 62·8)
						90-179	20·8 (13·7-27·4)			21-34	54·6 (41·1 to 65·0)
						≥180	-9·3 (-16·3 to -2·8)			≥35	38·6 (19·4 to 53·1)
					Severe disease	0-179	76·9 (19·2-93·4)				
						≥180	64·0 (39·1-78·7)				
Florentino[5] (Brazil)	Test-negative case control (age, gender, calendar time, geographic region, socioeconomic status, comorbidities, pregnancy and post-partum status, ethnicity)	Jan 1, 2022 - Mar 8, 2022	12-17 years	Pfizer BioNTech - Comirnaty	Symptomatic disease	14-27	62·8 (60·9-64·7)				
						28-41	49·4 (4·4-51·3)				
						42-55	37·4 (35·3-39·3)				
						56-69	29·6 (27·5-31·7)				
						70-83	21·7 (19·2-24·1)				
						84-97	16·6 (13·7- 19·5)				
						98-153	13·9 (10·9-16·9)				
						14-27	78·3 (75·3-80·9)				
						28-41	70·8 (66·6-74·5)				
						42-55	57·8 (50·8-63·8)				
						56-69	41·2 (28·8-51·4)				
						70-83	32·8 (13·9-47·6)				
						84-97	24·7 (-4·0-45·5)				
						98-153	31.3 (4·8-50·5)				
						14-27	75.4 (57·3-85·9)				

					Severe disease	28-41	82.1 (70·7-89·1)				
						42-55	82.8 (74·5-88·5)				
						56-69	81.2 (73·4-86·7)				
						70-83	83.0 (75·1-88·4)				
						84-97	89.8 (82·1-94·2)				
						98-153	84.9 (75·2-90·8)				
Fowlkes[6] (USA)	Prospective cohort (site, sociodemographic characteristics, comorbidities, influenza vaccination history, SARS-CoV-2 infection and vaccine knowledge, attitudes, and practices)	Jul 25, 2021 - Feb 12, 2022	12-15 years	Pfizer BioNTech - Comirnaty	Documented infection	14-149	59 (22-79)				
						150-202	62 (-28-89)				
Gray[7] (South Africa)	Test-negative case-control (age, sex, number of documented risk factors, surveillance week, period of prior infection, geographic region)	Nov 8, 2021 - Dec 17, 2021	Healthcare workers	Janssen - Ad26.COV2.S				Janssen - Ad26.COV2.S	Severe disease	14-27	84 (67-92)
										30-60	85 (54-95)
Hansen[8] (Denmark)	Retrospective cohort (age, sex, comorbidities, and region of residency)	Dec 28, 2021 - Feb 15, 2022	≥12	Pfizer BioNTech - Comirnaty	Documented infection	14-30	37·0 (35·6-38·3)	Pfizer BioNTech - Comirnaty	Documented infection	14-30	47·9 (47·4-48·3)
						31-60	27·4 (26·3-28·4)			31-60	41·0 (40·5-41·5)
						61-90	26·6 (25·3-27·9)			61-90	41·0 (40·3-41·7)
						91-120	27·4 (26·2-28·5)			91-120	38·6 (37·7-39·5)
						120-210	9·8 (9·2-10·4)			120-140	40·5 (38·9-42·2)
					Severe disease	14-30	50·5 (33·9-63·0)		Severe disease	14-30	88·8 (87·3-90·1)
						31-60	48·5 (36·6-58·2)			31-60	88·5 (87·4-89·6)
						61-90	42·6 (26·9-54·9)			61-90	84·9 (83·1-86·5)
						91-120	47·2 (33·7-57·9)			91-120	79·0 (76·5-81·3)
						120-210	51·6 (47·2-55·6)			120-140	66·2 (61·1-70·7)
				Moderna - mRNA-1273	Documented infection	14-30	37·9 (34·4-41·2)	Moderna - mRNA-1273	Documented infection	14-30	47·7 (47·0-48·3)
						31-60	27·1 (24·5-29·6)			31-60	45·5 (44·9-46·2)
						61-90	26·8 (23·8-29·6)			61-90	43·5 (42·2-44·7)
						91-120	23·3 (21·1-25·5)			91-120	36·9 (34·8-38·9)

						120-210	13·2 (12·3-14·2)			120-126	37·9 (33·4-42·0)
									Severe disease	14-30	90·2 (87·3-92·5)
										31-60	87·7 (85·3-89·7)
										61-90	87·8 (84·5-90·4)
										91-120	83·6 (77·7-88·0)
										120-126	77·3 (63·1-86·1)
Klein[9] (USA)	Test-negative case-control (age, geographic region, calendar time, local virus circulation in the community, and weighted for inverse propensity to be vaccinated or unvaccinated)	Dec 16, 2021 - Jan 9, 2022	12-15 years	Pfizer BioNTech - Comirnaty	Symptomatic disease	14-149	45 (30-57)				
						150-241	-2 (-25-17)				
			16-17 years			14-149	34 (8-53)				
						150-241	-3 (-30-18)				
Powell[10] (UK)	Test-negative case control (age, sex, index of multiple deprivation, ethnic group, geographic region, calendar week, clinical risk group, clinically extremely vulnerable, previous infection)	Sep 13, 2021 - Jan 12, 2022	16-17 years	Pfizer BioNTech - Comirnaty	Symptomatic disease	14-34	71·3 (69·3-73·1)				
						35-69	49·5 (45·7-53·0)				
						≥70	22·6 (14·5-29·9)				
Price[11] (United States)	Test-negative case control (U.S. Census region, calendar time of admission (biweekly intervals), age, sex, and race and ethnic group)	Dec 19, 2021 - Feb 17, 2022	12-18 years	Pfizer BioNTech - Comirnaty	Severe disease	14-160	43 (-1·0- 68·0)				
						161-314	38 (-3·0- 62·0)				
Šmíd[12] (Czech Republic)	Retrospective cohort (age group, sex and prior infection)	Dec 7,2021 - Feb 13, 2022	≥5 years	Pfizer BioNTech - Comirnaty	Documented infection	14-74	49 (48-50)	Pfizer BioNTech - Comirnaty	Documented infection	14-74	58 (58-59)
						75-135	27 (25-29)			75-243	24 (22-26)
						>135	11 (10-12)				
					Severe disease	14-74	46 (28-60)		Severe disease	14-74	86 (84-89)
						75-135	-10 (-51-19)			75-243	79 (74-82)
						>135	34 (24-42)				

