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Supplementary appendix

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Supplement to: Wu N, Joyal-Desmarais K, Ribeiro PAB, et al. Long-term effectiveness of COVID-19 vaccines against infections, hospitalisations, and mortality in adults: findings from a rapid living systematic evidence synthesis and meta-analysis up to December, 2022. *Lancet Respir Med* 2023; published online Feb 10. https://doi.org/10.1016/S2213-2600(23)00015-2.

– Supplemental File –

Long-term effectiveness of COVID-19 vaccines against infections, hospitalizations, and mortality in adults: findings from a rapid living systematic evidence synthesis and meta-analysis up to December 2022

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Section 1: PRISMA Checklist.

eTable 1. Completed PRISMA Checklist.

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	1*
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	4-5*
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	6*
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	6*
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	7-8* & S9
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	7-8*
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	S7
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	7-8*& S9
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	8-9*& S10
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	9-11* & S10-15
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	7* & S8-10
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	9*
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	9-11* & S15

Section and Topic	Item #	Checklist item	Location where item is reported
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	9-10*
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	S10-18
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	S10-18
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	8-11* & S10-18
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	10-11* & S18-20
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	S18-20
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	S15
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	N/A
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	11-12* & S21
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	11* & S34
Study characteristics	17	Cite each included study and present its characteristics.	22* S34
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Supplement
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	25-28* & S40-62
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	11-13*
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	11-14* & S40-84
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	13& S44-84
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	S55-84
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis	Supplement

Section and Topic	Item #	Checklist item	Location where item is reported
		assessed.	
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	N/A
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	14*
	23b	Discuss any limitations of the evidence included in the review.	14-16*
	23c	Discuss any limitations of the review processes used.	16-17*
	23d	Discuss implications of the results for practice, policy, and future research.	17-19*
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	7*
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	7*
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	7*
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	29*
Competing interests	26	Declare any competing interests of review authors.	29*
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	29*

Notes. NA=not applicable; S#= page number in the supplement; #*= page number in main paper.

Section 2. eMethods

2.01. Search Databases and Syntaxes

We searched the National Institutes of Health's (NIH) iSearch COVID-19 Portfolio, which is a comprehensive, expert-curated database covering publications and preprints related to COVID-19, as well as EMBASE via OVID.

eTable 2. Search Syntaxes Across Databases.

NIH iSEARCH COVID
(mRNA OR messenger OR "RNA messenger" OR vector* OR Pfizer OR Moderna OR Janssen OR AstraZeneca OR Oxford OR BioNTech OR BNT162b2 OR mRNA-1273 OR AZD1222 OR ChAdOx1 OR Ad26.COV2.S OR JNJ-78436735 OR COVISHIELD OR booster OR "third dose") AND vaccin* AND (effectiveness OR efficacy) **Limits:** Date: January 01, 2021 to November 3, 2022 **Fields:** Title and Abstract and Full-text
EMBASE Syntax
(mRNA or messenger or "RNA messenger" or vector* or Pfizer or Moderna or Janssen or AstraZeneca or Oxford or BioNTech).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]
("BNT162b2" or "mRNA-1273" or "AZD1222" or "ChAdOx1" or "Ad26.COV2.S" or "JNJ-78436735" or COVISHIELD).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]
(booster or "third dose").mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]
1 or 2 or 3
vaccination/ or Vaccin*.mp. or vaccine/
(effectiveness or efficacy).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]
4 and 5 and 6
limit 7 to dd=20210101-20221103
limit 8 to covid-19

2.02. Operationalisation of Inclusion and Exclusion Criteria

All studies that met the following criteria were included:

1. Studies that included results for populations of individuals exclusively more than 18 years of age, and studies that also included results for minors less than 18 years of age (in addition to adults) but did not stratify results into different age groups (e.g., < 12 years, > 12 years)
2. Studies that included participants who received a full primary series of any Canadian-licensed COVID-19 vaccines (specifically, BNT162b2, mRNA-1273, ChAdOx1/AZD1222, or Ad26.COV2.S) or received an additional dose (a booster) specifically from a Canadian-licensed vaccine (BNT162b2, mRNA-1273, ChAdOx1/AZD1222, or Ad26.COV2.S) beyond a primary series of doses (this primary series could be of any brand of vaccine, and did not have to be Canadian-licensed COVID-19 vaccines)
3. Studies that reported vaccine efficacy or effectiveness estimates that compared people who were fully vaccinated with those who were unvaccinated (including placebo groups), or compared people who were fully vaccinated and received an additional dose (i.e., those who received a booster) with those who were unvaccinated (or received a placebo)
4. Studies that reported vaccine effectiveness for COVID-19 infections (asymptomatic infection and/or symptomatic illness), hospitalisations, and/or mortality
5. Studies that provided baseline data (i.e., ≤42 days since the primary dose or ≤28 days since the booster dose) and at least one follow-up measurement (i.e., ≥112 days since the primary dose or ≥84 days since a booster dose)
6. Randomised controlled trials (RCT) or studies with longitudinal data designs
7. Studies written in English or French

All studies that met any of the following criteria were excluded:

1. Studies that only included populations of individuals less than 18 years of age
2. Studies that only included people who were partially vaccinated (for studies that had data for fully and partially vaccinated individuals (compared to unvaccinated) the data for fully vaccinated individuals was retained and the partially vaccinated data was excluded)
3. Studies that reported only severe COVID-19 illness without stratifying results into hospitalisations and mortality (e.g., excluding studies that combined both outcomes)
4. Studies that did not have discrete time intervals since the last dose of vaccine, e.g., only reported calendar time
5. Studies that did not explicitly report vaccine efficacy or effectiveness data, e.g., those who only presented the data in a metric other than vaccine effectiveness or risk, hazard or odds ratios
6. Studies using a non-human animal sample
7. The following report types: abstracts, reviews, conference reports, study protocols, author responses, case reports, case series, and cross-sectional studies
8. Articles written in any language other than English or French

2.03. Procedure for Coding Baseline and Follow-Up Time Points

eTable 3. Coding Procedure for Classifying Time Points.

Coding categories used to classify baseline and follow-up time points.	
For the **primary series** of COVID-19 vaccines, time was defined in relation to days since the last dose of the vaccine (i.e., days since completing the primary series, not days since effective date or full immunity). Classifications followed the designation below.	For COVID-19 vaccine **booster doses**, time was defined in relation to days since the last dose of the vaccine received (not since effective date or full immunity). Classifications followed the designation below.
Baseline 1: 0-13 days (since last dose) Baseline 2: 14-42 days FUP1: 112-139 days FUP2: 140-167 days FUP3: 168-195 days FUP4: 196-223 days FUP5: 224-251 days FUP6: 252-279 days FUP7: 280-307 days FUP8: 308-335 days FUP9: 336+ days	Baseline 1: 0-6 days (since last dose) Baseline 2: 7-28 days FUP1: 84-111 days FUP2: 112-139 days FUP3: 140-167 days FUP4: 168-195 days FUP5: 196-223 days FUP6: 224-251 days FUP7: 252-279 days FUP8: 280-307 days FUP9: 308+ days
When studies report time in more than one unit (days, weeks and months), we focus on extracting the more specific unit (i.e., prioritise days, then weeks, then months). All metrics are converted into days using specific conversion factors.	
When a study presents a single time point-estimate (e.g., day 120; at 20 weeks; at 6 months), we report that number as both the lower and upper limit. We will use the following conversions as needed: Months: 30.5x (for both lower/upper limits) Weeks: 7x (for both lower/upper limits)	Example: Code: Lower limit = 120; upper limit=120; Unit= Days *Conversion to days will be calculated separately
When we only have a lower limit for time, we anchor our extraction on the lower limit, and mark the upper limit as “N/A”. For example, "120+ days" is treated the same as "120 days to N/A". We will then apply the following conversion factors if needed: Months: 30.5x+1 Weeks: 7x+1 *Exception*: When the lower bound is a baseline period (e.g., 7 days +), this time point will not be extracted as it likely aggregates VE across the full sample, rather than presenting results at baseline.	Example: Code: Lower limit = 120; upper limit=N/A; Unit= Days *Conversion to days will be calculated separately
When we only have an upper limit for time (e.g. <2 months since the last dose of vaccine), we treat the lower limit as 0, and report the upper limit. We will then use the following conversion factors for the upper limit only: Months: 30.5y (e.g., 2 months = 61 days) Weeks: 7y (e.g., 2 weeks = 14 days)	Example: Lower limit = 0; upper limit= 2; Unit= Months *Conversion to days will be calculated separately
When studies state a range (e.g., "week 1-2") we extract the lower/upper limits as reported. We will then use the following conversion factors Months: 30.5x+1 for the lower limit; 30.5y for the upper limit (e.g., 2-3 months = 62-91.5 days) Weeks: 7x+1 for the lower limit; 7y for the upper limit (e.g., 2-3 weeks= 15-21 days)	Example: Code: Lower limit= 1, upper limit=2, Unit= Weeks. *Conversion to days will be calculated separately
If a time period is equally situated between 2 FUP periods (15 days overlap in FUP2 and 15 days overlap with FUP3), such that the midpoint is also between two categories, we pick the lower FUP category (FUP2). The rationale is that we assume there is attrition, so more data is concentrated in the 1st FUP. If reports a 181-210 day period. This overlaps equally between FUP3 and FUP4, and we would pick FUP3.	Example: Lower limit = 181; upper limit= 210; Unit= Days *FUP selection is set automatically in the codebook using formulae (i.e., whenever the median of the FUP range falls between 2 FUP periods, it will pick the lower category)

Notes. FUP = Follow-up time point.

2.04. Details of Meta-Analytic Procedure

Data were included for meta-analytic review when they met all the following criteria:

1. Reported percent vaccine effectiveness (VE), risk ratio (RR), odds risk (OR) or hazard ratio (HR) data, along with corresponding confidence intervals (CIs)
2. Provided the above with regards to: (a) cases; (b) hospitalisations; and/or (c) deaths due to COVID-19
3. Reported data for baseline (0-42 days since second dose of vaccine or 0-28 days since booster dose of vaccine) and for at least one follow-up time point (≥ 112 days since complete primary series of a vaccine or ≥ 84 days since an additional dose of the vaccine)

All estimates, and their corresponding CIs, were converted to risk ratios (RRs) when necessary. Conversions between percent VE and RRs used the following conventional equation: *VE = (1-RR)*100*. For the purpose of this review, ORs and HRs were assumed to be an equivalent metric to RRs (assuming equivalence between the metrics when using large sample sizes to study rare events such as COVID-19 infections, hospitalisations, and deaths). RRs were then log-transformed for use in meta-analytic models, and the CIs were used to derive a standard error for each effect size. The results of meta-analytic models were then converted back into a percent VE metric for presentation within our results.

Multilevel models were used to calculate pooled effects, as we anticipated meaningful heterogeneity across studies and group comparisons (e.g., follow-up time points). When data was available, subgroup analyses were computed to examine how patterns of findings varied according to:

1. Type of vaccine
    a) Overall (i.e., any vaccine)
    b) Any mRNA vaccines
        i) Moderna (mRNA-1273)
        ii) Pfizer-BioNTech (BNT162b2)
    c) Any adenovirus
        i) AstraZeneca/COVISHIELD (AZD1222/ChAdOx1)
        ii) Janssen (Johnson & Johnson: Ad26.COV2.S)
2. Variants of Concern (VOC):
    a) Any variant
    b) Delta
    c) Omicron

All analyses for the paper were computed using the *metafor* package in R (version 4.1.2). We used a multi-step procedure to determine which model to report according to the subgroups above.

(A) First, when multiple studies were available for a given subgroup (e.g., when examining the effects of any vaccine type on cases), we computed three-level meta-analytic models, nesting effect sizes within studies. These models used the Restricted Maximum Likelihood procedure to obtain estimates. All three-level meta-analytic models explicitly considered all time points for which we had data available. Time points (broken down according to the categories outlined in the preceding table) were entered as a moderator variable in each model. For the results reported in this manuscript, we always set the 2nd baseline period (e.g., 14-42 days for the primary vaccine schedule) as the comparison group. This allowed us to evaluate the effect of each time point relative to this baseline to establish whether a statistically significant decrease in VE had occurred by a given follow-up time period. The time point variable was treated as a categorical variable for this purpose in modelling. This was done for a few reasons. First, modelling the variable in this manner would allow us not to assume a particular form for the effect of time, allowing us to model a non-linear trend over time (indeed, VE does not vary in a monotonic manner over time; e.g., increasing between the first two baselines). Second, because authors report VE results in clusters (i.e., aggregate results over a range like 110-130 days) rather than report the effects of time in a continuous manner, and the exact range of these clusters differs across studies, assuming that the time variable reflects truly equal intervals may be an unrealistic assumption. Modelling the time variable as we do allowed us to avoid making this assumption. In our manuscript, we only report effects from these three-level meta-analytic models. Further, we only report results for time points for which 4 or more studies contributed data (in order to focus our report on results that have a higher chance of being reliable). Other time points, however, were nevertheless modelled, and their results are provided in this supplement.

As with traditional univariate models (e.g., a random effects model), three-level meta-analytic models will weight estimates used in pooling according to their level of uncertainty (their standard errors). However, three-level models extend the method used in random effects models by further accounting for the covariance structure between the observations. This process has been described in detail within texts on three-level models (e.g., see Konstantopoulos, 2011, below). A description can also be found within the metafor documentation (and is summarized at: https://www.metafor-project.org/doku.php/tips:weights_in_rma.mv_models).

(B) Second, when only a single study was available for a given subgroup, separate random-effects models were used to estimate VE at each time point, treating all cohorts as independent groups. These models were computed using the DerSimonian and Laird procedure. These models were not computed to draw any inferences, but rather for descriptive purposes only. Their results are only reported in the supplement and not within the main manuscript.

References for three-level meta-analytic models:

- Harrer, M., Cuijpers, P., Furukawa, T. A., & Ebert, D. D. (2021). Doing Meta-Analysis With R: A Hands-On Guide (1st ed.). Chapman & Hall/CRC Press.
- Konstantopoulos, S. (2011). Fixed effects and variance components estimation in three-level meta-analysis. *Research Synthesis Methods, 2*(1), 61-76. https://doi.org/10.1002/jrsm.35
- Moeyaert, M., Ugille, M., Natasha Beretvas, S., Ferron, J., Bunuan, R., & Van den Noortgate, W. (2017). Methods for dealing with multiple outcomes in meta-analysis: a comparison between averaging effect sizes, robust variance estimation and multilevel meta-analysis. *International Journal of Social Research Methodology, 20*(6), 559-572. https://doi.org/10.1080/13645579.2016.1252189
- Tipton, E., Pustejovsky, J. E., & Ahmadi, H. (2019a). A history of meta-regression: Technical, conceptual, and practical developments between 1974 and 2018. Research Synthesis Methods, 10(2), 161-179. https://doi.org/10.1002/jrsm.1338
- Tipton, E., Pustejovsky, J. E., & Ahmadi, H. (2019b). Current practices in meta-regression in psychology, education, and medicine. Research Synthesis Methods, 10(2), 180-194. https://doi.org/10.1002/jrsm.1339
- Van den Noortgate, W., López-López, J. A., Marín-Martínez, F., & Sánchez-Meca, J. (2013). Three-level meta-analysis of dependent effect sizes. *Behavior Research Methods*, 45(2), 576-594. https://doi.org/10.3758/s13428-012-0261-6
- Van den Noortgate, W., López-López, J. A., Marín-Martínez, F., & Sánchez-Meca, J. (2015). Meta-analysis of multiple outcomes: A multilevel approach. *Behavior Research Methods*, 47(4), 1274-1294. https://doi.org/10.3758/s13428-014-0527-2
- Van den Noortgate, W., & Onghena, P. (2003). Multilevel meta-analysis: A comparison with traditional meta-analytical procedures. *Educational and Psychological Measurement*, 63(5), 765-790. https://doi.org/10.1177/0013164403251027

2.05. Adjustments and Imputations to VE Estimates Prior to Meta-Analytic Modelling

To be included in meta-analytic models, each effect size extracted from studies needed to be accompanied by a corresponding standard error (SE). The standard error was always derived from the confidence intervals provided. However, several values were not usable for computation and needed adjustment. Similarly, a few VE point-estimates required adjustments to compute models. The table that follows lists each of the adjustments/imputations we applied, along with our rationale.

eTable 4. Rules Guiding the Adjustment/Imputation of VE Values.

Problem Case	Explanation and Solution
1. Provided CIs were asymmetric (when computed as log RRs).	Because standard errors (SEs) were derived from CIs, asymmetric CIs would produce two competing standard errors (SEs). To resolve this, we calculated the SE implied by both the upper and lower CI, and selected the larger of the 2 SEs for use in models. This represents the more conservative approach (assuming more, rather than less, error in estimates extracted).
2. VE estimates were negative in magnitude (or, equivalently, RRs were >1.0 in magnitude). Applies to point estimates and CIs.	If the original metric was an RR, OR, or HR, this was not a problem, and the estimate could be used directly in analyses. When the original metric was a VE, we needed to take into account that calculating VEs typically assumes a positive number, where: **VE** = (1-RR)*100 When an RR is less than 1, the plausible range of VE is 0% to 100%. If we extend the logic of VE to the negative range, then we could assume that a VE equal to -100% represents non-vaccination offering the highest protection. From this extension, VE can have a range of -100% to 100%. However, when a VE is negative, its relation to RR needs to be adjusted as the RR metric is unbounded in the positive range. Specifically, RR ranges from 0 to infinity, which should correspond to VEs from 100% to –100%). Consequently, when VE estimates were negative (or RR>1), we used the following formulas to convert between the two metrics. A negative VE was assumed to reflect the following formula: **VE** = (-1 + 1/RR)*100 **RR** = 1 / (VE/100 +1)
3. VE point estimate was 100%, or RR point estimate was 0.	Both these cases make it impossible to calculate a log-transformed RR (as the transformation cannot be applied to a value of zero). We therefore replaced/adjusted VE estimates of 100% with a VE value of 99.5% (equivalent RR would be .005). The choice of 99.5% stemmed from a recognition that VE is often reported without decimals, and that a value of 99.5% would be likely to be rounded up. This decision is more conservative than using a value between 99.5 and 100).
4. Upper CI was equal to VE = 100% or RR = 0.	Causes a similar problem as when the point estimate is VE = 100%. If a lower CI was available, we used that CI instead to derive the SE. Otherwise, we imputed a value of VE = 99.9% (or RR = .001). This allowed us to derive SEs while recognizing that the value may approach 100%.
5. Lower CI is VE = 100 or RR = 0.	Causes a similar problem as when the point estimate is VE = 100%. If an upper CI was available, we used that CI instead to derive the SE. Otherwise, we imputed a value of VE = 97.5% (or RR = .025). This allowed us to derive SEs while recognizing that the value may approach 100%. The values of 99.9% for the upper CI and 97.5% for the lower CI were chosen to be symmetrical (in the log RR scale) around the value of VE = 100%.
6. A study cohort had a point estimate for VE available, but no CIs.	No SE could be computed for such effects, and they were removed from the meta-analytic models.
7. A study cohort had a point estimate, but only one CI.	In such cases, we used the SE suggested by the CI that was provided.
8. A CI was reported as -/+ infinity or a CI was reported as less than -100% (i.e., -189.8%)	We treated “infinity” or “less than -100%”as a missing value. We reasoned such estimates would have large enough errors as to be too imprecise to warrant including within our models.

9. One of the CIs was equal in value to the point estimate.	When a CI is equal in magnitude to the point estimate, the implied standard error (SE) is effectively zero. SEs of zero cannot be used in analyses, so we used the other (provided) CI to derive an SE. This rule can be seen as a specific case of rule #1.
10. Both CIs were equal in magnitude to the point estimate.	When both CIs are equal in magnitude to the point estimate, both imply a standard error (SE) of zero, which cannot be used in meta-analytic models. Since SEs of zero are not usually plausible, such occurrences were taken to be artifacts of rounding estimates in reporting when SE was very low. Because low SEs are particularly valuable in meta-analytic reviews, we sought to retain these studies while accounting for this. Our solution was to add a 5 beyond the last decimal of the upper CI reported and subtract a 5 beyond the last decimal of the lower CI reported. For example: [CI = 15.5 - 15.5] -> [CI = 15.45 - 15.55] [CI = 15 - 15] -> [CI = 14.5 - 15.5] This rule was derived assuming that these cases derived from rounding error (i.e., rounding the imputed values to the right to have one fewer decimal point would lead to the values on the left). This rule allowed us to retain estimates for meta-analytic modelling while accounting for the fact that these studies would have small SE values. Since 2 CIs were imputed, the meta-analysis used the whichever produced the larger SE as per rule #1.
11. The point estimate was outside the range of the CI.	This was assumed to be an error in reporting. We thus operated under the assumption that the point-estimate was accurate and used the CI that had a plausible value to derive SEs (e.g., the upper CI if it was higher than the point estimate, or the lower CI if it was below the point estimate).

2.06. Indices of Heterogeneity

We computed three indices of effect size heterogeneity to qualify the findings from our meta-analytic models. These indices were computed whenever we produced three-level meta-analytic models and included:

1. **95% Prediction Intervals (PI).** Prediction intervals reflect the likely range within which a future effect size (i.e., a VE estimate from a new study, or VE observed in a new context) would be expected to fall. Prediction intervals are produced for every point estimate within the models (i.e., at each time point) and account for both sampling error and true variability in the population of effect sizes we are studying. Prediction intervals are represented in the same unit as our other estimates (i.e., VE as a percentage).
   a) *Formal Interpretation:* If we were to repeat our sampling of effect sizes (i.e., from primary studies) an infinite number of times, and then collected a new data point (i.e., a VE estimate from a new study), then 95% of the generated prediction intervals would be expected to capture the new data point.
   b) We provide details on the exact way in which PIs are calculated (with equations) in the section below.

2. **σ (Sigma)**: σ represents the estimated standard deviation in the (true) population of VE (i.e., without sampling error). The unit of this index is the same as used during the meta-analytic process; in our case, σ is provided in log odds ratios. In three-level models, σ can be divided into several levels.
   a) *Within-Study σ*: Indicates variability in VE within studies. This is the level 2 heterogeneity.
   b) *Between-Study σ*: Indicates variability in VE between studies. This is the level 3 heterogeneity. The between-study σ is comparable in interpretation to the tau (τ) parameter produced in traditional random effects models.
   c) *Total σ:* The variability within and between studies can be combined to represent the total heterogeneity across effect sizes in our review. This is the level 1 heterogeneity. We do not report level 1 heterogeneity in our manuscript as it can be derived from the other two levels:
      (1) $\sigma^2_{lvl\,1} = \sigma^2_{lvl\,2} + \sigma^2_{lvl\,3}$

3. **I^2**. The value of I^2 (which ranges from 0 to 1) captures the proportion of variability in observed effect sizes which cannot be attributed to sampling error. For example, a value of 0 indicates that most of the variability in VE estimates may be due to sampling errors, and a value of 1 indicates that most of the variability can be attributed to true variation in VE across studies (accounting for any sampling error). This relative index of heterogeneity can be broken down into two levels:
   a) *Within-Study I^2*: Indicates the relative heterogeneity in VE observed within studies.
   b) *Between-Study I^2*: Indicates the relative heterogeneity in VE observed between studies. The between-study I^2 is comparable in interpretation to the I^2 produced in traditional random effects models.

Calculation of Prediction Intervals (PIs), and How These Values Relate to Confidence Intervals (CIs)

In our modelling, PIs are calculated using the following formula.

$$PI = \hat{\mu} \pm z * \sqrt{SE^2 + \sigma^2}$$

Where, $\hat{\mu}$ is the estimated vaccine effectiveness (VE) at a given time point, z is the critical value for an alpha of a given value (i.e., for a two-tailed 96% test, it would be approximately 1.956), SE is the standard error corresponding to a given VE estimate, and σ is the estimate of τ given in a model. When calculating PIs, we relied on the total variability estimated (level 1 σ), to reflect how estimates often vary both across studies and within studies (e.g., for different subgroups).

Prediction intervals are calculated using the raw metric of the estimates being pooled in analyses, which in our case is a log transformation of a risk ratio. However, once the PI is calculated, it can be transformed back into a VE metric (i.e., a percentage ranging from -100% to 100%).

The above formula contrasts with the (narrower/simpler) formula of a confidence interval, which is calculated using the following formula instead:

$$CI = \hat{\mu} \pm z * SE$$

As an example, the following list provides the value of each component of these equations when calculating the VE of the primary series of COVID-19 vaccines, generally, against any COVID-19 infection (i.e., row 1 of Table 1 in our manuscript). Values are given for the 14-42 day baseline, obtained for the *November* update of our review, and we provide different metric conversions when meaningful. Of note, calculations are all conducted in a log RR metric. Consequently, the order of the lower/upper PIs and CIs will be flipped in that metric, relative to when it is expressed as a VE.

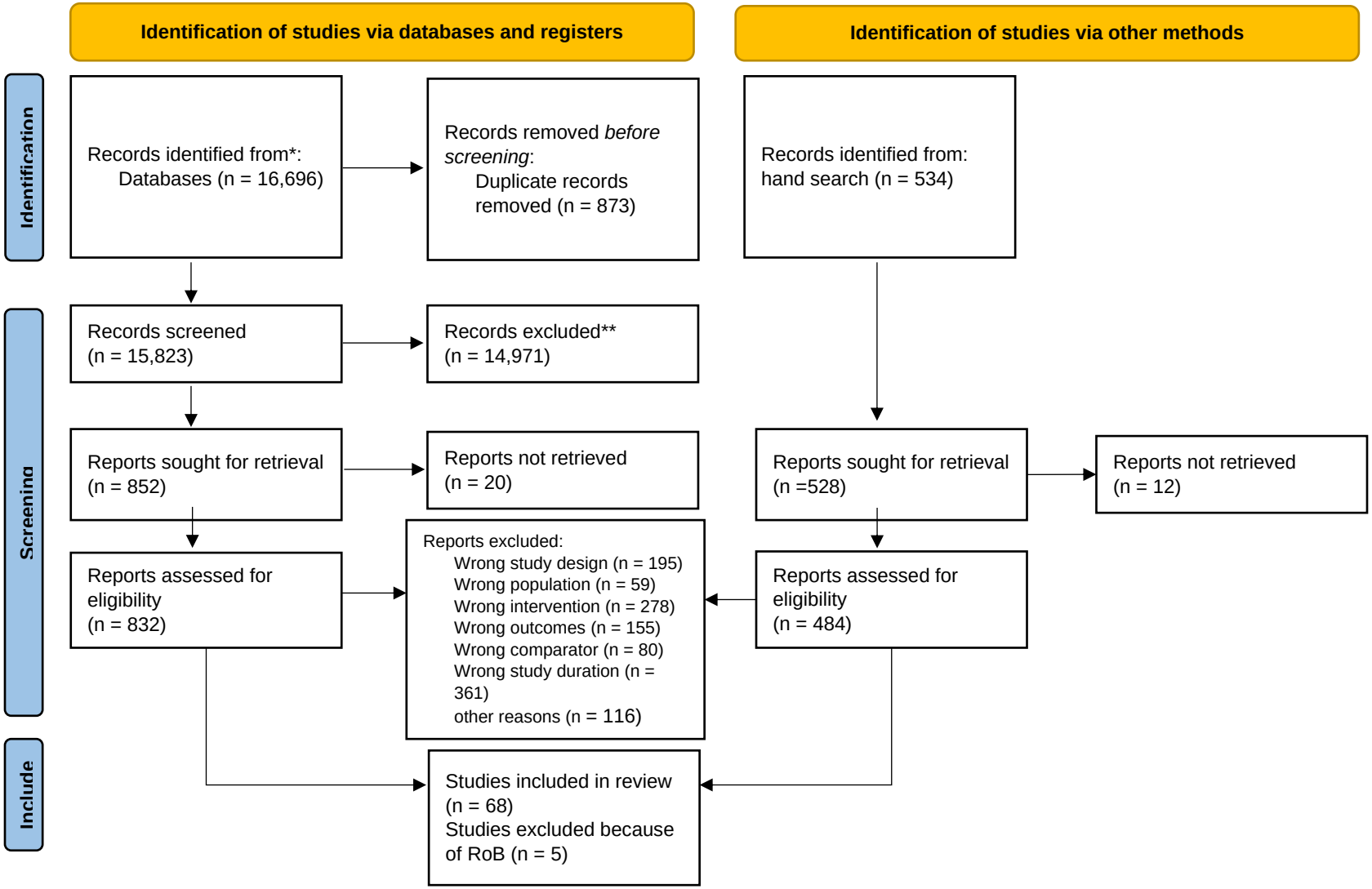
eTable 5. Descriptive Example for Calculating Prediction Intervals and Confidence Intervals.

Parameter	Value[a]	Description/Note
$\hat{\mu}$	Log RR: -1.7743 RR: 0.1696 VE: 83.04%	Estimate of vaccine effectiveness (VE). Calculated in the meta-analysis as a log RR value.
z	1.956	Critical value for a two-tailed 95% statistical test (i.e., for an α of 0.05).
SE	Log RR: 0.0886	Standard error for the parameter μ, calculated by the meta-analytic model. It is not explicitly provided in the manuscript but can be back-calculated using the CIs and the equation above.
σ^2	All in Log RR: Lvl 1: 0.4225 Lvl 2: 0.2052 Lvl 3: 0.2173	The level 1 value of σ^2 refers to the total variability and is the sum of the lvl 2 (within-study variability) and lvl 3 (between study variability) values of σ^2.
Lower CI[b]	Log RR: -1.9487 RR: 0.1425 VE: 85.75%	This is calculated on the log RR scale using the CI equation above. Barring rounding error for each term[a]: -1.95 = -1.77 – 1.96*(0.089)
Upper CI[b]	Log RR: -1.5999 RR: 0.2019 VE: 79.81%	This is calculated on the log RR scale using the CI equation above. Barring rounding error for each term[a]: -1.60 = -1.77 + 1.96*(0.089)
Lower PI[b]	Log RR: -3.0650 RR: 0.0467 VE: 95.33%	This is calculated on the log RR scale using the PI equation above. Barring rounding error for each term[a]: $-3.07 = -1.77 - 1.96 * \sqrt{.089^2 + 0.422}$
Upper PI[b]	Log RR: -0.4837 RR: 0.6165 VE: 38.35%	This is calculated on the log RR scale using the PI equation above. Barring rounding error for each term[a]: $-3.07 = -1.77 + 1.96 * \sqrt{.089^2 + 0.422}$

[a]Values are rounded, so using the values reported here in the equations will lead to slight deviations based on rounding when doing the calculations.

[b]The lower (CI or PI) values in a log RR or an RR metric, each correspond to the upper values in a VE metric. Likewise, the upper (CI or PI) values in a log RR or an RR metric, each correspond to the lower values in a VE metric.

Section 3. eResults A – Flowchart and Characteristics of Included Studies



eFigure 1. Literature Search Flow Diagram.
These are approximate numbers. Although all the steps were properly registered, some challenges were faced with the overlap between the searches, the same record may have been full-text assessed more than once (e.g., updates and peer-review publication of preprints). If there were multiple exclusion reasons for one study, we choose the primary exclusion reason.

eTable 6. Characteristics of Included Studies of Effectiveness of COVID-19 Vaccines.

Author, year	Study design	Analytic Design	Country	Population and age groups	Variant(s)	Vaccine(s)	Outcome measure	Days post-primary series*
Andeweg et al. 2022	Case-control	Test Negative (symptomatic and asymptomatic)	Netherland	1,460,458 aged ≥11 years	Delta Omicron	mRNA – 1273 BNT162b2 Ad26.CoV2.S	Documented infections Hospitalisations	0-29; 120-149; 150-179; 180-209; 210
Andrejko et al. 2022	Case-Control	Test-negative (symptomatic)	USA	2,238 persons aged 13+ years	Non-specific	BNT162b2 mRNA-1273	Documented infections	14; 120-121; 150; 180; 210; 240; 270
Andrews, et al. 2022 a	Case-Control	Test-negative (symptomatic)	England	2,663,549 Adults aged ≥18 years	Delta Omicron	BNT162b2 AZD1222(ChAdOx1) mRNA-1273	Documented infections	15-28; 141-168; 176+
Andrews, et al. 2022 b	Case-Control	Test-negative (symptomatic)	UK	5,233,372 persons aged >16 years	Delta	BNT162b2 AZD1222 (ChAdOx1)	Documented infections Hospitalisations Mortality	15 to 63; 141+
Baum et al. 2022	Cohort	Data-linked Cohort	Finland	897,932 Adults aged ≥70 years	Delta Omicron	BNT162b2 AZD1222(ChAdOx1) mRNA-1273	Hospitalisations	0-13; 181+;
Bedston et al. 2022	Cohort	Data-linkage	UK	82,959 HCWs aged ≥ 16 years	Non-specific	BNT162b2	Documented infections	8 - 35; 119 - 147; 147 - 175; 182+
Berec et al. 2022	Case-Control	Population Retrospective Cohort and Data-linkage	Czech Republic	7,428,968 Overall population	Non-specific	BNT162b2 Ad26.COV2.S mRNA-1273	Documented infections Hospitalisations Mortality	1-61; 214.5 – 244
Britton et al. 2022	Cohort	Test-negative (symptomatic)	USA	1,634,271 adults aged ≥20 years	Delta	BNT162b2 mRNA-1273 Ad26.CoV2.S	Documented infections	14-30; 121-150; 151-180; 181-210; 211-240; 241-270; 271-300
Bruxvoort et al. 2021	Case-Control	Test-negative (symptomatic and asymptomatic)	USA	352,878 unvaccinated and 352,878 vaccinated Kaiser Permanente	Delta	mRNA-1273	Documented infections	14-60; 121-150; 151-180

				Southern California (KPSC) members aged ≥18years				
Buchan et al. 2022	Case-Control	Test-negative (symptomatic)	Canada	134,435 Adults aged >18 years	Delta Omicron	BNT162b2 Ad26.CoV2.S AZD1222 (ChAdOx1) mRNA-1273	Documented infections	7-59; 120-179; 180-239; 240+
Carazo, et al. 2022 a	Case-Control	Test-negative (symptomatic and asymptomatic)	Canada	696,439 aged ≥ 12 years	Omicron	BNT162b2 mRNA-1273	Documented infections	0-67; 187-247; 277-337
Carazo, et al. 2022 b	Case-Control	Test-negative (symptomatic and asymptomatic)	Canada	111,239 HCWS aged ≥18years who were paid by the Quebec publicly funded health-care system	Omicron	BNT162b2 mRNA-1273	Documented infections Hospitalisations Mortality	7-59 183-364
Carazo, et al. 2022 c	Case-Control	Test-negative (symptomatic and asymptomatic)	Canada	696,439 individuals aged ≥12 years	Omicron	BNT162b2 mRNA-1273	Documented infections Hospitalisations	0-61 184-244 275.5-335.5
Castillo, et al.2022	Case-Control	Test-negative (symptomatic)	France	1,296,351 Adults aged ≥50 years	Delta	BNT162b2 Ad26.CoV2.S AZD1222 (ChAdOx1) mRNA-1273	Documented infections Hospitalisations	15-30; 123-152.5; 153.5-183; 184+
Cerqueira-Silva, et al. 2022 a	Cohort	Test-negative (symptomatic)	Brazil	899,050 Adults aged ≥18 years	Omicron	BNT162b2 AZD1222(ChAdOx1)	Documented infections	14-63; 141+
Cerqueira-Silva, et al. 2022 b	Case-Control	Test-negative (symptomatic)	Brazil	30,910 Adults aged >18 years	Non-specific	BNT162b2, AZD1222 (ChAdOx1) Ad26.CoV2.S	Documented infections	0-13; 180+
Chambers et al. 2022	Case-control	Test-negative (symptomatic and asymptomatic)	Canada	14,955 adults living with HIV aged ≥18 years	Omicron	BNT162b2 Ad26.CoV2.S AZD1222 (ChAdOx1) mRNA-1273	Documented infections Hospitalisations Mortality	7-59 120-179 180+
Chemaitell, et al. 2022 a	Case-Control	Test-negative (symptomatic and asymptomatic)	Qatar	84,884 Persons aged ≥12 years in Qatar	Omicron	BNT162b2	Documented infections	30; 120; 150; 180; 210; 240; 270; 300; 330; 360+
Chemaitelly et al. 2021 b	Case-Control	Test-negative (symptomatic and asymptomatic)	Qatar	494,859 Persons aged ≥12 years	Delta	BNT162b2	Documented infections	30; 120; 150; 180; 210; 240; 270; 300; 330; 360+
Chung et al. 2022	Case Control	Test-negative (symptomatic and asymptomatic)	Canada	3,045,059 Ontario residents aged ≥16 years, registered for provincial health	Omicron	BNT162b2 Ad26.CoV2.S AZD1222 (ChAdOx1) mRNA-1273	Hospitalisations	7-59 120-179 180-239 240+

				insurance, and not in a long-term care facility				
Collie et al. 2022	Case-control	Test-negative (symptomatic)	South Africa	38,367 patients aged ≥18 years that had been hospitalized for medical treatment	Omicron	BNT162b2	Hospitalisations	14-27 150-180 181-240
de Gier et al. 2021	Cohort	Retrospective Cohort	Netherlands	15,571 Persons aged ≥12 year in a nationwide registry of COVID-19 Hospitalisations	Delta	BNT162b2 Ad26.CoV2.S AZD1222 (ChAdOx1) mRNA-1273	Hospitalisations	1-28; 106 – 133; 141+
El Adam et al. 2022	Case-Control	Test-negative (symptomatic)	Canada	27,602 HCWs, (36,776 specimens) within the WHITE database aged ≥18 years	Non-specific	BNT162b2 mRNA-1273	Documented infections	14-20; 112-195; 197+
El Sahly et al. 2021	RCT - open phase	RCT	USA	28,451 Adults aged ≥18 years with high risk for Covid-19	Non-specific	mRNA-1273	Documented infections	15 - 60; 123+
Ferdinands et al. 2022	Case-Control	Test-negative (asymptomatic)	USA	839,461 Adults aged ≥18 years	Delta Omicron	BNT162b2 mRNA-1273	Documented infections Hospitalisations	14-61; 62-183; 184-244; 245-305; 306-366
Florea et al. 2022	Cohort	Prospective Cohort	USA	1,854,008 KPSC members aged >18 years	Non-specific	mRNA-1273	Documented infections Hospitalisations	0-61; 123 - 183; 184 - 244
Gray et al. 2022	Case-Control	Test-negative (symptomatic)	South Africa	162,637 Adults aged ≥18 years	Omicron	BNT162b2 Ad26.COV2.S mRNA-1273	Documented infections	14-27; 148-207
Gram et al. 2022	Cohort	Cohort	Denmark	7,351,244 Persons aged ≥12 years	Delta Omicron	BNT162b2 mRNA-1273	Documented infections Hospitalisations	14-30; 120+
Hall et al. 2022	Cohort	Prospective Cohort	UK	35,768 HCWs aged ≥18 years	Non-specific	BNT162b2 Ad26.CoV2.S AZD1222 (ChAdOx1) mRNA-1273	Documented infections	0-13; 134-193+; 194+
Hansen et al. 2022	Cohort	Cohort	Denmark	3,090,833 Persons aged ≥12 years	Omicron	BNT162b2 mRNA-1273	Documented infections Hospitalisations	14-30; 121+
Horne et al. 2022	Cohort	Cohort	England	13,841,107 Persons aged ≥18 years	Non-specific	BNT162b2 AZD1222 (ChAdOx1)	Documented infections Hospitalisations Mortality	22-42; 106-126; 134-154; 162-182
Katikireddi et al. 2022	Case-Control	Test-negative (symptomatic)	Scotland	2,534,527 Adults aged >18 years	Non-specific	AZD1222 (ChAdOx1)	Documented infections	15 - 21; 113 - 119; 127-133; 141-147
Kirsebom et al. 2022 a	Case-Control	Test-negative (symptomatic)	England	626,148 Adults aged ≥18 years	Omicron	BNT162b2 AZD1222(ChAdOx1) mRNA-1273	Documented infections Hospitalisations	1-14; 176+

Kissling et al. 2022	Case-Control	Test-negative (symptomatic)	European countries**	14,282 persons aged ≥ 30 years	Delta	BNT162b2 Ad26.COV2.S mRNA-1273	Documented infections	For people 30–59 years old: 14; 203 For people ≥60 years old: 16; 203
Lauring et al. 2022	Case-Control	Test-negative and Syndrome negative comparison groups (asymptomatic)	USA	11,690 Adults aged ≥18 years	Non-specific	BNT162b2 mRNA-1273	Hospitalisations	0-13; 151+
Lin, et al. 2022 a	Cohort	Surveillance data linkage	USA	10,600,823 Adults aged ≥18 years in North Carolina	Non-specific	BNT162b2 Ad26.CoV2.S mRNA-1273	Documented infections Hospitalisations Mortality	31.5; 123; 153.5; 184;
Lin, et al. 2022 b	Cohort	Surveillance data linkage	USA	10,600,823 Adults aged ≥18 years in North Carolina	Non-specific	BNT162b2 Ad26.CoV2.S mRNA-1273	Documented infections Hospitalisations Mortality	31.5; 123; 153.5; 184; 213.5; 244; 274.5; 305
Lind, et al. 2022 a	Case-Control	Test-negative (symptomatic and asymptomatic)	USA	130,073 Persons aged ≥5 years	Omicron	BNT162b2 mRNA-1273	Documented infections	0-14; 151+
Lind, et al. 2022 b	Case-control	Test-negative (symptomatic and asymptomatic)	USA	441,356 individuals enrolled in the Yale New Haven Health System (YNHH) (aged ≥16 years)	Alpha Delta	mRNA-1273 BNT162b2	Documented infections Hospitalisations	0-14 150+
Lyngse et al. 2022	Case-Control	Data-linkage	Denmark	24,693 primary cases, 53,584 household contacts, 11,631 secondary cases Danish population (0 - 80 years old)	Delta	BNT162b2 Ad26.CoV2.S AZD1222 (ChAdOx1) mRNA-1273	Documented infections	1-30.5; 123 – 152.5; 153.5 - 183; 214.5 - 244
Lytras et al. 2022	Cohort	Observational Cohort	Greece	9,200,000 Persons aged ≥15 years	Non-specific	BNT162b2 Ad26.CoV2.S AZD1222 (ChAdOx1) mRNA-1273	Mortality	0-30.5; 184
Machado et al. 2022	Cohort	Historical Cohort based on data linkage	Portugal	471,439,909 Adults aged ≥65 years Adults	Non-specific	BNT162b2 mRNA-1273	Documented infections Hospitalisations Mortality	14-41; 124-203
Nielsen et al. 2022	Cohort	Population-based Cohort	Denmark	748,322 individuals with prior SARS-CoV-2 infection.	Omicron	BNT162b2 Ad26.CoV2.S AZD1222 (ChAdOx1) mRNA-1273	Documented infections	14-43; 104-133; 134-163; 164-193;

								194-223; 224-253; 254-283; 284-313; 314-343; 344+
Ng et al. 2022	Case-Control	Retrospective Cohort	Singapore	8,470 contact cases aged 0+ with median age of 36 years	Delta	mRNA-1273 BNT162b2.	Documented infections	1-61; 184
Nordström, et al. 2022	Case-Control	Retrospective Cohort	Sweden	1,684,958 Adults aged >18 years in Sweden	Non-specific	BNT162b2 AZD1222 (ChAdOx1) mRNA-1273	Documented infections	15-30; 121-180; 181-210; 121+; 181+; 211+
Nyberg et al. 2022	Cohort	Retrospective Cohort	England	1,191,526 Adults aged ≥20 years	Delta Omicron	BNT162b2 AZD1222(ChAdOx1) mRNA-1273	Hospitalisations Mortality	15-49; 113 - 133; 141+
Petráš et al. 2022	Cohort	Retrospective Cohort	Prague	11,443 Hospital staff aged ≥18 years	Non-specific	BNT162b2 Ad26.CoV2.S AZD1222 (ChAdOx1) mRNA-1273	Documented infections	24; 163
Poukka et al. 2022	Cohort	Register-based Cohort	Finland	427,905 HCWs aged 16-69 years	Delta	BNT162b2 AZD1222 (ChAdOx1) mRNA-1273	Documented infections Hospitalisations	0-13; 181+
Robles-Fontán et al. 2022	Cohort	Data Linkage	Puerto Rico	88,044 Persons aged ≥12 years	Non-specific	BNT162b2 Ad26.CoV2.S mRNA-1273	Documented infections Hospitalisations Mortality	14; 144
Rosenberg et al. 2022	Cohort	Surveillance-based prospective Cohort	USA	8,690,825 Adults aged ≥18 years in New York State	Non-specific	BNT162b2 mRNA-1273 AZD1222 (ChAdOx1)	Documented infections Hospitalisations	14-44; 134-164;
Skowronski et al. 2021	Case-Control	Test-negative (asymptomatic)	Canada	872,440 Adults aged >18 years in British Columbia	Delta	BNT162b2 AZD1222 (ChAdOx1) mRNA-1273	Documented infections Hospitalisations	14-27; 15-21 113-133; 141-161; 169-189; 197-217; 225-245; 253-273
				1,973,637Adults aged >18 years in Quebec				15-21; 113-133; 141-161; 169-189; 197-217; 225-245; 253-273
Sobieszczyk et al. 2022	RCT	RCT	USA, Chile, Peru	32,380 Adults aged ≥18 years	Non-specific	AZD1222 (ChAdOx1)	Documented infections	0-15 180-360

Starrfelt et al. 2022	Cohort	Population-based Cohort	Norway	4,301,995 Adults aged ≥18 years	Non-specific	BNT162b2 AZD1222(ChAdOx1) mRNA-1273	Documented infections Hospitalisations	15-63; 127-175; 183-231; 232+
Stowe et al. 2022	Case-Control	Test-negative (symptomatic and asymptomatic)	England	409,985 Adults aged ≥18 years	Delta Omicron	BNT162b2 AZD1222(ChAdOx1) mRNA-1273	Hospitalisations	0-13; 175+
Syed, et al. 2022	Cohort	Prospective Cohort	Qatar	1,241,501 Persons aged ≥12 years	Non-specific	BNT162b2 mRNA-1273	Documented infections	14-43; 134-163; 164-333
Tartof et al. 2022	Cohort	Retrospective Cohort	USA	3,436,957 KPSC members aged >18 years	Non-specific	BNT162b2	Documented infections Hospitalisations	1-29; 120-149; 150-179; 180-209; 210-239
Thomas et al. 2021	RCT	RCT	Global	44,047 Persons aged ≥16 years	Non-specific	BNT162b2	Documented infections	8-61 123+
Thompson et al. 2021	Cohort	Test-negative (symptomatic)	USA	41,552 Adults aged ≥50 years	Non-specific	BNT162b2 Ad26.CoV2.S mRNA-1273	Hospitalisations	14-27; 112+

HCWs: healthcare workers; RCT: randomized controlled trial

*It includes the baseline.