				Moderna - mRNA-1273	Documented infection	14-74	48 (44-52)	Moderna - mRNA-1273	Documented infection	14-74	61 (60-62)
						75-135	41 (36-46)			75-243	33 (29-38)
						>135	20 (17-22)				
					Severe disease	14-74	51 (-20-80)		Severe disease	14-74	89 (84-93)
						75-135	39 (-92-81)			75-243	84 (72-91)
						>135	31 (9-49)				
				Janssen – Ad26.COV2.S	Documented infection	14-74	47 (45-49)				
						75-135	37 (35-40)				
						135+	35 (33-38)				
					Severe disease	14-74	28 (-22-57)				
						75-135	40 (-8-66)				
						>135	38 (8-58)				
				AstraZeneca - Vaxzevria	Documented infection	75-135	51 (23-69)				
						>135	5 (1-9)				
					Severe disease	75-135	-139 (-861-41)				
						>135	13 (-8-30)				
Ranzani[13] (Brazil)	Test-negative case control (age, comorbidities, race, prior symptomatic illness)	Sep 6, 2021 - Mar 10, 2022	≥18 years	Sinovac-CoronaVac	Symptomatic disease	14-59	26·9 (25·1-28·6)	Sinovac-CoronaVac	Symptomatic disease	8-59	15·0 (12·0-18·0)
						60-179	5·0 (4·2-5·9)			60-171	0·4 (-2·2-2·9)
						180-396	8·1 (7·0-9·1)		Severe disease	8-59	71·3 (60·3-79·2)
					Severe disease	14-59	49·9 (30·7-63·7)			60-171	65·4 (61·5-68·8)
						60-179	62·6 (58·5-66·3)	Pfizer BioNTech - Comirnaty	Symptomatic disease	8-59	56·8 (56·3-57·4)
						180-396	57·0 (53·5-60·2)			60-171	34·9 (34·3-35·6)
									Severe disease	8-59	85·5 (83·8-87·0)
										60-171	86·1 (85·0-87·1)
Stowe[14] (UK)	Test-negative case control (age, sex, index of multiple deprivation, ethnic group, care home residence status, geographic region, calendar time, health and social care worker status, clinical risk group, clinically extremely vulnerable, severely immunocompromised, and previously testing positive)	Nov 01, 2021 - Jan 01, 2022	18-64 years	Pfizer BioNTech - Comirnaty	Severe disease	14-174	73·8 (62·5-81·7)	Pfizer BioNTech - Comirnaty	Severe disease	7-13	85·2 (47·1-95·8)
						175-373	65·1 (51·3-74·9)			14-34	79·7 (66·3-87·7)
						14-174	87·6 (79·4-92·5)			35-69	86·6 (81·3-90·4)
						175-290	65·4 (56·6-72·5)			70-178	79·3 (71·3-85·0)
										105-178	66·0 (44·5-79·2)
								Moderna - mRNA-1273		14-34	94·3 (85·0-97·8)
										35-69	89·8 (77·9-95·3)
			≥65 years					Pfizer BioNTech - Comirnaty		7-13	86·4 (69·1-94·0)
										14-34	90·0 (85·4-93·2)
										35-69	88·4 (85·7-90·6)
										70-185	88·4 (86·2-90·2)
										105-185	85·2 (82·1-87·7)
								Moderna - mRNA-1273		7-13	92·9 (50·2-99·0)
										14-34	92·9 (83·0-97·1)
										35-69	90·9 (84·8-94·5)
										70-185	97·3 (90·8-99·2)

			18-64 years	AstraZeneca - Vaxzevria		14-174	59·0 (31·9-75·3)	Pfizer BioNTech - Comirnaty		7-13	90·2 (78·1-95·6)
						175-373	53·0 (41·7-62·0)			14-34	88·9 (83·8-92·4)
						14-174	71·2 (50·0-83·4)			35-69	83·9 (79·1-87·5)
						175-290	53·1 (43·4-61·2)			70-178	82·2 (76·3-86·7)
										105-178	69·0 (50·3-80·7)
								Moderna - mRNA-1273		7-13	97·2 (86·1-99·4)
										14-34	93·0 (86·4-96·4)
										35-69	89·2 (87·1-91·0)
			≥65 years					Pfizer BioNTech - Comirnaty		7-13	85·4 (73·4-92·0)
										14-34	91·3 (88·5-93·5)
										35-69	89·2 (87·1-91·0)
										70-178	87·6 (85·2-89·6)
										105-178	86·1 (82·5-88·9)
								Moderna - mRNA-1273		14-34	92·9 (87.7-95·9)
										35-69	92·7 (89·1-95·2)
										70-185	91·8 (85·9-95·3)
Tartof[15] (USA)†	Test-negative case control (age, sex, race/ethnicity, body mass index, comorbidities, prior infection)	Dec 1, 2021 - Jan 11, 2022	≥18 years	Pfizer BioNTech - Comirnaty	Symptomatic disease	7-89	64 (51-73)	Pfizer BioNTech - Comirnaty	Symptomatic disease	14-89	77 (72−81)
						90-179	47 (34-57)			≥ 90	53 (36−66)
						180-269	51 (43-59)				
						≥270	31 (16-43)				
					Severe disease	7-89	68 (48−80)		Severe disease	14-89	85 (80−89)
						90-179	68 (53−78)			≥ 90	55 (28−71)
						180-269	72 (63-79)				
						≥270	41 (21−55)				
Tseng[16] (USA)	Test-negative case control (age group, sex, race/ethnicity, comorbidities, frailty index, prior infection, number of healthcare encounters, specimen type, medical center area)	Dec 6, 2021 - Dec 31 2021	≥18 years	Moderna - mRNA-1273	Documented infection	14-90 days	44·0 (35·1-51·6)	Moderna - mRNA-1273	Documented infection	14-60	72·1 (70·2-73·9)
						91-180 days	23·5 (16·4-30·0)			>60	51·2 (44·2-57·3)
						181-270 days	13·8 (10·2-17·3)				
						>270 days	5·9 (0·4-11·0)				
UKHSA/ Andrews[17,18] (UK)‡	Test-negative case control (age group, sex, index of multiple deprivations (quintile), ethnic	Nov 27, 2021 - Jan 23, 2022.	≥18 years	Pfizer BioNTech - Comirnaty	Symptomatic disease	14-34	65·8 (64·4-67·2)	Pfizer BioNTech - Comirnaty	Symptomatic disease	14-34	67·6 (67·0-68·2)
						35-69	49·1 (47·7-50·6)			35-69	55·9 (55·1-56·6)
						70-104	31·0 (29·6-32·3)			70-104	46·2 (45·2-47·1)
						105-139	16·5 (15·3-17·6)			105-139	39·5 (36·0-42·8)
						140-174	13·3 (12·0-14·7)				
						≥175	9·4 (7·8-11·1)				

	group, geographic region, period (day of test), health and social care worker status, clinical risk group status, clinically extremely vulnerable, and previously testing positive)							Moderna - mRNA-1273	Symptomatic disease	14-34	73·9 (73·2-74·5)
										35-69	65·4 (63·9-66·9)
										70-104	64·1 (49·7-74·4)
				AstraZeneca - Vaxzevria	Symptomatic disease	14-34	49·8 (40·7-57·5)	Pfizer BioNTech - Comirnaty	Symptomatic disease	14-34	63·2 (62·6-63·8)
						35-69	35·7 (27·7-42·8)			35-69	54·0 (53·3-54·8)
						70-104	30·4 (23·2-36·9)			70-104	39·3 (37·9-40·8)
						105-139	18·8 (14·6-22·9)			≥105	29·4 (19·5-38·2)
						140-174	6·1 (4·1-8·1)				
						≥175	-1·0 (-2·4-0·3)				
								Moderna - mRNA-1273	Symptomatic disease	14-34	70·7 (70·1-71·2)
										35-69	62·1 (61·1-63·1)
										70-104	38·9 (18·8-54·1)
				Moderna - mRNA-1273	Symptomatic disease	14-34	76 (72-79)	Moderna - mRNA-1273	Symptomatic disease	14-34	68 (66-70)
						35-69	54 (49-58)			35-69	57 (35-71)
						70-104	36 (33-39)				
						105-139	26 (24-28)	Pfizer BioNTech - Comirnaty	Symptomatic disease	14-34	66 (64-68)
						140-174	17 (14-20)			35-69	49 (29-64)
						≥175	13 (3-22)				
Veneti (Norway)[19]	Retrospective cohort (sex, country of birth, county of residence, crowding and underlying comorbidities associated with increased risk of severe COVID-19)	Aug 25, 2021 - Jan 16, 2022	16-17 years	Pfizer BioNTech - Comirnaty	Documented infection	7-34	53·1 (42·6-61·7)				
						35-62	45·7 (34·8-54·7)				
						63-91	23·3 (2·7-39·5)				

*See section S13 for definitions of symptomatic disease and severe disease for each study.

†Publication date is after cutoff date for literature search; study is included because it replaces and provides updated estimates from an earlier preprint that had originally been included in the analysis.

‡Study provides estimates for severe disease; however, these estimates are not included here since a later publication (Stowe *et al*) provides estimates for severe disease for the same population.

S5: Characteristics and results of studies excluded at Step 2 due to combining vaccines for VE estimates against Omicron*