**European countries: Croatia, France, Ireland, the Netherlands (community testing: NL-CO), Portugal, Romania, three regions in Spain, the Navarre region in Spain, as well as England and Scotland in the United Kingdom.

eTable 7. Characteristics of included studies of effectiveness of booster COVID-19 vaccines.

Authors, year **ID**	**Study design**	**Analytic Design**	**Country**	**Population and age group**	**Variant**	**Booster** (Primary doses)	**Outcome measure**	**Days post booster dose***
Andeweg et al. 2022	Case-Control	Test-negative	Netherlands	1,460,458 Immunization <11 to 60+ years old	Delta, Omicron	**BNT162b2 mRNA-1273** (mRNA – 1273 BNT162b2 Ad26.CoV2.S)	Documented infections	0-29; 90-119; 120-149
Cerqueira-Silva, et al. 2022 c	Case-Control	Test-negative	Brazil	2,471,576 Persons aged ≥18 years	Omicron	**BNT162b2** (CoronaVac)	Documented infections Hospitalisations Mortality	14-30; 91-120; 120+
Cerqueira-Silva, et al. 2022 d	Cohort	Test-negative	Brazil and Scotland	4,590,259 individuals (4,653,517 tests) Persons aged ≥18 years	Omicron	**BNT162b2 mRNA-1273** (BNT162b2 AZD1222 (ChAdOx1) mRNA-1273)	Documented infections	14-28; 91+
Chemaitelly, et al. 2022 c	Case-Control	Test-negative	Qatar	138,182, total population of Qatar All age ranges (<10 to >70 years)	Omicron	**BNT162b2, mRNA-1273** (same)	Documented infections	15-21; 85-91; 98+
Collie et al. 2022	Case-Control	Test-negative	South Africa	38,367 Patients >18 years hospitalized for medical treatment	Omicron	**BNT162b2** (same)	Hospitalisations	14-27; 91.5-122
Consonni et al. 2022	Cohort	Cohort study	Italy	5,596 HCWs were included	Omicron	**BNT162b2** (same)	Documented infections	7-29; 90-119; 120+
Glatman-Freedman et al. 2022	Cohort	Retrospective cohort	Israel	1,561,812 Persons aged ≥16 years	Omicron	**BNT162b2** (same)	Documented infections Hospitalisations Mortality	8; 84; 106 - 112; 134-140;
Gram et al. 2022	Cohort	Cohort study	Denmark	7,351,244 Persons aged ≥12 years	Omicron	**BNT162b2 mRNA-1273** (same)	Documented infections Hospitalisations	14-30; 91-120; 120+
Hansen et al. 2022	Cohort	Nationwide cohort study	Denmark	3,090,833 Persons aged ≥18 years for the booster	Omicron	**BNT162b2 mRNA-1273** (same)	Documented infections Hospitalisations	14-30; 91-120; 121+
Kirsebom et al. 2022 a	Case-Control	Test-negative	England	626,1481,127,517 eligible tests Persons aged ≥18 years	Omicron	**BNT162b2 mRNA-1273** (BNT162b2 AZD1222l ChAdOx1, mRNA-1273)	Documented infections Hospitalisations	8; 105+
Kirsebom et al. 2022 b	Case-Control	Test-negative c	England	10,281,119 Persons aged ≥40 years	Omicron	**BNT162b2, ChAdOx1-S** (BNT162b2, ChAdOx1-S, mRNA-1273)	Documented infections	7-13; 105+
Nyberg et al. 2022	Cohort	Retrospective cohort study	England	1,191,526 All age ranges (<10 to >70 years)	Delta; Omicron	**BNT162b2 AZD1222(ChAdOx1) mRNA-1273** (same)	Hospitalisations Mortality	0-13; 84+
Richterman et al. 2022	Case-Control	Test-negative	USA	14,520 HCWs (7.098 Omicron period)	Omicron	**BNT162b2** (same)	Documented infections	1-56; 113+

Stowe et al. 2022	Case-Control	Test-negative	England	409,985 Persons aged ≥18 years	Omicron	**BNT162b2 AZD1222(ChAdOx1) mRNA-1273** (same)	Hospitalisations	7-13; 105+
Suphanchaimat et al. 2022	Case-Control	Test-negative	Thailand	1,460,458 Thai population	Delta	**BNT162b2 AZD1222l ChAdOx1** (CoronaVac)	Documented infections	15-29; 90+
Tseng et al. 2022	Case-Control	Test-negative	USA	123,236 Individuals aged ≥18 years	Omicron	**mRNA-1273** (same)	Documented infections	14-30; 91-150; 150+

Notes: HCWs: healthcare workers; USA: United States of America.
*It includes the baseline.

3.01. List of Included Studies

- **Andeweg,** Stijn P., Brechje de Gier, Dirk Eggink, Caroline van den Ende, Noortje van Maarseveen, Lubna Ali, Boris Vlaemynck, et al. 2022. "Protection of COVID-19 Vaccination and Previous Infection against Omicron BA.1, BA.2 and Delta SARS-CoV-2 Infections." Nature Communications 13 (1): 4738. https://doi.org/10.1038/s41467-022-31838-8.
- **Andrejko,** Kristin L., Jake Pry, Jennifer F. Myers, Megha Mehrotra, Katherine Lamba, Esther Lim, Nozomi Fukui, et al. 2022. "Waning of Two-Dose BNT162b2 and MRNA-1273 Vaccine Effectiveness against Symptomatic SARS-CoV-2 Infection Is Robust to Depletion-of-Susceptibles Bias." Preprint. Epidemiology. https://doi.org/10.1101/2022.06.03.22275958.
- **Andrews (a),** Nick, Julia Stowe, Freja Kirsebom, Samuel Toffa, Tim Rickeard, Eileen Gallagher, Charlotte Gower, et al. 2022. "Covid-19 Vaccine Effectiveness against the Omicron (B.1.1.529) Variant." New England Journal of Medicine 0 (0): null. https://doi.org/10.1056/NEJMoa2119451. (a)
- **Andrews (b),** Nick, Elise Tessier, Julia Stowe, Charlotte Gower, Freja Kirsebom, Ruth Simmons, Eileen Gallagher, et al. 2022. "Duration of Protection against Mild and Severe Disease by Covid-19 Vaccines." New England Journal of Medicine 386 (4): 340–50. https://doi.org/10.1056/NEJMoa2115481. (b)
- **Baum,** Ulrike, Eero Poukka, Tuija Leino, Terhi Kilpi, Hanna Nohynek, and Arto A Palmu. 2022. "High Vaccine Effectiveness against Severe Covid-19 in the Elderly in Finland before and after the Emergence of Omicron." MedRxiv Preprint, 15. https://doi.org/10.1101/2022.03.11.22272140.
- **Bedston,** Stuart, Ashley Akbari, Christopher I. Jarvis, Emily Lowthian, Fatemeh Torabi, Laura North, Jane Lyons, et al. 2022. "COVID-19 Vaccine Uptake, Effectiveness, and Waning in 82,959 Health Care Workers: A National Prospective Cohort Study in Wales." Vaccine 40 (8): 1180–89. https://doi.org/10.1016/j.vaccine.2021.11.061.
- **Berec,** Luděk, Martin Šmíd, Lenka Přibylová, Ondřej Májek, Tomáš Pavlík, Jiří Jarkovský, Milan Zajíček, Jakub Weiner, Tamara Barusová, and Jan Trnka. 2022. "Protection Provided by Vaccination, Booster Doses and Previous Infection against Covid-19 Infection, Hospitalisation or Death over Time in Czechia." Edited by Mohd Adnan. PLOS ONE 17 (7): e0270801. https://doi.org/10.1371/journal.pone.0270801.
- **Britton,** Amadea, Katherine E. Fleming-Dutra, Nong Shang, Zachary R. Smith, Tandin Dorji, Gordana Derado, Emma K. Accorsi, et al. 2022. "Association of COVID-19 Vaccination With Symptomatic SARS-CoV-2 Infection by Time Since Vaccination and Delta Variant Predominance." JAMA, February. https://doi.org/10.1001/jama.2022.2068.
- **Bruxvoort,** Katia J., Lina S. Sy, Lei Qian, Bradley K. Ackerson, Yi Luo, Gina S. Lee, Yun Tian, et al. 2021. "Effectiveness of MRNA-1273 against Delta, Mu, and Other Emerging Variants of SARS-CoV-2: Test Negative Case-Control Study." BMJ 375 (December): e068848. https://doi.org/10.1136/bmj-2021-068848.
- **Buchan,** Sarah A., Hannah Chung, Kevin A. Brown, Peter C. Austin, Deshayne B. Fell, Jonathan B. Gubbay, Sharifa Nasreen, et al. 2022. "Effectiveness of COVID-19 Vaccines against Omicron or Delta Symptomatic Infection and Severe Outcomes." https://doi.org/10.1101/2021.12.30.21268565.
- **Carazo (a),** Sara, Danuta M. Skowronski, Marc Brisson, Chantal Sauvageau, Nicholas Brousseau, Rodica Gilca, Manale Ouakki, Sapha Barkati, Judith Fafard, Denis Talbot, et al. 2022. "Protection against Omicron Re-Infection Conferred by Prior Heterologous SARS-CoV-2 Infection, with and without MRNA Vaccination," April. https://doi.org/10.1101/2022.04.29.22274455. (a)
- **Carazo (b),** Sara, Danuta M Skowronski, Marc Brisson, Sapha Barkati, Chantal Sauvageau, Nicholas Brousseau, Rodica Gilca, et al. 2022. "Protection against Omicron (B.1.1.529) BA.2 Reinfection Conferred by Primary Omicron BA.1 or Pre-Omicron SARS-CoV-2 Infection among Health-Care Workers with and without MRNA Vaccination: A Test-Negative Case-Control Study." The Lancet Infectious Diseases, September. https://doi.org/10.1016/S1473-3099(22)00578-3. (b)
- **Carazo (c),** Sara, Danuta M Skowronski, Marc Brisson, Chantal Sauvageau, Nicholas Brousseau, Rodica Gilca, Manale Ouakki, Sapha Barkati, Judith Fafard, and Denis Talbot. 2022. "Estimated Protection of Prior SARS-CoV-2 Infection Against Reinfection With the Omicron Variant Among Messenger RNA–Vaccinated and Nonvaccinated Individuals in Quebec, Canada." JAMA Network Open 5 (10): e2236670–e2236670. (c)

- **Castillo,** Milena Suarez, Hamid Khaoua, and Noémie Courtejoie. 2022. "Vaccine Effectiveness and Duration of Protection against Symptomatic and Severe Covid-19 during the First Year of Vaccination in France," March. https://doi.org/10.1101/2022.02.17.22270791.
- **Cerqueira-Silva (a),** Thiago, Vinicius de Araújo Oliveira, Enny S Paixão, Pilar Florentino, Gerson O Penna, Neil Pearce, Guilherme L Werneck, Maurício L Barreto, Viviane S Boaventura, and Manoel Barral-Netto. 2022. "Protection Conferred by Vaccine plus Previous Infection (Hybrid Immunity) with Vaccines of Three Different Platforms during the Omicron Variant Period in Brazil." MedRxiv. (a)
- **Cerqueira-Silva (b),** Thiago, Jason R Andrews, Viviane S Boaventura, Otavio T Ranzani, Vinicius de Araújo Oliveira, Enny S Paixão, Juracy Bertoldo Júnior, et al. 2022. "Effectiveness of CoronaVac, ChAdOx1 NCoV-19, BNT162b2, and Ad26.COV2.S among Individuals with Previous SARS-CoV-2 Infection in Brazil: A Test-Negative, Case-Control Study." The Lancet Infectious Diseases 22 (6): 791–801. https://doi.org/10.1016/S1473-3099(22)00140-2. (b)
- **Cerqueira-Silva (c),** Thiago, Vinicius de Araujo Oliveira, Enny S. Paixão, Juracy Bertoldo Júnior, Gerson O. Penna, Guilherme L. Werneck, Neil Pearce, Maurício L. Barreto, Viviane S. Boaventura, and Manoel Barral-Netto. 2022. "Duration of Protection of CoronaVac plus Heterologous BNT162b2 Booster in the Omicron Period in Brazil." Nature Communications 13 (1): 4154. https://doi.org/10.1038/s41467-022-31839-7. (c)
- **Cerqueira-Silva (d),** Thiago, Syed Ahmar Shah, Chris Robertson, Mauro Niskier Sanchez, Srinivasa Vittal Katikireddi, Vinicius de Araújo Oliveira, Enny S. Paixão, et al. 2022. "Waning of MRNA Boosters after Homologous Primary Series with BNT162b2 or ChadOx1 Against Symptomatic Infection and Severe COVID-19 in Brazil and Scotland: A Test-Negative Design Case-Control Study." SSRN Electronic Journal. https://doi.org/10.2139/ssrn.4082927. (d)
- **Chambers,** Catharine, Hasina Samji, Curtis L Cooper, Cecilia T Costiniuk, Naveed Z Janjua, Abigail E Kroch, Gordon Arbess, et al. 2022. "COVID-19 Vaccine Effectiveness among a Population-Based Cohort of People Living with HIV." AIDS (London, England), October. https://doi.org/10.1097/QAD.0000000000003405.
- **Chemaitelly (a),** Hiam, Houssein H. Ayoub, Sawsan AlMukdad, Patrick Tang, Mohammad R. Hasan, Hadi M. Yassine, Hebah A. Al Khatib, et al. 2022. "Duration of Protection of BNT162b2 and MRNA-1273 COVID-19 Vaccines against Symptomatic SARS-CoV-2 Omicron Infection in Qatar." https://doi.org/10.1101/2022.02.07.22270568. (a)
- **Chemaitelly (b),** Hiam, Patrick Tang, Mohammad R. Hasan, Sawsan AlMukdad, Hadi M. Yassine, Fatiha M. Benslimane, Hebah A. Al Khatib, et al. 2021. "Waning of BNT162b2 Vaccine Protection against SARS-CoV-2 Infection in Qatar." New England Journal of Medicine, October. https://doi.org/10.1056/NEJMoa2114114. (b)
- **Chemaitelly (c),** Hiam, Houssein H. Ayoub, Sawsan AlMukdad, Peter Coyle, Patrick Tang, Hadi M. Yassine, Hebah A. Al-Khatib, et al. 2022. "Duration of MRNA Vaccine Protection against SARS-CoV-2 Omicron BA.1 and BA.2 Subvariants in Qatar," March. https://doi.org/10.1101/2022.03.13.22272308. (c)
- **Chung,** Hannah, Peter C. Austin, Kevin A. Brown, Sarah A. Buchan, Deshayne B. Fell, Cindy Fong, Jonathan B. Gubbay, et al. 2022. "Effectiveness of COVID-19 Vaccines Over Time Prior to Omicron Emergence in Ontario, Canada: Test-Negative Design Study." Open Forum Infectious Diseases 9 (9): ofac449–ofac449. https://doi.org/10.1093/ofid/ofac449.
- **Collie,** Shirley, Jiren Nayager, Lesley Bamford, Linda-Gail Bekker, Matt Zylstra, and Glenda Gray. 2022. "Effectiveness and Durability of the BNT162b2 Vaccine against Omicron Sublineages in South Africa." New England Journal of Medicine 387 (14): 1332–33. https://doi.org/10.1056/NEJMc2210093.
- **Consonni,** Dario, Andrea Lombardi, Davide Mangioni, Patrizia Bono, Massimo Oggioni, Sara Uceda Renteria, Antonia Valzano, et al. 2022. "Immunogenicity and Effectiveness of BNT162b2 COVID-19 Vaccine in a Cohort of Healthcare Workers in Milan (Lombardy Region, Northern Italy)." Epidemiologia e Prevenzione 46 (4): 250–58. https://doi.org/10.19191/EP22.4.A513.065.
- **El Adam,** Shiraz, Macy Zou, Shinhye Kim, Bonnie Henry, Mel Krajden, and Danuta M Skowronski. 2022. "SARS-CoV-2 MRNA Vaccine Effectiveness in Health Care Workers by Dosing Interval and Time Since Vaccination: Test-Negative Design, British Columbia, Canada." Open Forum Infectious Diseases 9 (5): ofac178. https://doi.org/10.1093/ofid/ofac178.

- **El Sahly,** Hana M., Lindsey R. Baden, Brandon Essink, Susanne Doblecki-Lewis, Judith M. Martin, Evan J. Anderson, Thomas B. Campbell, et al. 2021. "Efficacy of the MRNA-1273 SARS-CoV-2 Vaccine at Completion of Blinded Phase." New England Journal of Medicine 385 (19): 1774–85. https://doi.org/10.1056/NEJMoa2113017.
- **Ferdinands,** Jill M, Suchitra Rao, Brian E Dixon, Patrick K Mitchell, Malini B DeSilva, Stephanie A Irving, Ned Lewis, et al. 2022. "Waning of Vaccine Effectiveness against Moderate and Severe Covid-19 among Adults in the US from the VISION Network: Test Negative, Case-Control Study." BMJ 379 (October): e072141. https://doi.org/10.1136/bmj-2022-072141.
- **Florea,** Ana, Lina S Sy, Yi Luo, Lei Qian, Katia J Bruxvoort, Bradley K Ackerson, Gina S Lee, Jennifer H Ku, Julia E Tubert, and Yun Tian. 2022. "Durability of MRNA-1273 against COVID-19 in the Time of Delta: Interim Results from an Observational Cohort Study." PloS One 17 (4): e0267824.
- **Gier,** Brechje de, Marjolein Kooijman, Jeanet Kemmeren, Nicolette de Keizer, Dave Dongelmans, Senna C.J.L. van Iersel, Jan van de Kassteele, et al. 2021. "COVID-19 Vaccine Effectiveness against Hospitalizations and ICU Admissions in the Netherlands, April- August 2021," September. https://doi.org/10.1101/2021.09.15.21263613.
- **Glatman-Freedman,** Aharona, Michal Bromberg, Yael Hershkovitz, Hanna Sefty, Zalman Kaufman, Rita Dichtiar, and Lital Keinan-Boker. 2022. "Effectiveness of BNT162b2 Vaccine Booster against SARS-CoV-2 Infection and Breakthrough Complications, Israel." Emerging Infectious Diseases 28 (5): 948–56. https://doi.org/10.3201/eid2805.220141.
- **Gram,** M. A., H. D. Emborg, A. B. Schelde, N. U. Friis, K. F. Nielsen, I. R. Moustsen-Helms, R. Legarth, et al. 2022. "Vaccine Effectiveness against SARS-CoV-2 Infection or COVID-19 Hospitalization with the Alpha, Delta, or Omicron SARS-CoV-2 Variant: A Nationwide Danish Cohort Study." PLoS Medicine 19. https://doi.org/10.1371/journal.pmed.1003992.
- **Gray,** Glenda, Shirley Collie, Ameena Goga, Nigel Garrett, Jared Champion, Ishen Seocharan, Lesley Bamford, Harry Moultrie, and Linda-Gail Bekker. 2022. "Effectiveness of Ad26.COV2.S and BNT162b2 Vaccines against Omicron Variant in South Africa." New England Journal of Medicine, May, NEJMc2202061. https://doi.org/10.1056/NEJMc2202061.
- **Hall,** Victoria, Sarah Foulkes, Ferdinando Insalata, Peter Kirwan, Ayoub Saei, Ana Atti, Edgar Wellington, et al. 2022. "Protection against SARS-CoV-2 after Covid-19 Vaccination and Previous Infection." New England Journal of Medicine 0 (0): null. https://doi.org/10.1056/NEJMoa2118691.
- **Hansen,** Christian, Astrid Schelde, Ida Moustsen-Helm, Hanne-Dorthe Embor, Rasmus Eriksen, Marc Stegger, Tyra Krause, Kåre Mølbak, and Palle Valentiner-Branth. 2022. "Vaccine Effectiveness against Infection and COVID-19-Associated Hospitalisation with the Omicron (B.1.1.529) Variant after Vaccination with the BNT162b2 or MRNA-1273 Vaccine: A Nationwide Danish Cohort Study," March. https://doi.org/10.21203/rs.3.rs-1486018/v1.
- **Horne,** Elsie M F, William J Hulme, Ruth H Keogh, Tom M Palmer, Elizabeth J Williamson, Edward P K Parker, Amelia Green, et al. 2022. "Waning Effectiveness of BNT162b2 and ChAdOx1 Covid-19 Vaccines over Six Months since Second Dose: OpenSAFELY Cohort Study Using Linked Electronic Health Records." BMJ, July, e071249. https://doi.org/10.1136/bmj-2022-071249.
- **Katikireddi,** Srinivasa Vittal, Thiago Cerqueira-Silva, Eleftheria Vasileiou, Chris Robertson, Sarah Amele, Jiafeng Pan, Bob Taylor, et al. 2022. "Two-Dose ChAdOx1 NCoV-19 Vaccine Protection against COVID-19 Hospital Admissions and Deaths over Time: A Retrospective, Population-Based Cohort Study in Scotland and Brazil." The Lancet 399 (10319): 25–35. https://doi.org/10.1016/S0140-6736(21)02754-9.
- **Kirsebom (a),** Freja CM, Nick Andrews, Julia Stowe, Samuel Toffa, Ruchira Sachdeva, Eileen Gallagher, Natalie Groves, Anne-Marie O'Connell, Meera Chand, and Mary Ramsay. 2022. "COVID-19 Vaccine Effectiveness against the Omicron (BA. 2) Variant in England." The Lancet Infectious Diseases. (a)
- **Kirsebom (b),** Freja, Nick Andrews, Ruchira Sachdeva, Julia Stowe, Mary Ramsay, and Jamie Lopez Bernal. 2022. "Effectiveness of ChAdOx1-S COVID-19 Booster Vaccination against the Omicron and Delta Variants in England," May. https://doi.org/10.1101/2022.04.29.22274483. (b)
- **Kissling,** Esther, Mariëtte Hooiveld, Iván Martínez-Baz, Clara Mazagatos, Naoma William, Ana-Maria Vilcu, Marjolein N Kooijman, et al. 2022. "Effectiveness of Complete Primary Vaccination against COVID-19 at Primary Care and Community Level during Predominant Delta Circulation in Europe: Multicentre Analysis, I-MOVE-COVID-

19 and ECDC Networks, July to August 2021." Eurosurveillance 27 (21). https://doi.org/10.2807/1560-7917.ES.2022.27.21.2101104.