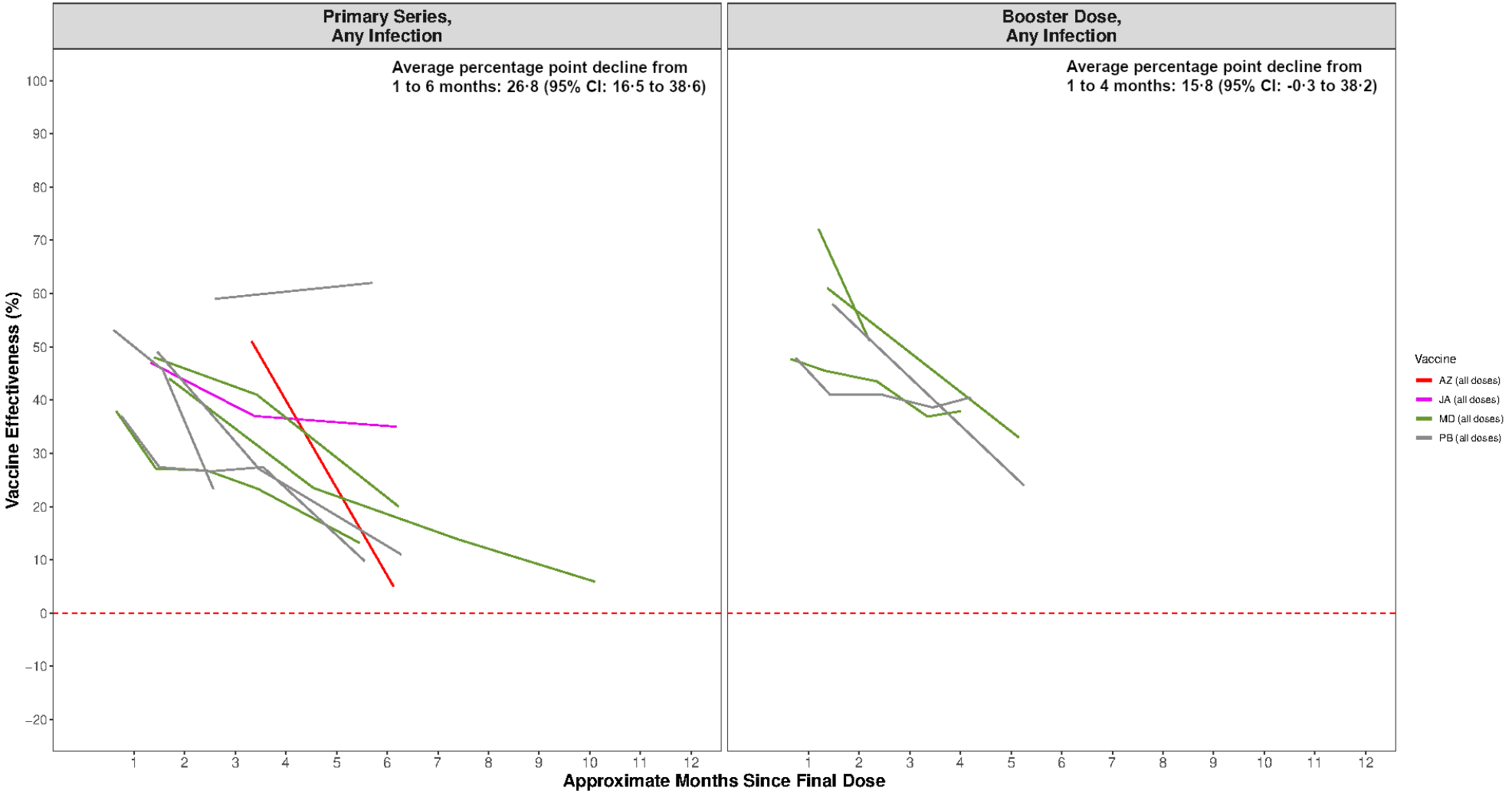
Study (Country)	Study Design (Variables controlled for in VE estimates)	Testing Period	Age group (years)	PRIMARY SERIES				BOOSTER			
				Vaccine	Disease Outcome	Time interval since final dose (days)	Vaccine effectiveness (95% CI)	Vaccine	Disease Outcome	Time interval since final dose (days)	Vaccine effectiveness (95% CI)
Buchan[20] (Canada)	Test negative case control (10-year age groups, sex, geographic region, number of SARS-CoV-2 PCR tests, prior infection, comorbidities, influenza vaccination, and neighborhood-level information on median household income, proportion of the working population employed as non-health essential workers, mean number of persons per dwelling, and proportion of the population who self-identify as a visible minority)	Dec 6, 2021 - Dec 26,2021	≥18 years	Pfizer BioNTech - Comirnaty or Moderna - mRNA-1273	Symptomatic disease	7-59	36 (24- 45)				
						60-119	12 (3-21)				
						120-179	15 (8-22)				
						180-239	1 (-8-10)				
						≥240	2 (-17-17)				
					Hospitalization	7-59	55 (-106- 90)				
						60-119	37 (-71-77)				
						120-179	75 (51- 87)				
						180-239	82 (62-91)				
						≥240	86 (-12-98)				
Ferdinands[21] (USA)	Test negative case control (calendar time, geographic area, age, local virus circulation, propensity to be vaccinated, other factors)	Dec 16, 2021 – Jan 22, 2022	≥18 years	Pfizer BioNTech - Comirnaty or Moderna - mRNA-1273	Emergency department and urgent care visits	<60	69 (62-75)	Pfizer BioNTech - Comirnaty or Moderna - mRNA-1273	Emergency department and urgent care visits	<60	87 (85-88)
						60-119	50 (45-55)			60-119	81 (79-82)
						120-149	48 (41-54)			120-149	66 (59-71)
						≥150	37 (34-40)			≥150	31 (-50-68)
					Hospitalization	<60	71 (51-83)		Hospitalization	<60	91 (88-93)
						60-119	65 (53-74)			60-119	88 (85-90)
						120-149	58 (38-71)			≥120	78 (67-85)
						≥150	54 (48-59)				
Gram[22] (Denmark)	Retrospective cohort (five-year age groups, sex, and geographical region)	Dec 21, 2021 - Jan 31, 2022	18-59 years	Pfizer BioNTech - Comirnaty or Moderna - mRNA-1273	Any infection	14-30	39·8 (38·4-41·2)	Pfizer BioNTech - Comirnaty or	Any infection	14-30	55·2 (54·7-55·6)
						31-60	31·6 (30·5-32·8)			31-60	50·8 (50·2-51·4)
						61-90	32·1 (30·6-33·5)			61-90	52·9 (52·0-53·7)
						91-120	31·4 (30·3-32·4)			91-120	51·1 (49·7-52·5)

						≥120	13·2 (12·5-13·9)	Moderna - mRNA-1273		≥120	49·9 (46·5-53·1)
					Hospitalization	14-30	62·4 (46·3-73·6)		Hospitalization	14-30	89·8 (87·9-91·3)
						31-60	51·4 (37·4-62·3)			31-60	87·4 (84·9-89·6)
						61-90	59·8 (43·7-71·3)			61-90	80·5 (75·4-84·5)
						91-120	61·4 (51·3-69·4)			91-120	72·8 (63·6-79·7)
						≥120	65·9 (62·0-69·4)			≥120	33·3 (0·9-55·1)
			≥60 years		Any infection	14-30	39·9 (26·4-50·9)		Any infection	14-30	57·6 (55·8-59·4)
						31-60	39·2 (27·8-48·8)			31-60	55·3 (53·6-56·9)
						61-90	26·4 (10·4-39·6)			61-90	58·3 (56·5-60·0)
						91-120	24·4 (11·9-35·1)			91-120	56·6 (54·4-58·7)
						≥120	4·7 (0·2-8·9)			≥120	52·8 (49·3-56·0)
									Hospitalization	14-30	94·4 (93·0-95·5)
										31-60	93·8 (92·7-94.7)
										61-90	91·7 (90·2-93.0)
										91-120	84·5 (81·6- 87·0)
										≥120	77·3 (70·9-82·3)
Grewal[23] (Canada)	Test-negative case-control (age, sex, geographic region, calendar time, prior infection, presence of outbreak at facility)	Dec 30, 2021 – Mar 2, 2022	≥60 years living in long-term care facilities	Pfizer BioNTech - Comirnaty or Moderna - mRNA-1273				Pfizer BioNTech - Comirnaty or Moderna - mRNA-1273	Any infection	<84	45 (38-52)
										≥84	42 (35-48)
									Symptomatic disease	<84	73 (63-81)
										≥84	66 (54-75)
									Hospitalization	<84	87 (80-91)
										≥84	92 (87-95)
Kim[24] (USA)	Test-negative case-control (age, site, illness onset week, and prior infection status)	Oct 1, 2021 - Feb 12, 2022	≥18 years	Pfizer BioNTech - Comirnaty or Moderna - mRNA-1273	Symptomatic disease	14-149	45 (14-46)				
						≥150	11 (-21-35)				
Lind[25] (USA)	Test-negative case-control (calendar time, age, sex, race/ethnicity, insurance, comorbidities, geographic region, prior infection, and number of non-emergent visits during the year before vaccine rollout)	Nov 1, 2021 - Jan 31, 2022	≥5 years	Pfizer BioNTech - Comirnaty or Moderna - mRNA-1273	Any infection	14-140	28·5 (20·0-36·2)	Pfizer BioNTech - Comirnaty or Moderna - mRNA-1273	Any infection	14-59	54 (48-60)
						≥150	15·3 (10·4-20.0)			60-89	47 (37-56)
										90-108	28 (9-43)
Thompson[26] (USA)	Test negative case control	Aug 26, 2021 - Dec 26, 2021	≥18 years	Pfizer BioNTech - Comirnaty	Emergency department or	14-179	52 (46-58)	Pfizer BioNTech - Comirnaty	Emergency department or	14+	94 (93-95)
						≥180	38 (32-43)				

	(age, geographic region, calendar time, local virus circulation)			or Moderna - mRNA-1273	urgent care visits			or Moderna - mRNA-1273	urgent care visits		
					Hospitalization	14-179	81 (65-90)		Hospitalization		90 (80-94)
						≥180	57 (39-70)				
Wang[27] (USA)	Test negative case control (age, sex, geographic region, prior infection, race/ethnicity, smoking status, comorbidities, week of testing)	Oct 1, 2021 - Jan 31, 2022	≥18 years	Pfizer BioNTech - Comirnaty or Moderna - mRNA-1273	Documented infection	14-179	26 (22-30)	Pfizer BioNTech - Comirnaty or Moderna - mRNA-1273	Documented infection	14-179	65 (63-66)
						180-378	7 (4-10)			180-378	50 (45-55)

*****Two additional studies excluded in step 2 not included in the table: 1) Cerqueira-Silva et al (this study provides estimates of a subset of a population in a second study already included in Table 1, reference #3) and 2) Patalon et al (study provided only estimates of relative VE and are not directly comparable to other included studies).

S6. Duration of COVID-19 primary series and first booster dose vaccine effectiveness (VE) against Omicron infection. Average percentage point decline in VE from 1 to 6 months post-vaccination from meta-regression (see S11 for methods).



Abbreviations: AZ, AstraZeneca; JA, Janssen; MD, Moderna; PB, Pfizer BioNTech

S7. Assessment and meta-regression on the duration of vaccine effectiveness against Omicron (main analysis)

Outcome	Primary series or booster	Number of vaccine-specific evaluations (number of studies)	Vaccines evaluated: Primary Series/Booster (number of studies)	Decrease in percentage points in VE from 1 to 4 months after final dose (95% CI), p value	Decrease in percentage points in VE from 1 to 6 months after final dose (95% CI), p value*
COVID-19 Severe Disease	Primary series	22 (12‡)	Pfizer BioNTech-Comirnaty (n=12) Moderna-mRNA-1273 (n=3) AstraZeneca-Vaxzevria (n=5) Janssen-Ad26.COV2.S (n=1) Sinovac-CoronaVac (n=1)	-1·7 (-6·2 to 3·6) p=0·50	1·0 (-3·9 to 6·6) p=0·70
	Booster	29 (10‡)	Pfizer BioNTech-Comirnaty/Pfizer BioNTech-Comirnaty (n=9) Pfizer BioNTech-Comirnaty/Moderna-mRNA-1273 (n=4) Moderna-mRNA-1273/Moderna-mRNA-1273 (n=3) Moderna-mRNA-1273/Pfizer BioNTech-Comirnaty (n=1) AstraZeneca-Vaxzevria/Pfizer BioNTech-Comirnaty (n=5) AstraZeneca-Vaxzevria/Moderna-mRNA-1273 (n=4) Janssen-Ad26.COV2.S/Janssen-Ad26.COV2.S (n=1) Sinovac (CoronaVac)/Sinovac (CoronaVac) (n=1) Sinovac (CoronaVac)/Pfizer BioNTech (Comirnaty) (n=1)	5·3 (2·4 to 8·7) P=0·0002	8·2 (3·7 to 14·3) p=0·0002
COVID-19 Symptomatic Disease	Primary series	17 (10‡)	Pfizer BioNTech-Comirnaty (n=11) Moderna-mRNA-1273 (n=2) AstraZeneca-Vaxzevria (n=3) Sinovac-CoronaVac (n=1)	40·3 (32·4 to 49·0) p<0·0001	47·6 (36·6 to 60·2) p<0·0001
	Booster	17 (6‡)	Pfizer BioNTech-Comirnaty/Pfizer BioNTech-Comirnaty (n=5) Pfizer BioNTech-Comirnaty/Moderna-mRNA-1273 (n=2) Moderna-mRNA-1273/Moderna-mRNA-1273 (n=2) Moderna-mRNA-1273/Pfizer BioNTech-Comirnaty (n=1) AstraZeneca-Vaxzevria/Pfizer BioNTech-Comirnaty (n=3) AstraZeneca-Vaxzevria/Moderna-mRNA-1273 (n=2) Sinovac (CoronaVac)/Sinovac (CoronaVac) (n=1) Sinovac (CoronaVac)/Pfizer BioNTech (Comirnaty) (n=1)	24·3 (19·9 to 29·1) p<0·0001	28·5 (18·3 to 40·5) p<0·0001
SARS-CoV-2 Infection	Primary series	9 (5)	Pfizer BioNTech-Comirnaty (n=4) Moderna-mRNA-1273 (n=3) AstraZeneca-Vaxzevria (n=1) Janssen-Ad26.COV2.S (n=1)	19.1 (11.8 to 27.3) p=0·0002	26·8 (16·5 to 38·6) p=0·0001
	Booster	5 (3)	Pfizer BioNTech-Comirnaty/Pfizer BioNTech-Comirnaty (n=2) Moderna-mRNA-1273/Moderna-mRNA-1273 (n=3)	15·8 (-0·3 to 38·2) P=0·0537	23·1 (0·4 to 57·7) P=0·0471

*From meta-regression modeling log(1-VE) regressed on log(months after final dose), Appendix S11; decrease for booster doses is projected out to 6 months.