- **Lauring,** Adam S, Mark W Tenforde, James D Chappell, Manjusha Gaglani, Adit A Ginde, Tresa McNeal, Shekhar Ghamande, et al. 2022. "Clinical Severity of, and Effectiveness of MRNA Vaccines against, Covid-19 from Omicron, Delta, and Alpha SARS-CoV-2 Variants in the United States: Prospective Observational Study." BMJ, March, e069761. https://doi.org/10.1136/bmj-2021-069761.
- **Lin (a),** Dan-Yu, Yu Gu, Bradford Wheeler, Hayley Young, Shannon Holloway, Shadia-Khan Sunny, Zack Moore, and Donglin Zeng. 2022. "Effectiveness of Covid-19 Vaccines over a 9-Month Period in North Carolina." New England Journal of Medicine 0 (0): null. https://doi.org/10.1056/NEJMoa2117128. (a)
- **Lin (b),** Dan-Yu, Yu Gu, Yangjianchen Xu, Bradford Wheeler, Hayley Young, Shadia Khan Sunny, Zack Moore, and Donglin Zeng. 2022. "Association of Primary and Booster Vaccination and Prior Infection with SARS-CoV-2 Infection and Severe COVID-19 Outcomes." JAMA 328 (14): 1415–26. (b)
- **Lind (a),** Margaret L., Alexander Robertson, Julio Silva, Frederick Warner, Andreas C. Coppi, Nathan Price, Chelsea Duckwall, et al. 2022. "Effectiveness of Primary and Booster COVID-19 MRNA Vaccination against Infection Caused by the SARS-CoV-2 Omicron Variant in People with a Prior SARS-CoV-2 Infection," April. https://doi.org/10.1101/2022.04.19.22274056. (a)
- **Lind (b),** Margaret L, Richard Copin, Shane McCarthy, Andreas Coppi, Fred Warner, David Ferguson, Chelsea Duckwall, et al. 2022. "Use of Whole Genome Sequencing to Estimate the Contribution of Immune Evasion and Waning Immunity to Decreasing COVID-19 Vaccine Effectiveness during Alpha and Delta Variant Waves," August. https://doi.org/10.1101/2022.08.25.22278443. (b)
- **Lyngse,** Frederik Plesner, Kåre Mølbak, Matt Denwood, Lasse Engbo Christiansen, Camilla Holten Møller, Morten Rasmussen, Arieh Sierra Cohen, et al. 2022. "Effect of Vaccination on Household Transmission of SARS-CoV-2 Delta Variant of Concern." Nature Communications 13 (1): 3764. https://doi.org/10.1038/s41467-022-31494-y.
- **Lytras,** Theodore, Flora Kontopidou, Angeliki Lambrou, and Sotirios Tsiodras. 2022. "Comparative Effectiveness and Durability of COVID 19 Vaccination against Death and Severe Disease in an Ongoing Nationwide Mass Vaccination Campaign." Journal of Medical Virology, June. https://doi-org.lib-ezproxy.concordia.ca/10.1002/jmv.27934.
- **Machado,** A., I. Kislaya, A. P. Rodrigues, D. Sequeira, J. Lima, C. Cruz, P. P. Leite, C. M. Dias, and B. Nunes. 2022. "COVID-19 Vaccine Effectiveness against Symptomatic SARS-CoV-2 Infections, COVID-19 Related Hospitalizations and Deaths, among Individuals Aged >=65 Years in Portugal: A Cohort Study Based on Data-Linkage of National Registries February-September 2021." PLoS ONE 17. https://doi.org/10.1371/journal.pone.0274008.
- **Ng,** Oon Tek, Vanessa Koh, Calvin J Chiew, Kalisvar Marimuthu, Natascha May Thevasagayam, Tze Minn Mak, Joon Kiat Chua, et al. 2022. "Impact of SARS-CoV-2 Vaccination and Paediatric Age on Delta Variant Household Transmission." Clinical Infectious Diseases, March, ciac219. https://doi.org/10.1093/cid/ciac219.
- **Nielsen,** Katrine Finderup, Ida Rask Moustsen-Helms, Astrid Blicher Schelde, Mie Agermose Gram, Hanne-Dorthe Emborg, Jens Nielsen, Christian Holm Hansen, Michael Asger Andersen, Marianna Meaidi, and Jan Wohlfahrt. 2022. "Vaccine Effectiveness against SARS-CoV-2 Reinfection during Periods of Alpha, Delta, or Omicron Dominance: A Danish Nationwide Study." PLoS Medicine 19 (11): e1004037.
- **Nordström,** Peter, Marcel Ballin, and Anna Nordström. 2022. "Risk of Infection, Hospitalisation, and Death up to 9 Months after a Second Dose of COVID-19 Vaccine: A Retrospective, Total Population Cohort Study in Sweden." The Lancet 399 (10327): 814–23. https://doi.org/10.1016/S0140-6736(22)00089-7.
- **Nyberg,** Tommy, Neil M Ferguson, Sophie G Nash, Harriet H Webster, Seth Flaxman, Nick Andrews, Wes Hinsley, et al. 2022. "Comparative Analysis of the Risks of Hospitalisation and Death Associated with SARS-CoV-2 Omicron (B.1.1.529) and Delta (B.1.617.2) Variants in England: A Cohort Study." The Lancet 399 (10332): 1303–12. https://doi.org/10.1016/S0140-6736(22)00462-7.
- **Petráš,** Marek, Ivana Králová Lesná, Livia Večeřová, Elka Nyčová, Jana Malinová, Petr Klézl, Martina Nezvedová, et al. 2022. "The Effectiveness of Post-Vaccination and Post-Infection Protection in the Hospital Staff of Three Prague Hospitals: A Cohort Study of 8-Month Follow-Up from the Start of the COVID-19 Vaccination Campaign (COVANESS)." Vaccines 10 (1): 9. https://doi.org/10.3390/vaccines10010009.

- **Poukka,** Eero, Ulrike Baum, Arto A. Palmu, Toni O. Lehtonen, Heini Salo, Hanna Nohynek, and Tuija Leino. 2022. "Cohort Study of Covid-19 Vaccine Effectiveness among Healthcare Workers in Finland, December 2020 - October 2021." Vaccine 40 (5): 701–5. https://doi.org/10.1016/j.vaccine.2021.12.032.
- **Richterman,** Aaron, Amy Behrman, Patrick J Brennan, Judith A O'Donnell, Christopher K Snider, and Krisda H Chaiyachati. 2022. "Durability of SARS-CoV-2 MRNA Booster Vaccine Protection Against Omicron Among Health Care Workers with a Vaccine Mandate." Clinical Infectious Diseases, no. ciac454 (June). https://doi.org/10.1093/cid/ciac454.
- **Robles-Fontán,** Mónica M, Elvis G Nieves, Iris Cardona-Gerena, and Rafael A Irizarry. 2022. "Effectiveness Estimates of Three COVID-19 Vaccines Based on Observational Data from Puerto Rico." The Lancet Regional Health-Americas 9: 100212.
- **Rosenberg,** Eli S., Vajeera Dorabawila, Delia Easton, Ursula E. Bauer, Jessica Kumar, Rebecca Hoen, Dina Hoefer, et al. 2022. "Covid-19 Vaccine Effectiveness in New York State." New England Journal of Medicine 386 (2): 116–27. https://doi.org/10.1056/NEJMoa2116063.
- **Skowronski,** Danuta M, Solmaz Setayeshgar, Yossi Febriani, Manale Ouakki, Macy Zou, Denis Talbot, Natalie Prystajecky, et al. 2021. "Two-Dose SARS-CoV-2 Vaccine Effectiveness with Mixed Schedules and Extended Dosing Intervals: Test-Negative Design Studies from British Columbia and Quebec, Canada." Preprint. Infectious Diseases (except HIV/AIDS). https://doi.org/10.1101/2021.10.26.21265397.
- **Sobieszczyk,** Magdalena E., Jill Maaske, Ann R. Falsey, Stephanie Sproule, Merlin L. Robb, Robert W. Frenck Jr., Hong-Van Tieu, et al. 2022. "Durability of Protection and Immunogenicity of AZD1222 (ChAdOx1 NCoV-19) COVID-19 Vaccine over 6 Months." The Journal of Clinical Investigation 132 (18). https://doi.org/10.1172/JCI160565.
- **Starrfelt,** Jostein, Anders Skyrud Danielsen, Eirik Alnes Buanes, Lene Kristine Juvet, Trude Marie Lyngstad, Gunnar Øyvind Isaksson Rø, Lamprini Veneti, Sara Viksmoen Watle, and Hinta Meijerink. 2022. "Age and Product Dependent Vaccine Effectiveness against SARS-CoV-2 Infection and Hospitalisation among Adults in Norway: A National Cohort Study, July–November 2021." BMC Medicine 20 (1): 278. https://doi.org/10.1186/s12916-022-02480-4.
- **Stowe,** Julia, Nick Andrews, Freja Kirsebom, Mary Ramsay, and Jamie Lopez Bernal. 2022. "Effectiveness of COVID-19 Vaccines against Omicron and Delta Hospitalisation: Test Negative Case-Control Study," April. https://doi.org/10.1101/2022.04.01.22273281.
- **Suphanchaimat,** Rapeepong, Natthaprang Nittayasoot, Chuleeporn Jiraphongsa, Panithee Thammawijaya, Punsapach Bumrungwong, Atthavit Tulyathan, Nontawit Cheewaruangroj, Chakkarat Pittayawonganon, and Piyanit Tharmaphornpilas. 2022. "Real-World Effectiveness of Mix-and-Match Vaccine Regimens against SARS-CoV-2 Delta Variant in Thailand: A Nationwide Test-Negative Matched Case-Control Study." Vaccines 10 (7): 1080. https://doi.org/10.3390/vaccines10071080.
- **Syed,** Mohamed Ahmed, Hamda Abdulla A/Qotba, and Ahmed Sameer Alnuaimi. 2022. "Effectiveness of COVID-19 Vaccines." Journal of Infection 0 (0). https://doi.org/10.1016/j.jinf.2022.02.034.
- **Tartof,** Sara Y., Jeff M. Slezak, Laura Puzniak, Vennis Hong, Timothy B. Frankland, Bradley K. Ackerson, Harpreet S. Takhar, et al. 2022. "Effectiveness of a Third Dose of BNT162b2 MRNA COVID-19 Vaccine in a Large US Health System: A Retrospective Cohort Study." The Lancet Regional Health - Americas, February, 100198. https://doi.org/10.1016/j.lana.2022.100198.
- **Thomas,** Stephen J., Edson D. Moreira, Nicholas Kitchin, Judith Absalon, Alejandra Gurtman, Stephen Lockhart, John L. Perez, et al. 2021. "Safety and Efficacy of the BNT162b2 MRNA Covid-19 Vaccine through 6 Months." New England Journal of Medicine, September, NEJMoa2110345. https://doi.org/10.1056/NEJMoa2110345.
- **Thompson,** Mark G., Edward Stenehjem, Shaun Grannis, Sarah W. Ball, Allison L. Naleway, Toan C. Ong, Malini B. DeSilva, et al. 2021. "Effectiveness of Covid-19 Vaccines in Ambulatory and Inpatient Care Settings." New England Journal of Medicine, September, NEJMoa2110362. https://doi.org/10.1056/NEJMoa2110362.
- **Tseng,** Hung Fu, Bradley K. Ackerson, Katia J. Bruxvoort, Lina S. Sy, Julia E. Tubert, Gina S. Lee, Jennifer H. Ku, et al. 2022. "Effectiveness of MRNA-1273 against Infection and COVID-19 Hospitalization with SARS-CoV-2 Omicron Subvariants: BA.1, BA.2, BA.2.12.1, BA.4, and BA.5." MedRxiv, January, 2022.09.30.22280573. https://doi.org/10.1101/2022.09.30.22280573.

Section 4. eResults B – Full Detailed Meta-Analytic Findings.

eTable 8. Vaccine Effectiveness for Any Primary COVID-19 Vaccine Series Against Infections, Hospitalisations, and Mortality.

Vaccine Type & Outcome	Model Estimates	Baseline days (weeks)		Follow-up days (weeks)									I^2 [w, b]	σ [w, b]
		0-13 (0-2)	14-42 (2-6)	112-139 (16-20)	140-167 (20-24)	168-195 (24-28)	196-223 (28-32)	224-251 (32-36)	252-279 (36-40)	280-307 (40-44)	308-335 (44-48)	336+ (48+)		
ANY VACCINE														
Any variant														
Documented infections	VE	67%	83%	61%*	55%*	50%*	57%*	50%*	47%*	50%*	46%*	53%*	[51, 49]	[.47, .45]
	95% CI	[53, 77]	[80, 86]	[52, 68]	[46, 63]	[39, 60]	[43, 67]	[34, 62]	[23, 63]	[20, 69]	[-31, 80]	[6, 77]		
	95% PI	[-20, 91]	[38, 95]	[-29, 89]	[-39, 88]	[-45, 86]	[-38, 88]	[-46, 86]	[-50, 86]	[-49, 87]	[-63, 89]	[-50, 89]		
	k (obs)	8 (14)	39 (94)	21 (48)	31 (75)	20 (47)	14 (21)	12 (19)	7 (10)	5 (6)	1 (1)	2 (2)		
Hospitalisations	VE	88%	92%	89%*	86%*	83%*	82%*	79%*	80%*	80%	-	74%*	[34, 64]	[.51, .70]
	95% CI	[75, 94]	[89, 94]	[84, 92]	[81, 90]	[74, 88]	[70, 89]	[65, 87]	[62, 90]	[38, 93]	-	[46, 87]		
	95% PI	[21, 98]	[53, 99]	[36, 98]	[22, 98]	[0, 97]	[-7, 97]	[-20, 96]	[-19, 97]	[-36, 97]	-	[-41, 96]		
	k (obs)	4 (7)	21 (55)	11 (37)	16 (37)	10 (19)	6 (8)	7 (9)	3 (4)	1 (1)	-	2 (3)		
Mortality	VE	-	91%	91%	85%*	86%	85%	83%	88%	85%	-	80%	[26, 69]	[.46, .75]
	95% CI	-	[85, 95]	[81, 95]	[73, 91]	[73, 93]	[61, 94]	[64, 92]	[61, 96]	[52, 95]	-	[34, 94]		
	95% PI	-	[45, 99]	[37, 99]	[3, 98]	[9, 98]	[-11, 98]	[-13, 98]	[0, 99]	[-20, 98]	-	[-40, 98]		
	k (obs)	-	10 (23)	4 (7)	8 (15)	4 (8)	2 (2)	3 (5)	1 (1)	1 (1)	-	1 (1)		
Omicron														
Documented infections	VE	58%	61%	36%*	33%*	23%*	36%*	21%*	30%*	18%*	20%*	34%	[31, 69]	[.24, .36]
	95% CI	[34, 73]	[50, 69]	[16, 52]	[13, 48]	[-2, 41]	[15, 52]	[-18, 49]	[-10, 56]	[-19, 46]	[-28, 54]	[-15, 62]		
	95% PI	[-10, 84]	[5, 84]	[-36, 74]	[-39, 73]	[-47, 69]	[-37, 74]	[-52, 70]	[-46, 73]	[-53, 68]	[-55, 71]	[-46, 76]		
	k (obs)	2 (3)	11 (20)	5 (9)	6 (13)	4 (9)	5 (7)	2 (2)	2 (2)	3 (3)	1 (1)	1 (1)		
Hospitalisations	VE	69%	71%	70%	60%	52%*	48%	38%	51%	69%	-	-	[40, 55]	[.24, .00]
	95% CI	[2, 90]	[58, 80]	[55, 80]	[35, 75]	[29, 67]	[1, 73]	[-21, 70]	[7, 75]	[2, 90]	-	-		
	95% PI	[-18, 92]	[32, 88]	[29, 87]	[2, 84]	[-12, 79]	[-29, 81]	[-43, 78]	[-24, 82]	[-18, 92]	-	-		
	k (obs)	2 (2)	6 (7)	3 (4)	2 (3)	4 (4)	1 (1)	1 (1)	1 (1)	2 (2)	-	-		
Mortality	VE	-	49%	62%	18%	-	-	-	-	-	-	-	-	-
	95% CI	-	[-64, 90]	[-76, 97]	[2, 31]	-	-	-	-	-	-	-		
	95% PI	-				-	-	-	-	-	-	-		
	k (obs)	-	1 (2)	1 (2)	1 (2)	-	-	-	-	-	-	-		

Vaccine Type & Outcome	Model Estimates	Baseline days (weeks)		Follow-up days (weeks)									I^2 [w, b]	σ [w, b]
		0-13 (0-2)	14-42 (2-6)	112-139 (16-20)	140-167 (20-24)	168-195 (24-28)	196-223 (28-32)	224-251 (32-36)	252-279 (36-40)	280-307 (40-44)	308-335 (44-48)	336+ (48+)		
(Continued from previous page)														
Delta														
Documented infections	VE	72%	86%†	67%*	66%*	62%*	66%*	64%*	61%*	62%	-	-	[34, 64]	[.32, .43]
	95% CI	[48, 85]	[82, 89]	[57, 75]	[56, 74]	[49, 71]	[53, 75]	[49, 74]	[40, 74]	[-49, 93]	-	-		
	95% PI	[6, 92]	[58, 95]	[3, 89]	[-1, 88]	[-12, 87]	[-3, 89]	[-9, 88]	[-18, 87]	[-62, 95]	-	-		
	k (obs)	2 (2)	14 (30)	8 (15)	10 (24)	9 (19)	6 (10)	6 (7)	3 (4)	1 (1)	-	-		
Hospitalisations	VE	88%	95%	92%	90%*	87%*	86%	-	77%*	-		68%*	[53, 45]	[.60, .56]
	95% CI	[61, 96]	[91, 97]	[87, 96]	[83, 94]	[74, 93]	[65, 95]	-	[7, 94]	-		[-24, 92]		
	95% PI	[10, 98]	[69, 99]	[57, 99]	[45, 98]	[21, 98]	[8, 98]	-	[-50, 97]	-		[-64, 96]		
	k (obs)	2 (3)	7 (17)	5 (14)	5 (14)	4 (8)	2 (3)	-	1 (1)	-		1 (1)		
Mortality	VE	-	94%	91%	83%*	-	-	-	-	-	-	-	[22, 69]	[.41, .73]
	95% CI	-	[74, 99]	[42, 99]	[32, 96]	-	-	-	-	-	-	-		
	95% PI	-	[29, 100]	[-27, 99]	[-48, 98]	-	-	-	-	-	-	-		
	k (obs)	-	2 (4)	1 (2)	2 (4)	-	-	-	-	-	-	-		

Notes. I^2 = Higgin's and Thompson's I^2 presented at the within-study (w) and between-study levels (b); σ = estimate of τ, the standard deviation of effect sizes in the population, presented at the within-study (w) and between-study levels (b); VE = vaccine effectiveness; CI = confidence interval; PI = prediction interval; k = number of studies pooled; obs = number of cohorts/observations pooled; greyed-out cells= fewer than 4 studies.

†VE at this follow-up time point is statistically different from the VE observed at baseline 1 (0-13 days);

*VE at this follow-up time point is statistically different from the VE observed at baseline 2 (14-42 days).

eTable 9. Vaccine Effectiveness for mRNA/Adenovirus Primary COVID-19 Vaccine Series Against Infections, Hospitalisations, and Mortality.

Vaccine Type & Outcome	Model Estimates	Baseline days (weeks)		Follow-up days (weeks)									I^2 [w, b]	σ [w, b]
		0-13 (0-2)	14-42 (2-6)	112-139 (16-20)	140-167 (20-24)	168-195 (24-28)	196-223 (28-32)	224-251 (32-36)	252-279 (36-40)	280-307 (40-44)	308-335 (44-48)	336+ (48+)		
ANY mRNA VACCINE														
Any variant														
Documented infections	VE	71%	87%	66%*	57%*	52%*	52%*	48%*	48%*	51%*	51%*	59%*	[32, 68]	[.37, .54]
	95% CI	[56, 80]	[84, 90]	[57, 74]	[46, 65]	[39, 63]	[35, 64]	[30, 61]	[24, 64]	[22, 69]	[-10, 78]	[7, 82]		
	95% PI	[-12, 92]	[53, 97]	[-20, 91]	[-38, 88]	[-44, 87]	[-45, 87]	[-49, 86]	[-50, 86]	[-49, 87]	[-56, 89]	[-47, 91]		
	k (obs)	6 (8)	28 (59)	14 (28)	25 (48)	13 (26)	11 (13)	9 (14)	5 (7)	4 (5)	1 (1)	1 (1)		
Hospitalisations	VE	87%	93%	89%*	87%*	84%*	82%*	80%*	79%*	-	-	73%*	[26, 73]	[.47, .78]
	95% CI	[70, 95]	[89, 95]	[83, 93]	[80, 91]	[73, 90]	[69, 90]	[64, 88]	[57, 90]	-	-	[38, 88]		
	95% PI	[6, 98]	[53, 99]	[31, 98]	[14, 98]	[-5, 98]	[-15, 97]	[-27, 97]	[-32, 97]	-	-	[-50, 96]		
	k (obs)	3 (4)	18 (33)	8 (20)	13 (20)	6 (9)	5 (7)	6 (7)	2 (3)	-	-	1 (2)		
Mortality	VE	-	94%	96%	87%*	90%	88%	87%	-	-	-	-	[25, 71]	[.49, .81]
	95% CI	-	[88, 97]	[86, 99]	[73, 94]	[76, 96]	[45, 97]	[59, 96]	-	-	-	-		
	95% PI	-	[55, 99]	[59, 100]	[-2, 98]	[17, 99]	[-30, 99]	[-19, 99]	-	-	-	-		
	k (obs)	-	8 (15)	2 (3)	6 (8)	2 (6)	1 (1)	2 (3)	-	-	-	-		
Omicron														
Documented infections	VE	32%	67%	49%*	32%*	25%*	29%*	16%*	26%*	16%*	22%*	35%*	[9, 91]	[.15, .49]
	95% CI	[-26, 66]	[53, 77]	[25, 65]	[2, 53]	[-10, 50]	[-5, 53]	[-26, 49]	[-13, 53]	[-23, 45]	[-21, 52]	[-6, 61]		
	95% PI	[-58, 81]	[0, 89]	[-36, 83]	[-51, 78]	[-56, 76]	[-54, 77]	[-62, 74]	[-57, 76]	[-62, 73]	[-59, 76]	[-52, 80]		
	k (obs)	1 (1)	8 (12)	3 (5)	4 (6)	2 (3)	3 (3)	1 (1)	2 (2)	3 (3)	1 (1)	1 (1)		
Hospitalisations	VE	76%	72%	74%	59%	52%	48%*	40%*	51%	-	-	55%	[24, 72]	[.17, .31]
	95% CI	[-69, 98]	[58, 81]	[60, 83]	[35, 74]	[26, 69]	[6, 71]	[-15, 69]	[12, 73]	-	-	[19, 75]		
	95% PI	[-73, 98]	[32, 88]	[36, 89]	[-2, 83]	[-14, 81]	[-28, 81]	[-41, 79]	[-23, 82]	-	-	[-16, 83]		
	k (obs)	1 (1)	6 (6)	3 (3)	2 (2)	3 (3)	1 (1)	1 (1)	1 (1)	-	-	1 (1)		
Mortality	VE	-	3%	91%	19%	-	-	-	-	-	-	-	-	-
	95% CI	-	[-53, 56]	[19, 99]	[-6, 38]	-	-	-	-	-	-	-		
	95% PI	-	-	-	-	-	-	-	-	-	-	-		
	k (obs)	-	1 (1)	1 (1)	1 (1)	-	-	-	-	-	-	-		
Delta														
Documented infections	VE	77%	91%†	73%*	72%*	69%*	63%*	65%*	59%†*	67%	-	-	[20, 80]	[.18, .37]
	95% CI	[64, 86]	[88, 93]	[63, 80]	[63, 79]	[58, 77]	[48, 74]	[51, 75]	[40, 72]	[-37, 93]	-	-		
	95% PI	[41, 91]	[78, 96]	[33, 89]	[33, 88]	[25, 87]	[10, 85]	[14, 86]	[-3, 84]	[-49, 95]	-	-		
	k (obs)	2 (2)	7 (12)	4 (6)	7 (11)	4 (8)	2 (3)	3 (4)	2 (3)	1 (1)	-	-		

(Continued from previous page)

Hospitalisations	VE	87%	93%	89%*	87%*	84%*	82%*	80%*	79%*	-	-	73%*	[26, 73]	[.47, .78]
	95% CI	[70, 95]	[89, 95]	[83, 93]	[80, 91]	[73, 90]	[69, 90]	[64, 88]	[57, 90]	-	-	[38, 88]		
	95% PI	[6, 98]	[53, 99]	[31, 98]	[14, 98]	[-5, 98]	[-15, 97]	[-27, 97]	[-32, 97]	-	-	[-50, 96]		
	k (obs)	3 (4)	18 (33)	8 (20)	13 (20)	6 (9)	5 (7)	6 (7)	2 (3)	-	-	1 (2)		
Mortality	VE	-	94%	96%	87%*	90%	88%	87%	-	-	-	-	[25, 71]	[.49, .81]
	95% CI	-	[88, 97]	[86, 99]	[73, 94]	[76, 96]	[45, 97]	[59, 96]	-	-	-	-		
	95% PI	-	[55, 99]	[59, 100]	[-2, 98]	[17, 99]	[-30, 99]	[-19, 99]	-	-	-	-		

Vaccine Type & Outcome	Model Estimates	Baseline days (weeks)		Follow-up days (weeks)									I^2 [w, b]	σ [w, b]
		0-13 (0-2)	14-42 (2-6)	112-139 (16-20)	140-167 (20-24)	168-195 (24-28)	196-223 (28-32)	224-251 (32-36)	252-279 (36-40)	280-307 (40-44)	308-335 (44-48)	336+ (48+)		
	k (obs)	-	8 (15)	2 (3)	6 (8)	2 (6)	1 (1)	2 (3)	-	-	-	-		
ANY adenovirus VACCINE														
Any variant														
Documented infections	VE	48%	69%	56%*	50%*	47%*	59%	60%	32%*	41%*	-	45%	[30, 69]	[.26, .39]
	95% CI	[15, 68]	[60, 75]	[42, 66]	[37, 61]	[31, 59]	[27, 77]	[40, 73]	[-14, 60]	[-6, 68]	-	[0, 70]		
	95% PI	[-33, 82]	[18, 88]	[-15, 83]	[-24, 81]	[-30, 80]	[-19, 86]	[-11, 85]	[-50, 77]	[-44, 81]	-	[-40, 82]		
	k (obs)	2 (4)	14 (23)	7 (12)	12 (20)	7 (13)	2 (2)	3 (3)	2 (3)	1 (1)	-	1 (1)		
Hospitalisations	VE	-	90%	89%	85%	82%	82%	79%	82%	79%	-	76%	[33, 65]	[.45, .63]
	95% CI	-	[83, 94]	[81, 94]	[75, 91]	[66, 90]	[46, 94]	[52, 91]	[47, 94]	[39, 93]	-	[25, 92]		
	95% PI	-	[46, 98]	[42, 98]	[23, 97]	[2, 97]	[-18, 97]	[-18, 97]	[-16, 97]	[-28, 97]	-	[-40, 96]		
	k (obs)	-	9 (15)	5 (11)	8 (11)	4 (6)	1 (1)	2 (2)	1 (1)	1 (1)	-	1 (1)		
Mortality	VE	-	84%	77%	75%	82%	77%	79%	82%	76%	-	69%	[67, 25]	[.57, .35]
	95% CI	-	[72, 91]	[47, 90]	[53, 86]	[62, 91]	[9, 94]	[46, 92]	[26, 95]	[10, 94]	-	[-19, 92]		
	95% PI	-	[28, 96]	[-15, 95]	[-14, 94]	[11, 96]	[-39, 97]	[-11, 96]	[-24, 97]	[-39, 97]	-	[-55, 96]		
	k (obs)	-	7 (10)	3 (4)	5 (6)	3 (5)	1 (1)	2 (2)	1 (1)	1 (1)	-	1 (1)		
Omicron														
Documented infections	VE	-	47%	52%	22%	-3%	-	-	-	-	-	-	[100,0]	[.26, .00]
	95% CI	-	[24, 63]	[-2, 77]	[-13, 47]	[-51, 48]	-	-	-	-	-	-		
	95% PI	-	[-13, 75]	[-25, 83]	[-41, 65]	[-63, 61]	-	-	-	-	-	-		
	k (obs)	-	3 (4)	1 (1)	2 (3)	1 (1)	-	-	-	-	-	-		
Hospitalisations	VE	-	60%	46%	45%	-	-	-	-	-	-	-	-	-
	95% CI	-	[33, 76]	[21, 63]	[-89, 97]	-	-	-	-	-	-	-		
	95% PI	-				-	-	-	-	-	-	-		
	k (obs)	-	1 (1)	1 (1)	1 (1)	-	-	-	-	-	-	-		

Vaccine Type & Outcome	Model Estimates	Baseline days (weeks)		Follow-up days (weeks)									I^2 [w, b]	σ [w, b]
		0-13 (0-2)	14-42 (2-6)	112-139 (16-20)	140-167 (20-24)	168-195 (24-28)	196-223 (28-32)	224-251 (32-36)	252-279 (36-40)	280-307 (40-44)	308-335 (44-48)	336+ (48+)		
(Continued from previous page)														
Mortality	VE	-	84%	-7%	17%	-	-	-	-	-	-	-	-	-
	95% CI	-	[-22, 98]	[-68, 63]	[-4, 34]	-	-	-	-	-	-	-		
	95% PI	-	-	-	-	-	-	-	-	-	-	-		
	k (obs)	-	1 (1)	1 (1)	1 (1)	-	-	-	-	-	-	-		
Delta														
Documented infections	VE	-	75%	59%*	58%*	54%*	64%*	64%	64%	-	-	-	[23, 76]	[.14, .25]
	95% CI	-	[67, 81]	[45, 70]	[46, 68]	[39, 66]	[49, 75]	[47, 76]	[47, 76]	-	-	-		
	95% PI	-	[51, 87]	[20, 79]	[19, 78]	[11, 76]	[29, 82]	[27, 83]	[27, 83]	-	-	-		
	k (obs)	-	5 (8)	2 (4)	5 (8)	3 (6)	2 (3)	1 (1)	1 (1)	-	-	-		
Hospitalisations	VE	-	93%	93%	86%	83%	-	-	-	-	-	-	[31, 65]	[.39, .57]
	95% CI	-	[80, 97]	[80, 98]	[65, 94]	[5, 97]	-	-	-	-	-	-		
	95% PI	-	[54, 99]	[55, 99]	[14, 98]	[-43, 98]	-	-	-	-	-	-		
	k (obs)	-	3 (4)	2 (3)	3 (4)	1 (2)	-	-	-	-	-	-		
Mortality	VE	-	93%	82%	79%	-	-	-	-	-	-	-	[0, 79]	[.00, .42]
	95% CI	-	[69, 98]	[-72, 99]	[19, 95]	-	-	-	-	-	-	-		
	95% PI	-	[29, 99]	[-83, 99]	[-49, 98]	-	-	-	-	-	-	-		
	k (obs)	-	2 (2)	1 (1)	2 (2)	-	-	-	-	-	-	-		

Notes. I^2 = Higgin's and Thompson's I^2 presented at the within-study (w) and between-study levels (b); σ = estimate of τ, the standard deviation of effect sizes in the population, presented at the within-study (w) and between-study levels (b); VE = vaccine effectiveness; CI = confidence interval; PI = prediction interval; k = number of studies pooled; obs = number of cohorts/observations pooled; greyed-out cells= fewer than 4 studies.

*VE at this follow-up time point is statistically different from the VE observed at baseline 2 (14-42 days).

eTable 10. Vaccine Effectiveness for Individual Brands of Primary COVID-19 Vaccine Series Against Infections, Hospitalisations, and Mortality.

Vaccine Type & Outcome	Model Estimates	Baseline days (weeks)		Follow-up days (weeks)									I^2 [w, b]	σ [w, b]
		0-13 (0-2)	14-42 (2-6)	112-139 (16-20)	140-167 (20-24)	168-195 (24-28)	196-223 (28-32)	224-251 (32-36)	252-279 (36-40)	280-307 (40-44)	308-335 (44-48)	336+ (48+)		
BNT162b2 VACCINE														
Any variant														
Documented infections	VE	73%	86%†	62%*	52%*	49%*	46%*	44%*	46%*	40%*	46%*	55%*	[24, 76]	[.29, .53]
	95% CI	[59, 82]	[81, 89]	[49, 71]	[38, 63]	[33, 61]	[24, 61]	[24, 59]	[19, 65]	[1, 64]	[-5, 72]	[12, 77]		
	95% PI	[4, 92]	[51, 96]	[-24, 89]	[-39, 86]	[-43, 85]	[-47, 84]	[-48, 84]	[-48, 85]	[-54, 84]		[-44, 89]		
	k (obs)	4 (5)	18 (29)	9 (15)	18 (28)	12 (20)	6 (7)	8 (9)	3 (4)	2 (2)	1 (1)	1 (1)		
Hospitalisations	VE	88%	92%	88%*	84%*	81%*	77%*	77%*	74%*	-	-	68%*	[24, 74]	[.43, .76]
	95% CI	[47, 97]	[87, 95]	[80, 93]	[73, 90]	[67, 89]	[55, 88]	[56, 88]	[44, 88]	-	-	[27, 86]		
	95% PI	[-15, 99]	[52, 99]	[27, 98]	[0, 97]	[-15, 97]	[-34, 96]	[-34, 96]	[-43, 96]	-	-	[-55, 95]		
	k (obs)	1 (1)	13 (20)	6 (11)	7 (12)	6 (8)	3 (5)	5 (5)	2 (3)	-	-	1 (2)		
Mortality	VE	-	95%	93%	89%*	89%*	-	83%*	-	-	-	-	[86, 4]	[.43, .10]
	95% CI	-	[93, 97]	[77, 98]	[81, 94]	[82, 94]	-	[55, 94]	-	-	-	-		
	95% PI	-	[86, 98]	[67, 98]	[67, 97]	[68, 96]	-	[34, 96]	-	-	-	-		
	k (obs)	-	5 (7)	1 (1)	3 (3)	2 (4)	-	1 (1)	-	-	-	-		
Omicron														
Documented infections	VE	-	56%	22%*	23%*	11%*	9%*	-8%*	1%*	-18%*	-1%*	16%*	[85, 15]	[.21, .09]
	95% CI	-	[44, 66]	[-12, 46]	[0, 41]	[-22, 38]	[-34, 45]	[-45, 34]	[-39, 40]	[-51, 27]	[-41, 39]	[-30, 50]		
	95% PI	-	[23, 75]	[-32, 58]	[-27, 57]	[-40, 52]	[-46, 56]	[-55, 47]	[-51, 52]	[-60, 41]	[-52, 51]	[-43, 60]		
	k (obs)	-	4 (5)	2 (2)	3 (4)	2 (2)	1 (1)	1 (1)	1 (1)	1 (1)	1 (1)	1 (1)		
Hospitalisations	VE	79%	68%	52%	54%	59%	42%	38%	44%	-	-	51%	[94, 0]	[.33, .00]
	95% CI	[-77, 99]	[44, 82]	[-13, 80]	[-10, 81]	[31, 75]	[-28, 76]	[-36, 76]	[-24, 76]	-	-	[-14, 79]		
	95% PI	[-80, 99]	[12, 89]	[-38, 86]	[-36, 87]	[-11, 85]	[-49, 83]	[-54, 83]	[-47, 83]	-	-	[-39, 85]		
	k (obs)	1 (1)	4 (4)	1 (1)	1 (1)	3 (3)	1 (1)	1 (1)	1 (1)	-	-	1 (1)		
Delta														
Documented infections	VE	-	91%	76%*	73%*	72%*	70%*	69%*	69%*	-	-	-	[13, 86]	[.12, .32]
	95% CI	-	[86, 94]	[63, 85]	[60, 82]	[57, 82]	[52, 81]	[50, 81]	[48, 82]	-	-	-		
	95% PI	-	[79, 96]	[45, 90]	[39, 88]	[35, 88]	[29, 87]	[26, 87]	[24, 87]	-	-	-		
	k (obs)	-	3 (5)	1 (2)	3 (5)	2 (4)	1 (2)	1 (2)	1 (2)	-	-	-		
Hospitalisations	VE	89%	97%	94%	92%*	89%*	88%*	-	82%*	-	-	74%*	[25, 73]	[.37, .64]
	95% CI	[7, 99]	[92, 99]	[82, 98]	[80, 97]	[69, 96]	[67, 95]	-	[41, 95]	-	-	[9, 92]		
	95% PI	[-38, 99]	[80, 100]	[57, 99]	[47, 99]	[25, 98]	[18, 98]	-	[-25, 98]	-	-	[-51, 97]		
	k (obs)	1 (1)	3 (4)	1 (2)	3 (4)	2 (3)	2 (3)	-	1 (1)	-	-	1 (1)		
(Continued from previous page)														
Mortality	VE	-	99%	-	92%	-	-	-	-	-	-	-	-	-
	95% CI	-	[97, 99]	-	[89, 94]	-	-	-	-	-	-	-		
	95% PI	-	-	-	-	-	-	-	-	-	-	-		
	k (obs)	-	1 (1)	-	1 (1)	-	-	-	-	-	-	-		
mRNA-1273 VACCINE														
Any variant														
Documented infections	VE	-	92%	76%*	72%*	68%*	59%*	62%*	52%*	66%	-	-	[41, 59]	[.43, .51]

Vaccine Type & Outcome	Model Estimates	Baseline days (weeks)		Follow-up days (weeks)									I^2 [w, b]	σ [w, b]
		0-13 (0-2)	14-42 (2-6)	112-139 (16-20)	140-167 (20-24)	168-195 (24-28)	196-223 (28-32)	224-251 (32-36)	252-279 (36-40)	280-307 (40-44)	308-335 (44-48)	336+ (48+)		
	95% CI	-	[88, 94]	[64, 85]	[59, 80]	[49, 80]	[33, 76]	[39, 76]	[5, 76]	[-49, 94]	-	-		
	95% PI	-	[67, 98]	[5, 94]	[-11, 93]	[-23, 92]	[-41, 90]	[-36, 91]	[-53, 89]	[-68, 96]	-	-		
	k (obs)	-	14 (23)	6 (10)	10 (17)	4 (7)	4 (5)	6 (7)	2 (3)	1 (1)	-	-		
Hospitalisations	VE	87%	96%	95%	91%*	87%*	88%*	84%*	82%*	-	-	77%*		
	95% CI	[-24, 99]	[93, 97]	[91, 97]	[85, 95]	[69, 95]	[76, 94]	[59, 94]	[60, 92]	-	-	[46, 91]	[64, 31]	[.49, .35]
	95% PI	[-44, 99]	[83, 99]	[80, 99]	[67, 98]	[42, 97]	[51, 97]	[26, 97]	[23, 96]	-	-	[-2, 95]		
	k (obs)	1 (1)	6 (11)	3 (6)	4 (7)	2 (3)	3 (5)	2 (2)	2 (3)	-	-	1 (2)		
Mortality	VE	-	97%	-	93%	95%	-	88%*	-	-	-	-		
	95% CI	-	[92, 99]	-	[77, 98]	[89, 98]	-	[75, 94]	-	-	-	-	[14, 0]	[.17, .00]
	95% PI	-	[91, 99]	-	[75, 98]	[87, 98]	-	[71, 95]	-	-	-	-		
	k (obs)	-	3 (4)	-	1 (1)	1 (2)	-	1 (1)	-	-	-	-		
Omicron														
Documented infections	VE	-	61%	31%	-6%	-6%	-	-	-	-	-	-		
	95% CI	-	[-99, 100]	[-100, 100]	[-100, 100]	[-100, 100]	-	-	-	-	-	-	[50, 50]	[.45, .45]
	95% PI	-	[-100, 100]	[-100, 100]	[-100, 100]	[-100, 100]	-	-	-	-	-	-		
	k (obs)	-	2 (2)	1 (1)	1 (1)	1 (1)	-	-	-	-	-	-		
Delta														
Documented infections	VE	-	94%	83%*	79%*	77%*	58%*	70%*	62%*	75%	-	-		
	95% CI	-	[92, 95]	[79, 86]	[76, 82]	[72, 81]	[45, 69]	[62, 76]	[51, 71]	[-20, 95]	-	-	[75, 16]	[.14, .07]
	95% PI	-	[91, 96]	[75, 88]	[70, 86]	[66, 84]	[36, 73]	[55, 80]	[42, 75]	[-22, 95]	-	-		
	k (obs)	-	4 (6)	3 (4)	4 (6)	3 (5)	1 (2)	2 (3)	2 (3)	1 (1)	-	-		