‡One study (Cerqueira-Silva et al) presents estimates separately from two different countries and is counted twice in the number of studies.

S8. Schematic of meta-regression results: average decline in COVID-19 vaccine effectiveness against severe and symptomatic disease*

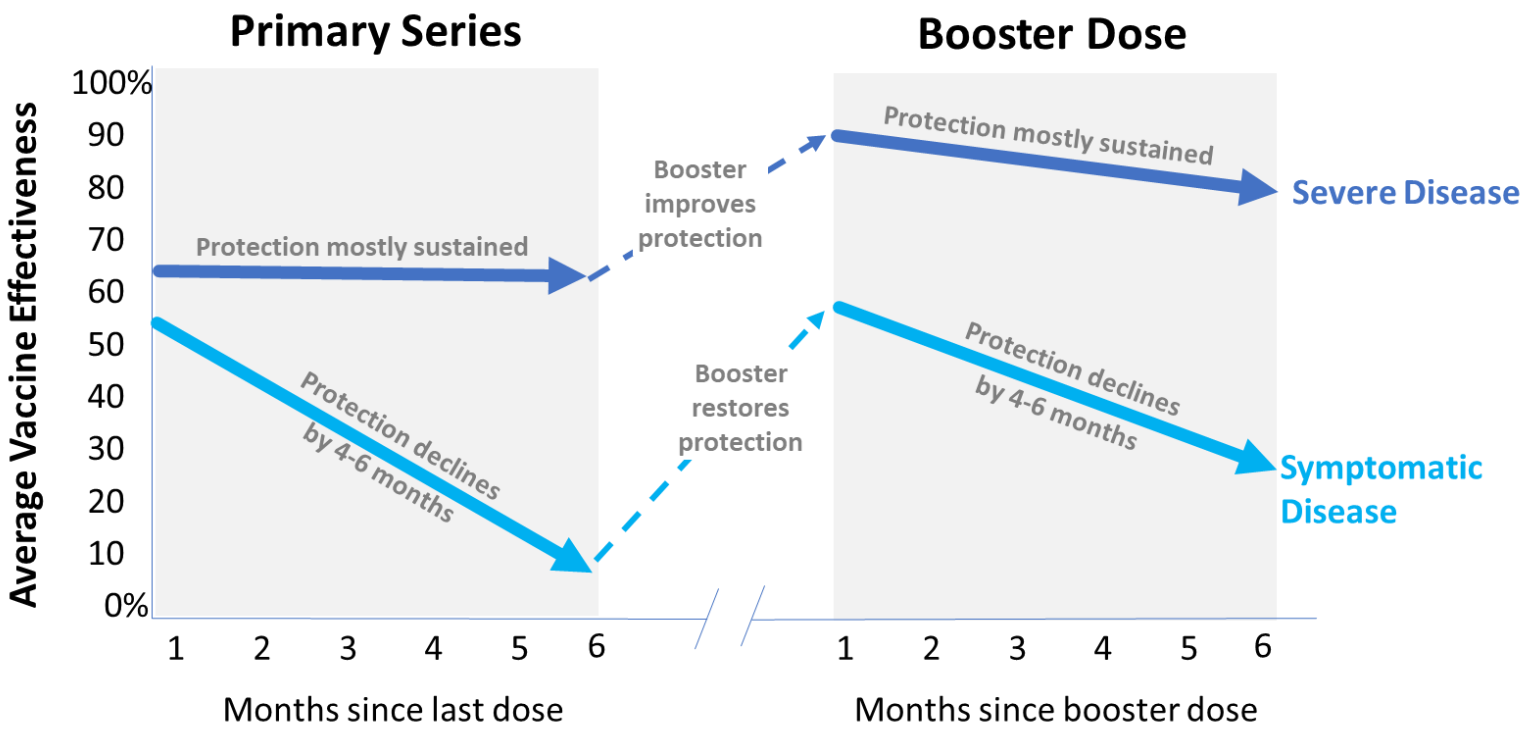


*Illustration of the average 6-month decline in vaccine effectiveness from meta-regression results shown in S7 across all studies and all included vaccines.

S9. PICO questions

Participants/population: Male and female participants of all age groups

Intervention: Any vaccine against COVID-19 that has received Emergency Use Listing by the World Health Organization, including only full dosing schedules

Comparators/control: Unvaccinated persons. For booster dose vaccine effectiveness, the comparator may also be persons having completed COVID-19 primary series vaccination. Partially vaccinated persons are excluded as comparators.

Outcomes: 1. Effectiveness of COVID-19 vaccines for the following outcomes: any SARS-CoV2 infection (confirmed by PCR, genomic sequencing or rapid antigen testing); any symptomatic COVID-19 disease (confirmed by PCR or genomic sequencing); severe COVID-19 disease (confirmed by PCR, genomic sequencing or rapid antigen testing), defined as hospitalisation, ICU admission, intubation, and death due to COVID-19 (confirmed by PCR, genomic sequencing or rapid antigen testing).