Vaccine Type & Outcome	Model Estimates	Baseline days (weeks)		Follow-up days (weeks)									I^2	σ
		0-13 (0-2)	14-42 (2-6)	112-139 (16-20)	140-167 (20-24)	168-195 (24-28)	196-223 (28-32)	224-251 (32-36)	252-279 (36-40)	280-307 (40-44)	308-335 (44-48)	336+ (48+)	[w, b]	[w, b]
(Continued from previous page)														
Hospitalisations	VE	-	98%	97%	93%*	92%*	89%*	-	82%*	-	-	77%*		
	95% CI	-	[95, 99]	[95, 98]	[92, 95]	[78, 97]	[86, 91]	-	[77, 86]	-	-	[61, 86]	[0, 33]	[.00, .10]
	95% PI	-	[95, 99]	[95, 98]	[91, 95]	[77, 97]	[84, 92]	-	[75, 87]	-	-	[59, 87]		
	k (obs)	-	2 (3)	1 (2)	2 (3)	1 (2)	2 (3)	-	1 (1)	-	-	1 (1)		
ChAdOx1 VACCINE														
Any variant														
Documented infections	VE	43%	72%	55%*	50%*	40%*	94%	70%	-31%*	-	-	-		
	95% CI	[-5, 69]	[61, 79]	[35, 69]	[31, 64]	[15, 57]	[48, 99]	[38, 86]	[-78, 52]	-	-	-	[23, 77]	[.26, .46]
	95% PI	[-49, 83]	[14, 91]	[-28, 85]	[-34, 84]	[-46, 80]	[33, 100]	[-8, 92]	[-85, 69]	-	-	-		
	k (obs)	2 (3)	10 (18)	4 (8)	8 (16)	4 (9)	1 (1)	1 (1)	1 (2)	-	-	-		
Hospitalisations	VE	-	92%	92%	87%*	84%*	-	78%	-	-	-	-		
	95% CI	-	[87, 96]	[86, 95]	[78, 93]	[70, 92]	-	[31, 93]	-	-	-	-	[36, 62]	[.42, .55]
	95% PI	-	[67, 98]	[63, 98]	[43, 97]	[26, 97]	-	[-25, 96]	-	-	-	-		
	k (obs)	-	7 (12)	4 (9)	6 (8)	3 (5)	-	1 (1)	-	-	-	-		
Mortality	VE	-	94%	82%	79%*	88%	-	82%*	-	-	-	-		
	95% CI	-	[89, 96]	[9, 96]	[65, 88]	[76, 94]	-	[65, 91]	-	-	-	-	[0, 64]	[.00, .28]
	95% PI	-	[85, 97]	[-4, 97]	[51, 91]	[68, 95]	-	[54, 93]	-	-	-	-		
	k (obs)	-	4 (5)	1 (1)	2 (2)	1 (2)	-	1 (1)	-	-	-	-		
Omicron														
Documented infections	VE	-	40%	-	22%	-3%	-	-	-	-	-	-		
	95% CI	-	[14, 59]	-	[-10, 46]	[-48, 45]	-	-	-	-	-	-	[100, 0]	[.22, .00]
	95% PI	-	[-19, 71]	-	[-37, 62]	[-60, 57]	-	-	-	-	-	-		
	k (obs)	-	2 (3)	-	2 (3)	1 (1)	-	-	-	-	-	-		
Delta														
Documented infections	VE	-	78%	62%*	57%*	49%*	92%	-	-	-	-	-		
	95% CI	-	[69, 85]	[44, 75]	[40, 70]	[27, 65]	[30, 99]	-	-	-	-	-	[9, 91]	[.10, .30]
	95% PI	-	[54, 90]	[18, 83]	[9, 80]	[-8, 76]	[23, 99]	-	-	-	-	-		
	k (obs)	-	4 (6)	1 (2)	4 (6)	2 (4)	1 (1)	-	-	-	-	-		
Hospitalisations	VE	-	93%	93%	86%	83%	-	-	-	-	-	-		
	95% CI	-	[80, 98]	[80, 98]	[65, 94]	[5, 97]	-	-	-	-	-	-	[31, 66]	[.39, .57]
	95% PI	-	[54, 99]	[55, 99]	[14, 98]	[-43, 98]	-	-	-	-	-	-		
	k (obs)	-	3 (4)	2 (3)	3 (4)	1 (2)	-	-	-	-	-	-		
(Continued from previous page)														
Ad26.COV2.S VACCINE														
Any variant														
Documented infections	VE	17%	61%	56%	52%	57%	55%	56%	45%	43%	-	46%		
	95% CI	[-46, 63]	[48, 70]	[41, 67]	[37, 64]	[42, 67]	[27, 72]	[37, 70]	[10, 66]	[7, 65]	-	[13, 67]	[55, 44]	[.20, .17]
	95% PI	[-55, 69]	[27, 79]	[17, 77]	[10, 74]	[19, 77]	[6, 79]	[14, 78]	[-14, 74]	[-17, 73]	-	[-11, 75]		
	k (obs)	1 (1)	4 (5)	3 (4)	4 (4)	4 (4)	1 (1)	2 (2)	1 (1)	1 (1)	-	1 (1)		
Hospitalisations	VE		74%	79%	73%	74%	70%	70%	70%	65%	-	59%		
	95% CI	-	[23, 91]	[24, 94]	[31, 90]	[9, 93]	[-13, 92]	[-6, 92]	[-12, 92]	[-20, 90]	-	[-42, 90]	[86, 0]	[.28, .00]
	95% PI	-	[-24, 95]	[-19, 96]	[-20, 94]	[-32, 95]	[-46, 95]	[-42, 95]	[-45, 95]	[-50, 94]	-	[-63, 94]		

Vaccine Type & Outcome	Model Estimates	Baseline days (weeks)		Follow-up days (weeks)									I^2 [w, b]	σ [w, b]
		0-13 (0-2)	14-42 (2-6)	112-139 (16-20)	140-167 (20-24)	168-195 (24-28)	196-223 (28-32)	224-251 (32-36)	252-279 (36-40)	280-307 (40-44)	308-335 (44-48)	336+ (48+)		
	k (obs)	-	2 (2)	1 (1)	2 (2)	1 (1)	1 (1)	1 (1)	1 (1)	1 (1)	-	1 (1)		
Mortality	VE	-	63%	83%*	77%*	78%*	74%	77%	80%	74%	-	66%		
	95% CI	-	[47, 75]	[74, 88]	[68, 84]	[70, 84]	[57, 85]	[66, 84]	[64, 89]	[61, 82]	-	[40, 81]	[0, 28]	[.00, .13]
	95% PI	-	[42, 77]	[71, 90]	[64, 86]	[67, 86]	[54, 86]	[63, 86]	[61, 89]	[57, 84]	-	[35, 82]		
	k (obs)	-	4 (4)	2 (2)	3 (3)	3 (3)	1 (1)	1 (1)	1 (1)	1 (1)	-	1 (1)		

Notes. I^2 = Higgin's and Thompson's I^2 presented at the within-study (w) and between-study levels (b); σ = estimate of τ, the standard deviation of effect sizes in the population, presented at the within-study (w) and between-study levels (b); VE = vaccine effectiveness; CI = confidence interval; PI = prediction interval; k = number of studies pooled; obs = number of cohorts/observations pooled; greyed-out cells= fewer than 4 studies.

[†]VE at this follow-up time point is statistically different from the VE observed at baseline 1 (0-13 days);

*VE at this follow-up time point is statistically different from the VE observed at baseline 2 (14-42 days).

eTable 11. Vaccine Effectiveness for Booster COVID-19 Vaccine Series Against Infections, Hospitalisations, and Mortality.

Vaccine type & Outcomes	Model Estimates	Baseline days (weeks)		Follow-up days (weeks)			I^2 [w/b]	σ [w/b]
		0-6 (0-1)	7-28 (1-4)	84-111 (12-16)	112-139 (16-20)	140-167 (20-24)		
ANY VACCINE								
Any variants								
Documented infections	VE	-	69%	55%*	42%*	-14%*	[24, 76]	[.34, .61]
	95% CI	-	[56, 79]	[35, 69]	[13, 61]	[-48, 30]		
	95% PI	-	[-23, 93]	[-48, 89]	[-60, 86]	[-81, 74]		
	k (obs)	-	14 (29)	12 (24)	8 (16)	2 (6)		
Hospitalisations	VE	78%	89%†	74%*	71%*	87%	[34, 64]	[.35, .47]
	95% CI	[60, 88]	[82, 93]	[60, 83]	[51, 83]	[60, 95]		
	95% PI	[17, 94]	[59, 97]	[8, 93]	[-6, 92]	[33, 97]		
	k (obs)	1 (4)	7 (11)	8 (15)	4 (5)	1 (1)		
Mortality	VE	83%	87%	86%	85%	73%	[61, 31]	[.31, .22]
	95% CI	[67, 91]	[74, 93]	[76, 92]	[66, 93]	[-37, 96]		
	95% PI	[49, 94]	[60, 96]	[61, 95]	[50, 95]	[-48, 96]		
	k (obs)	1 (4)	2 (2)	3 (6)	1 (1)	1 (1)		
Omicron								
Documented infections	VE	-	66%	50%*	39%*	-19%*	[33, 67]	[.35, .50]
	95% CI	-	[53, 76]	[30, 64]	[11, 58]	[-49, 24]		
	95% PI	-	[-15, 90]	[-43, 86]	[-54, 83]	[-78, 67]		
	k (obs)	-	12 (25)	10 (20)	7 (14)	2 (6)		
Hospitalisations	VE	69%	89%	74%*	71%*	87%	[30, 68]	[.32, .48]
	95% CI	[36, 85]	[82, 93]	[60, 83]	[51, 83]	[62, 95]		
	95% PI	[-20, 92]	[59, 97]	[8, 93]	[-6, 92]	[35, 97]		
	k (obs)	1 (2)	7 (11)	8 (13)	4 (5)	1 (1)		
Mortality	VE	76%	86%	86%	83%	75%	[33, 60]	[.22, .29]
	95% CI	[43, 90]	[72, 93]	[73, 92]	[63, 92]	[-45, 96]		
	95% PI	[14, 93]	[56, 96]	[55, 95]	[42, 95]	[-56, 97]		
	k (obs)	1 (2)	2 (2)	3 (4)	1 (1)	1 (1)		
Delta								
Documented infections	VE	-	92%	90%	-	-	-	-
	95% CI	-	[80, 97]	[88, 91]	-	-		
	95% PI	-	-	-	-	-		
	k (obs)	-	1 (2)	1 (2)	-	-		

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Hospitalisations	VE	88%	-	78%	-	-		
	95% CI	[84, 90]	-	[62, 88]	-	-	-	-
	95% PI	-	-	-	-	-		
	k (obs)	1 (2)	-	1 (2)	-	-		
Mortality	VE	87%	-	88%	-	-		
	95% CI	[81, 91]	-	[77, 94]	-	-	-	-
	95% PI	-	-	-	-	-		
	k (obs)	1 (2)		1 (2)	-	-		
ANY mRNA VACCINE								
Any variants								
Documented infections	VE	-	66%	49%*	36%*	-21%*		
	95% CI	-	[53, 75]	[30, 63]	[9, 55]	[-50, 21]	[34, 66]	[.34, .48]
	95% PI	-	[-14, 90]	[-42, 85]	[-55, 81]	[-78, 65]		
	k (obs)	-	13 (25)	11 (20)	8 (16)	2 (6)		
Hospitalisations	VE	79%	90%	78%*	75%*	87%		
	95% CI	[58, 90]	[85, 93]	[69, 84]	[60, 84]	[62, 95]	[52, 45]	[.35, .33]
	95% PI	[31, 94]	[71, 96]	[37, 92]	[25, 91]	[44, 97]		
	k (obs)	1 (2)	7 (12)	8 (14)	4 (5)	1 (1)		
Mortailty	VE	81%	87%	87%	84%	76%		
	95% CI	[63, 90]	[80, 92]	[81, 92]	[75, 90]	[-35, 96]	[0, 85]	[.00, .24]
	95% PI	[52, 92]	[73, 94]	[73, 94]	[66, 92]	[-42, 97]		
	k (obs)	1 (2)	2 (2)	3 (4)	1 (1)	1 (1)		
Omicron								
Documented infections	VE	-	66%	50%*	38%*	-19%*		
	95% CI	-	[53, 76]	[30, 65]	[10, 58]	[-50, 24]	[34, 66]	[.35, .50]
	95% PI	-	[-17, 91]	[-44, 86]	[-55, 83]	[-78, 67]		
	k (obs)	-	12 (23)	10 (18)	7 (14)	2 (6)		
Hospitalisations	VE	75%	90%	77%*	74%*	86%		
	95% CI	[38, 90]	[85, 93]	[68, 84]	[59, 84]	[61, 95]	[53, 44]	[.36, .33]
	95% PI	[4, 94]	[70, 96]	[35, 92]	[23, 92]	[42, 97]		
	k (obs)	1 (1)	7 (12)	8 (13)	4 (5)	1 (1)		
Mortality	VE	72%	87%	87%	84%	76%		
	95% CI	[16, 91]	[77, 93]	[78, 92]	[73, 91]	[-58, 98]	[0, 88]	[.00, .24]
	95% PI	[-7, 93]	[67, 95]	[68, 95]	[59, 94]	[-63, 98]		
	k (obs)	1 (1)	2 (2)	3 (3)	1 (1)	1 (1)		

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Delta

Hospitalisations	VE	86%	-	83%	-	-		
	95% CI	[82, 89]	-	[74, 89]	-	-	-	-
	95% PI	-	-		-	-		
	k (obs)	1 (1)	-	1 (1)	-	-		
Mortality	VE	84%	-	87%	-	-		
	95% CI	[74, 90]	-	[74, 93]	-	-	-	-
	95% PI	-	-	-	-	-		
	k (obs)	1 (1)	-	1 (1)	-	-		
ANY adenovirus VACCINE								
Any variants								
Documented infections	VE	82%	75%	-	-	-		
	95% CI	[-30, 98]	[-51, 97]	-	-	-	[9, 90]	[.37, 1.17]
	95% PI	[-85, 100]	[-90, 99]	-	-	-		
	k (obs)	2 (4)	2 (4)	-	-	-		
Hospitalisations	VE	82%	-	76%	-	-		
	95% CI	[54, 93]	-	[72, 80]	-	-	-	-
	95% PI	-	-	-	-	-		
	k (obs)	1 (2)	-	1 (2)	-	-		
Mortality	VE	83%	-	82%	-	-		
	95% CI	[61, 93]	-	[50, 94]	-	-	-	-
	95% PI	-	-	-	-	-		
	k (obs)	1 (2)	-	1 (2)	-	-		

Notes. I^2 = Higgin's and Thompson's I^2 presented at the within-study (w) and between-study levels (b); σ = estimate of τ, the standard deviation of effect sizes in the population, presented at the within-study (w) and between-study levels (b); VE = vaccine effectiveness; CI = confidence interval; PI = prediction interval; k = number of studies pooled; obs = number of cohorts/observations pooled; greyed-out cells= fewer than 4 studies.
*VE at this follow-up time point is statistically different from the VE observed at baseline 2 (7-28 days).

eTable 12. Vaccine Effectiveness for Individual Brands of Booster COVID-19 Vaccines Against Infections, Hospitalisations, and Mortality.

Vaccine Type & Outcome	Model Estimates	Baseline days (weeks)		Follow-up days (weeks)			I^2 [w, b]	σ [w, b]
		0-6 (0-1)	7-28 (1-4)	84-111 (12-16)	112-139 (16-20)	140-167 (20-24)		
BNT162b2 VACCINE								
Any variant								
Documented infections	VE	-	71%	60%*	50%*	-29%*	[13, 87]	[.33, .84]
	95% CI	-	[48, 84]	[27, 78]	[4, 74]	[-72, 45]		
	95% PI	-	[-49, 96]	[-63, 94]	[-71, 93]	[-91, 82]		
	k (obs)	-	9 (16)	8 (15)	5 (7)	1 (1)		
Hospitalisations	VE	-	86%	77%*	71%*	85%	[41, 56]	[.28, .33]
	95% CI	-	[78, 91]	[65, 85]	[51, 83]	[60, 94]		
	95% PI	-	[60, 95]	[37, 92]	[17, 90]	[43, 96]		
	k (obs)	-	5 (7)	5 (7)	3 (3)	1 (1)		
Mortality	VE	-	87%	87%	83%	78%	[0, 96]	[.00, .41]
	95% CI	-	[48, 97]	[47, 97]	[33, 96]	[-83, 99]		
	95% PI	-	[-19, 99]	[-21, 99]	[-38, 98]	[-89, 99]		
	k (obs)	-	2 (2)	2 (2)	1 (1)	1 (1)		
Omicron								
Documented infections	VE	-	65%	53%	46%	-36%*	[20, 80]	[.35, .69]
	95% CI	-	[38, 80]	[16, 74]	[-4, 72]	[-76, 40]		
	95% PI	-	[-47, 93]	[-60, 91]	[-66, 90]	[-90, 75]		
	k (obs)	-	7 (13)	6 (12)	4 (5)	1 (1)		
Hospitalisations	VE	-	86%	77%*	71%*	85%	[41, 56]	[.28, .33]
	95% CI	-	[78, 91]	[65, 85]	[51, 83]	[60, 94]		
	95% PI	-	[60, 95]	[37, 92]	[17, 90]	[43, 96]		
	k (obs)	-	5 (7)	5 (7)	3 (3)	1 (1)		
Mortality	VE	-	87%	87%	83%	78%	[0, 96]	[.00, .41]
	95% CI	-	[48, 97]	[47, 97]	[33, 96]	[-83, 99]		
	95% PI	-	[-19, 99]	[-21, 99]	[-38, 98]	[-89, 99]		
	k (obs)	-	2 (2)	2 (2)	1 (1)	1 (1)		
Delta								
Documented infections	VE	-	95%	91%	-	-	-	-
	95% CI	-	[94, 96]	[89, 92]	-	-		
	95% PI	-	-	-	-	-		
	k (obs)	-	1 (1)	1 (1)	-	-		

Vaccine Type & Outcome	Model Estimates	Baseline days (weeks)		Follow-up days (weeks)			I^2 [w, b]	σ [w, b]
		0-6 (0-1)	7-28 (1-4)	84-111 (12-16)	112-139 (16-20)	140-167 (20-24)		
(Continued from previous page)								
mRNA-1273 VACCINE								
Any variant								
Documented infections	VE	-	71%	31%*	32%*	-6%*	[99, 0]	[.43, .00]
	95% CI	-	[54, 81]	[-25, 64]	[1, 54]	[-38, 30]		
	95% PI	-	[19, 89]	[-53, 77]	[-45, 75]	[-65, 61]		
	k (obs)	-	3 (7)	2 (2)	2 (6)	1 (5)		
Hospitalisations	VE	-	90%	84%	77%	-	-	-
	95% CI	-	[87, 93]	[78, 88]	[63, 86]	-		
	95% PI	-	-	-	-	-		
	k (obs)	-	1 (1)	1 (1)	1 (1)	-		
Omicron								
Documented infections	VE	-	71%	31%*	32%*	-6%*	[99, 0]	[.43, .00]
	95% CI	-	[54, 81]	[-25, 64]	[1, 54]	[-38, 30]		
	95% PI	-	[19, 89]	[-53, 77]	[-45, 75]	[-65, 61]		
	k (obs)	-	3 (7)	2 (2)	2 (6)	1 (5)		
Mortality	VE	-	-	-	-	-	-	-
	95% CI	-	-	-	-	-		
	95% PI	-	-	-	-	-		
	k (obs)	-	-	-	-	-		
ChAdOx1 VACCINE								
Any variant								
Documented infections	VE	-	77%	78%	-	-	[3, 95]	[.15, .90]
	95% CI	-	[-27, 96]	[-26, 96]	-	-		
	95% PI	-	[-80, 99]	[-80, 99]	-	-		
	k (obs)	-	2 (3)	2 (3)	-	-		
Hospitalisations	VE	82%	-	76%	-	-	-	-
	95% CI	[54, 93]	-	[72, 80]	-	-		
	95% PI		-		-	-		
	k (obs)	1 (2)	-	1 (2)	-	-		
Mortality	VE	83%	-	82%	-	-	-	-
	95% CI	[61, 93]	-	[50, 94]	-	-		
	95% PI		-		-	-		
	k (obs)	1 (2)	-	1 (2)	-	-		
(Continued from Previous page)								
Omicron								
Documented infections	VE	-	62%	27%	-	-	-	-
	95% CI	-	[44, 74]	[-42, 69]	-	-		

Vaccine Type & Outcome	Model Estimates	Baseline days (weeks)		Follow-up days (weeks)			I^2 [w, b]	σ [w, b]
		0-6 (0-1)	7-28 (1-4)	84-111 (12-16)	112-139 (16-20)	140-167 (20-24)		
	95% PI	-			-	-		
	k (obs)	-	1 (2)	1 (2)	-	-		
Hospitalisations	VE	71%	-	77%	-	-		
	95% CI	[67, 74]	-	[72, 81]	-	-		
	95% PI		-		-	-	-	-
	k (obs)	1 (1)	-	1 (1)	-	-		
Delta								
Documented infections	VE	87%	89%	-	-	-		
	95% CI	[85, 89]	[88, 90]	-	-	-		
	95% PI	[--, --]	[--, --]	-	-	-	-	-
	k (obs)	1 (1)	1 (1)	-	-	-		
Hospitalisations	VE	89%	-	70%	-	-		
	95% CI	[87, 91]	-	[45, 83]	-	-		
	95% PI		-		-	-	-	-
	k (obs)	1 (1)	-	1 (1)	-	-		

Notes. I^2 = Higgin's and Thompson's I^2 presented at the within-study (w) and between-study levels (b); σ = estimate of τ, the standard deviation of effect sizes in the population, presented at the within-study (w) and between-study levels (b); VE = vaccine effectiveness; CI = confidence interval; PI = prediction interval; k = number of studies pooled; obs = number of cohorts/observations pooled; greyed-out cells= fewer than 4 studies.

*VE at this follow-up time point is statistically different from the VE observed at baseline 2 (7-28 days).

Section 5. eResults C – Publication Bias Analyses

5.01. Publication Bias – Sensitivity/Moderation Analyses

Our primary strategy to examine the operation of publication bias was to compare the results of studies that were published in peer-reviewed journals to those from preprint manuscripts. To do so, we used a meta-regression model, specified in a similar way to the primary analyses in our paper (e.g., 3-level model), but added an interaction term to the model between follow-up period and publication status (i.e., both of which were set as moderators in the model). The results of these analyses are presented in the table below (time points with fewer than 4 studies from which to pool results have been greyed out to signify a lower confidence in these numbers relative to those in black font).

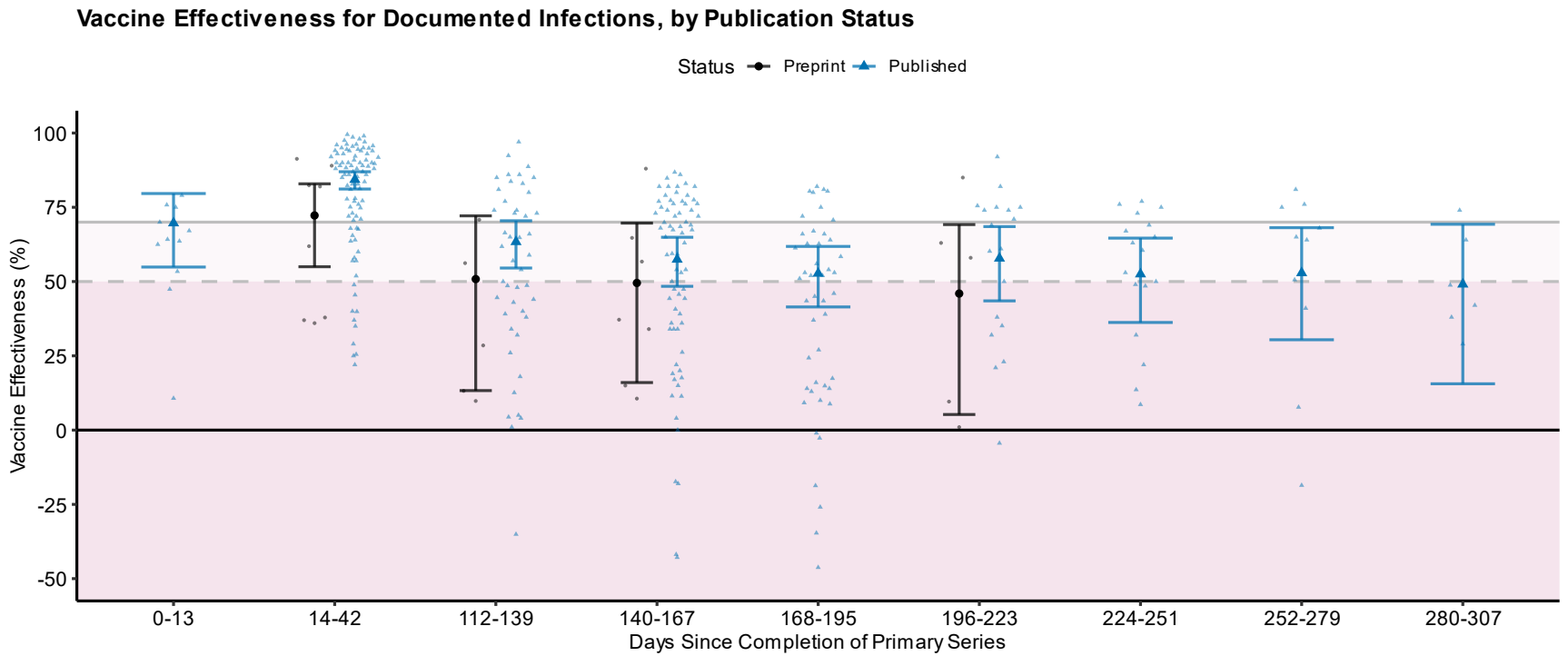
None of the interaction effects between time point and publication status were significant. This was true either when setting the 0-13 days baseline as the comparison group, or the 14-42 days baseline as the comparison group. However, in the latter case, there was a significant main effect of publication status such that the vaccine effectiveness (VE) estimate in the preprint condition was significantly *lower* in the preprint group relative to the published group (log OR = .57 [95% CI: .05, 1.09], p = .031). This pattern suggests that, overall, estimated VEs are lower in the preprint-group at baseline (at 14-42 days), but that there is no significant evidence that the *decline* in VE differs across the two groups. In other words, both published and unpublished (preprint) studies show similar evidence of decline in VE over time. However, the lower starting VE value in the preprint group is carried over across time points; in fact, the estimated VE in the model was lower at every time point for the preprint group compared to the published group. This suggests that the pattern of lower VE in unpublished studies is fairly consistent across time points. Examining the table below qualifies this assertion further.

We qualify the above pattern further by plotting the results of our model. The figure below depicts estimated VEs for published articles and preprint manuscripts across time points, limiting findings to cases when at least 4 studies informed an estimate. Additionally, we plot the VE estimates extracted from the studies that were used for our analyses. These results visually demonstrate a noticeable tendency for preprints to report lower VE estimates than do published studies.

eTable 13. Publication Bias Results – Effects of Any Vaccine for Documented Infections (Primary Series)

Status	Model Estimates	Baseline days		Follow-up days									I^2	σ
		0-13	14-42	112-139	140-167	168-195	196-223	224-251	252-279	280-307	308-335	336+	[w, b]	[w, b]
Published	VE	70%	84%	63%	57%	53%	58%	52%	53%	49%	32%	46%	[54, 45]	[.48, .44]
	95% CI	[55, 80]	[81, 87]	[55, 70]	[48, 65]	[41, 62]	[43, 68]	[36, 65]	[30, 68]	[16, 69]	[-50, 77]	[-13, 74]		
	95% PI	[-14, 92]	[43, 96]	[-25, 90]	[-36, 88]	[-42, 87]	[-36, 89]	[-43, 87]	[-44, 88]	[-50, 87]	[-72, 87]	[-58, 88]		
	k (obs)	6 (11)	34 (88)	18 (45)	26 (70)	18 (46)	11 (18)	10 (17)	6 (10)	4 (6)	1 (1)	2 (2)		
Preprint	VE	55%	72%	51%	50%	42%	46%	34%	25%	33%	32%	43%		
	95% CI	[3, 79]	[55, 83]	[13, 72]	[16, 70]	[-13, 71]	[5, 69]	[-19, 65]	[-41, 67]	[-34, 70]	[-49, 76]	[-39, 80]		
	95% PI	[-50, 90]	[-8, 93]	[-50, 88]	[-50, 87]	[-59, 87]	[-54, 87]	[-64, 84]	[-71, 84]	[-67, 85]	[-72, 87]	[-67, 89]		
	k (obs)	2 (3)	6 (8)	4 (5)	5 (7)	3 (3)	4 (5)	3 (4)	2 (2)	2 (2)	1 (1)	1 (1)		

Notes. I^2 = Higgin's and Thompson's I^2 presented at the within-study (w) and between-study levels (b); σ = estimate of τ, the standard deviation of effect sizes in the population, presented at the within-study (w) and between-study levels (b); VE = vaccine effectiveness; CI = confidence interval; PI = prediction interval; k = number of studies pooled; obs = number of cohorts/observations pooled. The findings aggregate VE estimates from 40 published studies (providing 314 observations) and 8 pre-prints (providing 41 observations). Numbers in grey font are for time points with fewer than 4 studies available for pooling.



eFigure 2. VE Estimates according to the Publication Status of Scientific Studies (Primary Series Against Infections)

In addition to the above analyses, we can also compute a meta-analytic model that ignores time points and examines the main moderating effect of publication status (i.e., a 3-level model, nesting estimates within studies, and only including publication status a moderator). With this model, we find:

1. A non-significant (marginal) moderation effect of publication status such that the vaccine effectiveness (VE) estimate in the preprint condition was significantly *lower* in the preprint group relative to the published group (log OR = **.40** [95% CI: -.01, .82], p = .058);
2. In the published condition the estimated VE is **69%** (95% CI = 63 to 73 [95% PI = -32 to 93]; using 314 observations from 40 studies); and
3. In the preprint condition the estimated VE is **53%** (95% CI = 31 to 68 [95% PI = -56 to 90]; using 41 observations from 8 studies).

Finally, we also conducted the above analyses examining the effects of publication status for VE against hospitalisations (for the primary series only). We computed a full model specified as we did in the initial table we presented for documented infections. The results are provided in the next table. In contrast to our findings for documented infections, there was no main effect of publication status at the baselines (i.e., baseline VEs did not significantly differ across published and unpublished studies at baseline), nor were there any significant interactions between publication status and any of the follow up periods. Although interaction effects were not significant, the estimated VE at each follow-up time point was lower than the corresponding estimated VEs for the published studies, for all but one time point. This could indicate a tendency for published studies to report a higher VE against Hospitalisations generally (compared to unpublished studies). That said, most time points had too few estimates from pre-prints to reliably evaluate the impact of publishing bias (i.e., fewer than 4 studies). As with infections, we also evaluated a model that did not take into account time points (only publication status), and this model did not find a significant effect of publication status.

eTable 14. Publication Bias Results – Effects of Any Vaccine for Hospitalisations (Primary Series)

Status	Model Estimates	Baseline days		Follow-up days									I^2	σ
		0-13	14-42	112-139	140-167	168-195	196-223	224-251	252-279	280-307	308-335	336+	[w, b]	[w, b]
Published	VE	87%	92%	90%	87%	84%	83%	80%	81%	81%	-	75%	[33, 66]	[.51, .72]
	95% CI	[48, 97]	[89, 95]	[85, 93]	[81, 91]	[75, 90]	[71, 90]	[66, 88]	[63, 91]	[40, 94]	-	[48, 88]		
	95% PI	[-17, 99]	[54, 99]	[39, 98]	[21, 98]	[3, 97]	[-6, 97]	[-19, 97]	[-18, 97]	[-35, 98]	-	[-40, 96]		
	k (obs)	1 (1)	18 (50)	8 (32)	13 (33)	6 (13)	6 (8)	7 (9)	3 (4)	1 (1)	0 (0)	2 (3)		
Preprint	VE	86%	88%	81%	87%	79%	-	-	-	-	-	-		
	95% CI	[65, 95]	[70, 95]	[53, 92]	[63, 95]	[52, 91]	-	-	-	-	-	-		
	95% PI	[-1, 98]	[12, 98]	[-28, 97]	[0, 98]	[-31, 97]	-	-	-	-	-	-		
	k (obs)	3 (6)	3 (5)	3 (5)	2 (4)	3 (6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)		

Notes. I^2 = Higgin's and Thompson's I^2 presented at the within-study (w) and between-study levels (b); σ = estimate of τ, the standard deviation of effect sizes in the population, presented at the within-study (w) and between-study levels (b); VE = vaccine effectiveness; CI = confidence interval; PI = prediction interval; k = number of studies pooled; obs = number of cohorts/observations pooled. The findings aggregate VE estimates from 19 published studies (providing 154 observations) and 6 pre-prints (providing 26 observations). Numbers in grey font are for time points with fewer than 4 studies available for pooling.

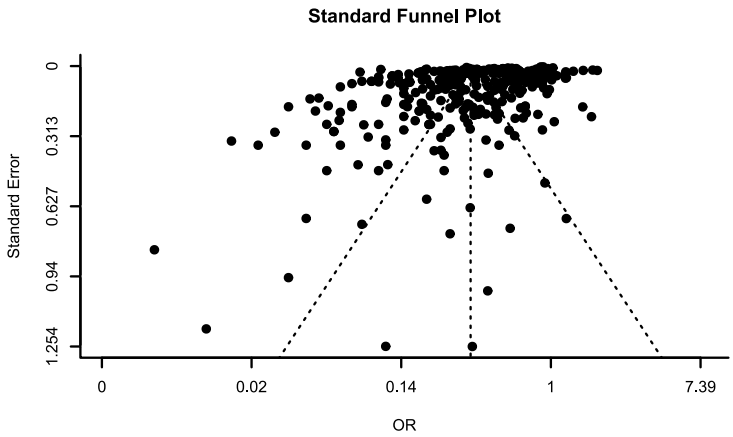
Finally, we considered whether to examine publication bias when it comes to VE against COVID-19 related mortality. However, too few studies were available for this purpose (i.e., we only have data from 1 preprint study examining general mortality data).

5.02. Publication Bias – Funnel Plots

In addition to the above meta-regression analyses, we also generated funnel plots for descriptive purposes. These analyses should not be used to draw strong inferences, as funnel plots are not well adapted to nested data (i.e., three-level meta-analyses). Further, it is important to consider that factors other than publication bias can cause skewness in funnel plots, which could render their interpretation misleading. For example, if we use a funnel plot to consider all VE estimates pooled in the current study (for documented infections), we may theoretically expect the following:

a. VE should wane over time, such that data points associated with longer follow ups show lower VE estimates;
b. That studies show attrition over time (i.e., follow-up VEs rely on increasingly smaller samples); and
c. As a consequence of the above two factors, in the absence of publication bias, we would expect funnel plots to be skewed, such that samples with smaller sample sizes (i.e., translating to larger standard errors) should be associated with low VE by virtue of the two forces described above.

The following figure shows the funnel plot associated with a random-effects model that ignores nesting across studies (i.e., plots all VE estimates, regardless of time point, ignoring that multiple VE estimates are produced by different studies).

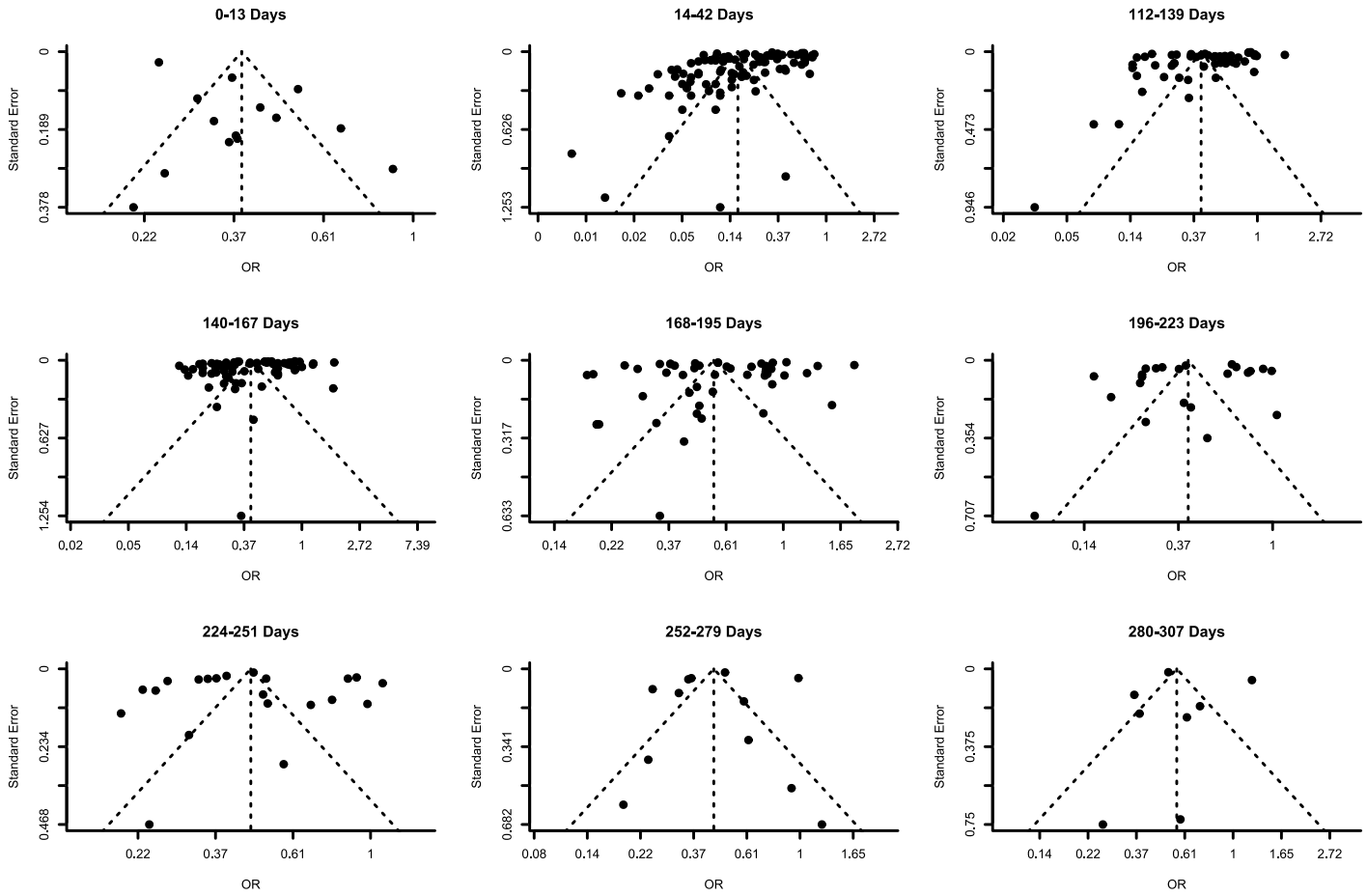


eFigure 3. Funnel Plot Aggregating All VE Estimates Against Documented Infections (Primary Series)

Interestingly, although we would expect a skew in the funnel plot for VE data, the observed skew is in the opposite direction than what we would theoretically expect. Studies with smaller sample sizes show higher VE (as indicated by a smaller OR; the pattern we outlined above would instead show larger OR values being associated with larger standard errors). Although this pattern is plotted in a descriptive manner, this could indicate the presence of publication bias.

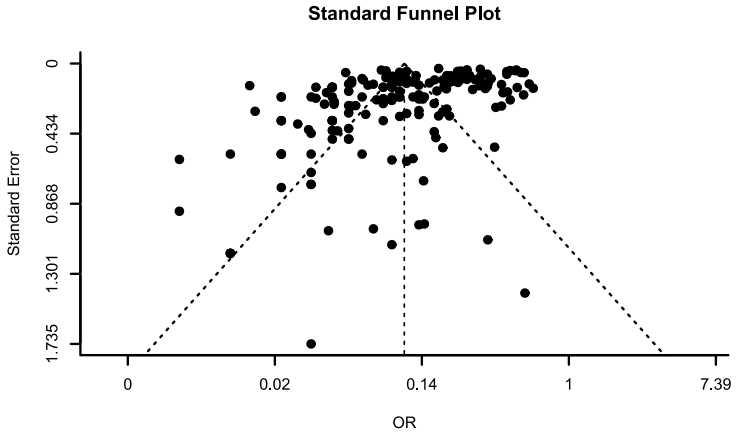
***Overcoming the limitation of funnel plots*.** Although funnel plots do not consider the nesting of the data, and their interpretation can be skewed due to factors such as waning VE and attrition within studies, these two limitations can be partially overcome by subsetting the data we use. Specifically, we can limit funnel plots to consider only a single follow-up period at a given time (e.g., generating a funnel plot at 0-14 days, another at 14-42 days, and so forth). Each of the following funnel plots were therefore generated in this manner. Each relied on analyses computed from random-effects models, limited to one time-point at a time, which pooled VE estimates from across studies. Each study could contribute multiple VE estimates, but only when these estimates were generated from distinct subsamples (i.e., "cohorts"). In line with the convention used above to evaluate publication bias, we only generated funnel plots when at least 4 studies could contribute data for a given time point.

Although many of these funnel plots provide too few data points to reliably comment on the skewness of the VE estimates, there does appear to be considerable skewness for at least a few time points, most notably the 14-42 day interval, and the 112-139 day interval. These results, taken together with the meta-regression analyses above, suggest that publication bias *could* be skewing some of our findings.

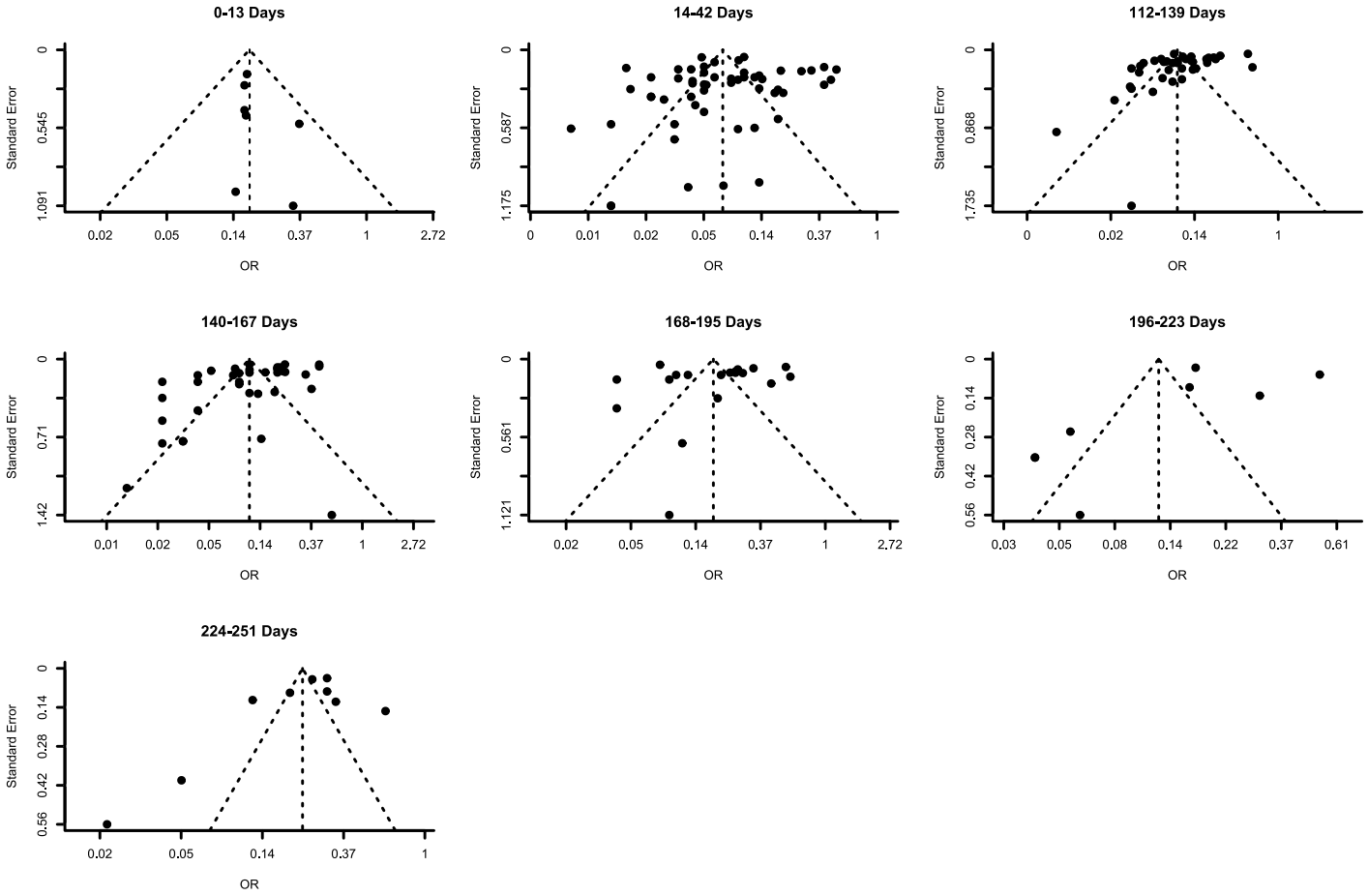


eFigure 4. Funnel Plot Aggregating VE Estimates Against Documented Infections, Broken Down by Time Point (Primary Series)

The above analyses were also repeated for the hospitalisation outcome. The results are in the plots below. Overall, there is again some evidence of skewness, depending on the time point being considered. Notably, most follow-up periods (112 days and above) show skewness in the plots. As with VE against documented infections, the direction of the skewness indicates that estimates with larger standard errors (e.g., from smaller studies) are associated with higher VE levels (i.e., smaller ORs). This again suggests that bias could be skewing our findings.



eFigure 5. Funnel Plot Aggregating All VE Estimates Against Hospitalisations (Primary Series)



eFigure 6. Funnel Plot Aggregating VE Estimates Against Hospitalisations, Broken Down by Time Point (Primary Series).