S10. Methods for figure in main text

Studies that met the inclusion criteria were included in the figure of the duration of VE. A study could contribute data for any or all of the 3 outcomes (i.e., infection, symptomatic disease and severe disease), one or both age groups (i.e., all ages and older), and for multiple vaccines. In order to standardize the way in which the time period was defined for all studies, we set all time intervals as time since the final dose in days. For final time intervals that were open-ended (e.g. ≥ 120 days), we determined the end of the interval by calculating the maximum duration of time a participant could have been fully vaccinated in the study given the date of introduction of vaccine in the study country and the data cut-off date for testing/analysis; we then used the median time point of the interval to plot the estimate for this final period. We only present time intervals from the time we considered someone as fully vaccinated and having had time for immunologic protection to develop (i.e., $\geq$7 days from the final dose for Pfizer/BioNTech-Comirnaty, and $\geq$14 days from the final dose for AstraZeneca-Vaxzevria, Moderna-mRNA-1273, Janssen-Ad26.COV2.S, and Sinovac-CoronaVac as determined in vaccine efficacy trials[28-32]), with some exceptions for early time intervals that includes days 0-7 or 0-14 post vaccination but for which the median time point for the interval extends beyond 7 or 14 days.

S11: Additional methods for meta-regression

The average (mean) change in VE over time was estimated using a Gaussian linear mixed effects model for the repeated measures within each study-vaccine group (PROC MIXED; SAS 9.4). This meta-regression regressed the log of 1-VE on log of months since vaccination (to maintain a linear relationship between VE and time in months). Random intercepts and slopes were included. Standard errors (SEs) of the ln(1-VE)s, derived from the 95% confidence intervals for the VEs reported by each study, were squared to produce estimates of residual variances for inverse weighting in the linear mixed effects model.

The SAS code used for the regression is given below. Study_vaccine_group refers to the multiple VE estimates over time for one vaccine in one study, represented by a line in the plots in Figure.

```
PROC MIXED cl method=reml;
CLASS  study_vaccine_group;
MODEL LN_RR = ln_5months_rescaled / SOLUTION cl;
RANDOM int ln_5months_rescaled / subject=study_vaccine_group SOLUTION;
WEIGHT Inverse_SEsqrd;
REPEATED /subject=study_vaccine_group;
```

The addition of a quadratic term (i.e., square of ln_5months_rescaled) to the MODEL statement was also evaluated for all analyses and was retained in the model when statistically significant ($p<.05$). It was statistically significant for three models: primary series severe disease, primary series symptomatic disease and booster symptomatic disease.

Confidence intervals for VE estimates of 100% were undefined in manuscripts, so SEs were approximated using formulas for SEs of the odds ratio and relative rate as relevant and adding 0.5 cases to each group to address the issue of dividing by zero:

	Vaccinated	Unvaccinated
Outcome	a	b
No Outcome	c	d

$$\widehat{se}_{logOR} = \sqrt{\frac{1}{(a+½)} + \frac{1}{(b+½)} + \frac{1}{(c+½)} + \frac{1}{(d+½)}}$$

$$\widehat{se}_{logRR} = \sqrt{\frac{c}{(a+½)(a+c+1)} + \frac{d}{(b+½)(b+d+1)}}$$

Because ln(1-VE) is not defined for estimates of VE=100%, the formulas above were also used to produce an estimate of VE <100%.

We obtained the 5-month change in predicted VE from 1 to 6 months of follow-up. Each predicted value of VE is 1-exp(predicted log relative rate). We did not directly calculate this change from the regression coefficients in the linear mixed model. A 1 unit change in the beta coefficient for Ln(time) was made to represent a period of 5 months. Each month's time value was calculated as ln[1 + (Months-1) * (exp(1) – exp(0))/5]:

	5-month change		3-month change	
Month	**Rescaled* Month**	**Ln(rescaled month)****	**Rescaled Month**	**Ln(rescaled month)****
1	1	**0**	1	**0**
2	1.343656366	**0.295395**	1.572761	**0.4528**
3	1.687312731	**0.523137**	2.145521	**0.7634**
4	2.030969097	**0.708513**	2.718282	**1**
5	2.374625463	**0.86484**	3.291042	**1.1912**
6	2.718281828	**1**	3.863803	**1.3517**

=1+(month-1)((EXP(1)-EXP(0))/5) = increments of 0.343536

**used in model

The Ln of the rescaled time values have a linear relationship with Ln(RR). The VE at Month 1 = 1 - exp(intercept), and the VE at Month 6 = 1 -exp(intercept + beta coeff). The 5-month change in VE from Month 1 to 6 = VE at month 1 - VE at month 6 = exp(beta coeff) when using ln(rescaled month). The 95% lower and upper confidence bounds for the 5-month change in VE = 1-exp(upper limit of beta coeff) and 1-exp(lower limit of beta coeff). Similar logic was applied for the 3-month change analyses (i.e., month 1 to 4 after vaccination). The addition of the quadratic term to relevant models where that improved fit facilitated modeling non-linear relationships between Ln(RR) and Ln(rescaled month).

Models were run for each outcome and dosing (i.e., primary series vs booster) combination.

S12. Risk of bias assessments

Using the ROBINS-I tool for observational studies: www.riskofbias.com

Study (by first author's last name)	Bias due to confounding	Bias in selection of participants into the study	Bias in classification of interventions	Bias due to departures from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result	Overall Bias
Baum et al	Moderate	Low	Low	Low	Low	Moderate	Moderate	Moderate
Buchan et al	Moderate	Low	Low	Low	Low	Low	Moderate	Moderate
Cerqueria Silva et al	Moderate	Low	Low	Low	Low	Moderate	Moderate	Moderate
Chemaitelly et al	Serious	Low	Low	Low	Low	Low	Moderate	Serious
Florentino et al	Moderate	Low	Low	Low	Low	Moderate	Moderate	Moderate
Fowlkes et al	Moderate	Low	Low	Low	Low	Low	Low	Moderate
Gray et al	Moderate	Low	Moderate	Low	Low	Low	Low	Moderate
Holm Hansen et al	Moderate	Low	Low	Low	Low	Moderate	Moderate	Moderate
Klein et al	Moderate	Low	Low	Low	Low	Low	Low	Moderate
Powell et al	Moderate	Low	Low	Low	Low	Low	Moderate	Moderate
Price et al	Moderate	Low	Low	Low	Low	Low	Low	Moderate
Ranzani et al	Moderate	Low	Low	Low	Low	Moderate	Moderate	Moderate
Šmíd et al	Serious	Low	Low	Low	Moderate	Moderate	Moderate	Serious
Stowe et al	Moderate	Low	Low	Low	Low	Low	Moderate	Moderate
Tartof et al	Serious	Low	Low	Low	Low	Low	Low	Serious
Tseng et al	Moderate	Low	Low	Low	Low	Low	Moderate	Moderate
Veneti et al	Moderate	Low	Low	Low	Low	Moderate	Moderate	Moderate
UKHSA/Andrews et al	Moderate	Low	Low	Low	Low	Low	Moderate	Moderate

S13. Study definitions for symptomatic and severe disease

Symptomatic disease

Study	Symptomatic disease definition
Buchan et al	At least one relevant covid-19 symptom (based on self-report or observation, such as measured temperature), at the time of testing.
Cerqueira-Silva et al	COVID-19-symptomatic infection
Chemaitelly et al.	Symptomatic disease was defined as a PCR- positive swab collected during the Omicron wave because of clinical suspicion due to the presence of symptoms compatible with a respiratory tract infection
Florentino et al.	COVID-19-symptomatic infection
Klein et al.	Emergency Department and Urgent Care encounters with COVID-19-like-illness diagnosis who received a positive SARS-CoV-2 molecular test (primary by RT-PCR) during the 14 days before through 72 hours after the encounter. COVID-19-like-illness was defined using ICD-9 and ICD-10, and four categories of codes were considered: 1) acute respiratory illness, including COVID-19, respiratory failure, viral or bacterial pneumonia, asthma exacerbation, influenza, and viral illness not otherwise specified; 2) non-respiratory COVID-19–like illness diagnoses including cause-unspecified gastroenteritis, thrombosis, and acute myocarditis; 3) respiratory signs and symptoms consistent with COVID-19–like illness, including hemoptysis, cough, dyspnea, painful respiration, or hypoxemia; and 4) signs and symptoms of acute febrile illness. One code in any of the four categories was sufficient for inclusion.
Powell et al.	Symptomatic disease: Cases who reported symptoms and gave a symptom onset date within the 10 days before a positive PCR test, tested in Pillar 2 (swab testing for the virus in the wider population, through commercial partnerships, either processed in a lab or more rapidly via LFD tests)
Ranzani et al.	COVID-19-symptomatic infection
Tartof et al.	Emergency department admission (without subsequent hospital admission) with ≥1 COVID-19 symptom and a positive Kaiser Permanente Southern California (KPSC) laboratory-confirmed SARS-CoV-2 PCR test from a sample collected within 14 days prior to the initial admission date through 3 days after the admission
UKHSA/ Andrews et al.	Positive PCR or LFT among individuals tested in Pillar 2 (community testing) who reported symptoms consistent with COVID-19 (high temperature, new continuous cough, or loss or change in sense of smell or taste)

Severe disease

Study	Severe disease definition
Baum et al.	Any inpatient encounter with a primary diagnosis of Covid-19, acute respiratory tract infection, or severe complications of lower respiratory tract infections
Buchan et al.	Hospitalization or death (specific guidance is provided to report only hospitalizations due to COVID, i.e. persons who received treatment for COVID-19)
Cerqueira-Silva et al.	COVID-19 hospital admission or death. COVID-19 hospitalization was defined as a positive specimen being collected up to 14 days before to three days after the hospital admission; cases of COVID-19 death were defined by death occurring within 28 days of the sample collection date.
Chemaitelly et al.	WHO definitions of severe, critical and death from COVID-19:

	Severe disease definition: SARS-CoV-2 infected person with “oxygen saturation of <90% on room air, and/or respiratory rate of >30 breaths/minute in adults and children >5 years old (or ≥60 breaths/minute in children <2 months old or ≥50 breaths/minute in children 2-11 months old or ≥40 breaths/minute in children 1–5 years old), and/or signs of severe respiratory distress (accessory muscle use and inability to complete full sentences, and, in children, very severe chest wall indrawing, grunting, central cyanosis, or presence of any other general danger signs)". Critical disease definition: SARS-CoV-2 infected person with “acute respiratory distress syndrome, sepsis, septic shock, or other conditions that would normally require the provision of life sustaining therapies such as mechanical ventilation (invasive or non-invasive) or vasopressor therapy” COVID-19 death definition: death resulting from a clinically compatible illness, in a probable or confirmed COVID-19 case, unless there is a clear alternative cause of death that cannot be related to COVID-19 disease (e.g. trauma). There should be no period of complete recovery from COVID-19 between illness and death. A death due to COVID-19 may not be attributed to another disease (e.g. cancer) and should be counted independently of preexisting conditions that are suspected of triggering a severe course of COVID-19.
Florentino et al.	Hospitalizations reported through the SIVEP-Gripe system which reports cases of severe acute respiratory infection, which can be defined as an acute respiratory infection with onset, within the past 10 days, of fever and cough, and typically requires hospitalization.
Gray et al.	COVID-19-related hospital admission
Hansen et al.	Any hospital admission lasting at least 12 hours and occurring no earlier than two days before, and no later than 14 days after, a positive PCR test
Price et al.	Hospitalization with COVID 19 as primary reason for admission or with a clinical syndrome consistent with acute COVID-19: one or more fever, cough, shortness of breath, loss of taste, loss of smell, gastrointestinal symptoms, receipt of respiratory support, or new pulmonary findings on chest imaging.
Ranzani et al.	Hospitalizations reported through the SIVEP-Gripe system which reports cases of severe acute respiratory infection, which can be defined as an acute respiratory infection with onset, within the past 10 d, of fever and cough, and typically requires hospitalization.
Šmíd et al.	Hospitalization: Hospital admission of a person, who tested positive on a PCR test, within two weeks after the confirmed infection or earlier
Stowe et al.	Hospitalization for at least 2 days stay and ARI code in primary diagnostic field.
Tartof et al.	Hospitalization: Hospital admission with ≥1 COVID-19 symptom and a positive Kaiser Permanente Southern California (KPSC) laboratory-confirmed SARS-CoV-2 PCR test from a sample collected within 14 days prior to the initial admission date through 3 days after the admission

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