Section 6. eResults D – Robustness Analyses, Moderation By Study Design

Our meta-analysis evaluated results from three types of study designs: (1) Case control studies, predominantly using test-negative designs; (2) cohort-based studies; and (3) randomised control trials [RCTs]. To examine the impact of different study designs, we computed a three level meta-analytic model which examined moderation according to an interaction effect between time point and study design. The table below summarizes the predicted vaccine effectiveness (VE) estimates of this model for each time point.

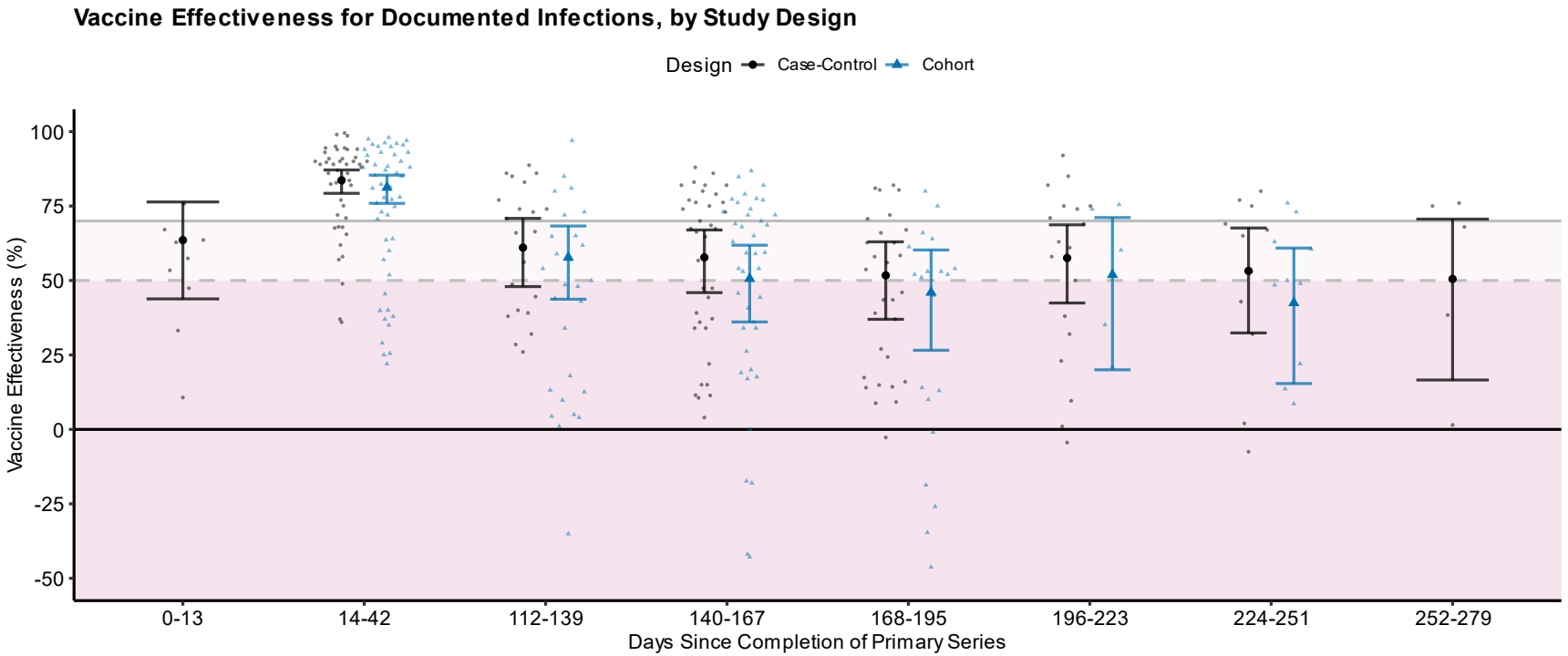
Overall, there was no significant difference between studies that used a case control or a cohort-based design (at any time point). Examining the table below further shows that roughly similar findings are available across both groups. RCTs did lead to significant differences against the 2nd baseline (14-42 days) and against the 252-279 day follow-up, when compared to either the case control or the cohort studies. All other comparisons were not statistically significant. However, these results are based on only 2 RCT studies at baseline and 1 RCT study at the follow up. Thus, the estimates specific to RCT designs may not be accurate, and particularly so for the 252-279 day follow-up, which has a very wide confidence interval (-75% to 73%). For the 14-42 day baseline, if the results are accurate, the higher VE estimate could be linked to the fact that RCTs were generally conducted early on in the pandemic, before the emergence of new variants of COVID-19. Nevertheless, the overall set of analyses provides little support for concerns that a different pattern of findings may emerge across the different designs. If RCTs were to have a tendency to produce different results than other designs, this should be monitored by future studies. However, for the purpose of our review, the addition of RCTs to our model likely has little overall impact on our results given that they make up a very small portion of the studies we synthesized.

eTable 15. Moderation by Study Design – Effects of Any Vaccine for Documented Infections (Primary Series)

Design	Model Estimates	Baseline days		Follow-up days									I^2	σ
		0-13	14-42	112-139	140-167	168-195	196-223	224-251	252-279	280-307	308-335	336+	[w, b]	[w, b]
Case	VE	64%	84%	61%	58%	52%	58%	53%	50%	49%	47%	56%		
Control	95% CI	[44, 76]	[79, 87]	[48, 71]	[46, 67]	[37, 63]	[42, 69]	[32, 68]	[17, 71]	[2, 74]	[-32, 81]	[-19, 84]		
	95% PI	[-28, 90]	[41, 95]	[-30, 89]	[-34, 88]	[-43, 87]	[-36, 88]	[-43, 87]	[-48, 87]	[-53, 88]	[-63, 89]	[-56, 91]		
	k (obs)	5 (9)	21 (45)	10 (21)	15 (36)	12 (29)	11 (18)	7 (11)	4 (5)	3 (3)	1 (1)	1 (1)	[57, 43]	[.48, .42]
Cohort	VE	72%	81%	58%	51%	46%	52%	42%	49%	41%	22%	38%		
	95% CI	[41, 87]	[76, 85]	[44, 68]	[36, 62]	[27, 60]	[20, 71]	[15, 61]	[14, 70]	[-5, 66]	[-57, 74]	[-25, 71]		
	95% PI	[-18, 93]	[32, 95]	[-35, 88]	[-44, 86]	[-49, 85]	[-47, 88]	[-53, 85]	[-50, 87]	[-58, 85]	[-76, 85]	[-63, 86]		
	k (obs)	2 (3)	17 (49)	10 (27)	16 (41)	9 (20)	4 (5)	6 (10)	3 (5)	3 (5)	1 (1)	2 (2)		
RCT	VE	63%	94%	88%	-	-	-	-	-4%	-	-	-		
	95% CI	[-10, 88]	[85, 98]	[67, 96]	-	-	-	-	[-75, 73]	-	-	-		
	95% PI	[-49, 93]	[71, 99]	[40, 98]	-	-	-	-	[-85, 84]	-	-	-		
	k (obs)	1 (2)	2 (2)	2 (2)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)		

Notes. RCT = randomized control trial; I^2 = Higgin's and Thompson's I^2 presented at the within-study (w) and between-study levels (b); σ = estimate of τ, the standard deviation of effect sizes in the population, presented at the within-study (w) and between-study levels (b); VE = vaccine effectiveness; CI = confidence interval; PI = prediction interval; k = number of studies pooled; obs = number of cohorts/observations pooled. The findings aggregate VE estimates from 26 case control studies (providing 179 observations), 19 cohort studies (providing 168 observations), and 3 RCTs (providing 8 observations). Numbers in grey font are for time points with fewer than 4 studies available for pooling.

The figure below summarizes our results by plotting all estimates (and observations) for time points for which 4 or more studies contributed data points.



eFigure 7. VE Estimates according to the Design of Scientific Studies.

Section 7. eResults E – Robustness Analyses, Leave-One-Out Analyses

To evaluate whether our meta-analytic modelling may be robust to the inclusion/exclusion of any given study from our analyses, we conducted a "leave-one-out" set of analyses. These focused on estimating levels of VE (across time points) for the primary vaccine series and the first booster against infections and hospitalizations (caused by any variant, and when considering any vaccine type). The figures in this section are forest plots that provide the results of these analyses, for each time point considered (i.e., baseline and follow up periods). These correspond to the results from the Figures in our main text.

First, a single three-level analysis was conducted to evaluate VE when including **all** reviewed studies that provided data on the VE of primary series. The results of this analysis are provided at the bottom row of each forest plot. For example, the bottom row for section 7.01 (effects of the primary series against infections) corresponds to the first row of Table 1 in our main manuscript (this row is labelled "Total" under the Source column of the forest plots). These estimates serve as a baseline when examining the effects of leaving any given study out of the analysis. Importantly, the estimates for this row all come from a single model (i.e., a single model provided estimates for all time points separately). The results of each time points are presented in different figures solely due to the large number of estimates provided by these analyses.

Second, a new three-level meta-analytic model was computed for each study in our review, dropping the study from our analysis. For example, the top row of the first set of figures provides VE data when study "01A-3" is dropped from the analysis (each code in the "Source" column stands for a different study; see our raw dataset to see which code corresponds to which study). Because our VE estimates pooled the results of 48 studies, the forest plots each include 48 rows specific to excluding each study individually.

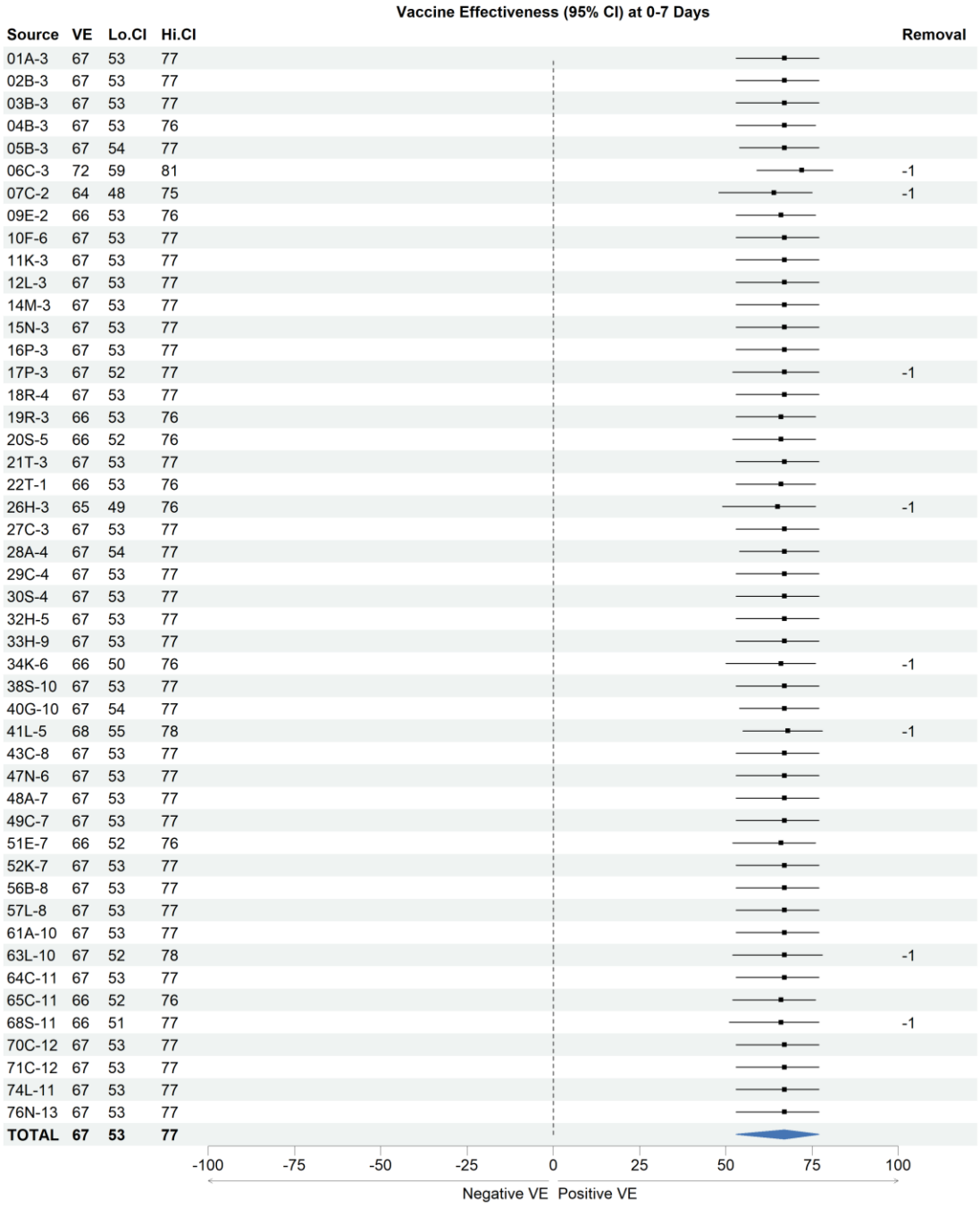
Estimates are provided for each of the studies (and for the total) for *every* time point, even though any given study provided data for only a subset of time points at a time. The reason for this, is that VEs across *all* time points are estimated simultaneously in a *single* multi-level model. Consequently, VE estimates at one time point not only consider data from that time point alone, but also across other time points (to account for baseline differences across studies). The column labelled "Removal" indicates whether the study provided an observation at the time point plotted or not in a specific figure (this is indicated by the presence of a "-1" indicating that the study was removed from contributing data for a given line).

Lastly, we also included some columns indicating whether the significance of our moderation tests differed based on the exclusion of any given study. For the baseline at 14-42 days (the 2nd forest plot), a column "increase" indicated whether the estimated VE at 14-42 days is significantly different (i.e., higher) than the VE from the 1st first plot at 0-7 days. In the 3rd plot, and each plot after, a column labelled "Waning" indicates whether the VE at that follow up period (e.g., at 112-139 days) was significantly different from the VE established at the baseline period of 14-42 days.

Findings. All leave-one-out analyses indicate that dropping any given study would have a negligible influence on our estimates. The point estimates and their 95% confidence intervals remain fairly stable (and similar) across all exclusions. Further, the significance of the moderation test comparing the 2nd baseline to each other time point is also very stable across exclusions.

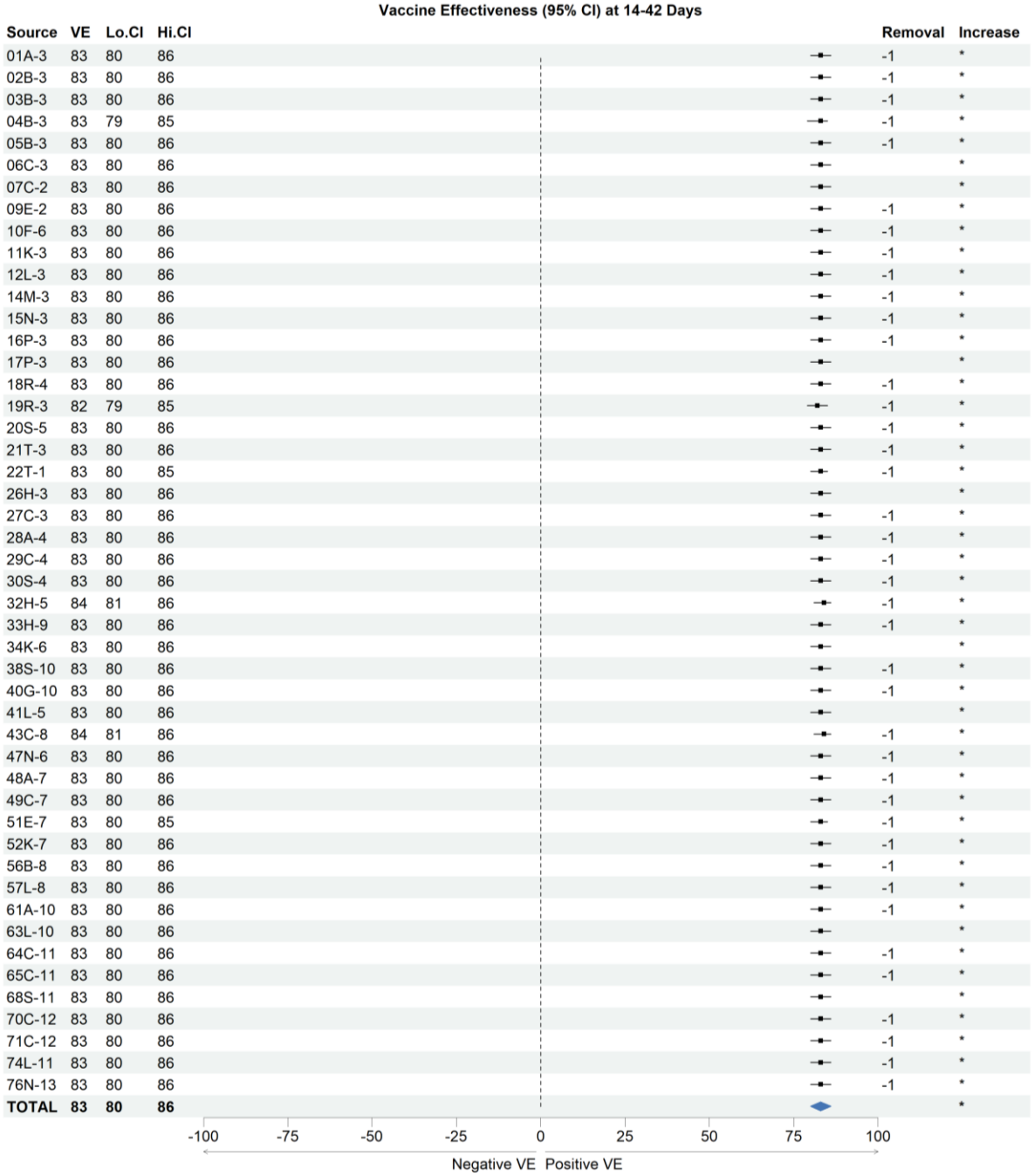
7.01. Leave-One-Out Analyses for the Primary Series Against Infections

eFigure 8. ***Leave-one-Out Analyses, Depicting the Impact of the Primary Series Against Infections at 0-7 Days.***



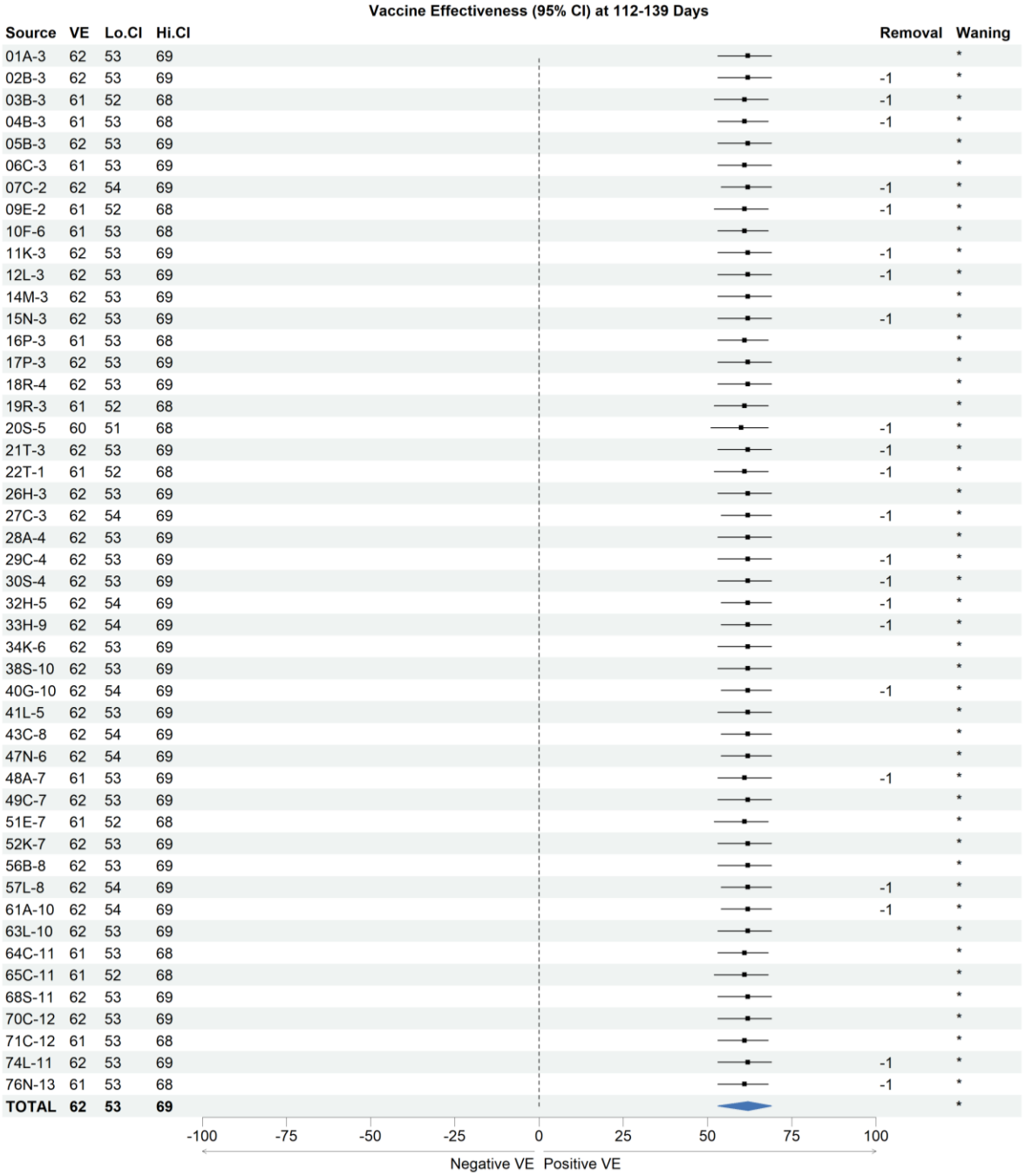
Notes. Source = individual studies from the review where each row indicates results when a specific study is excluded from the analysis (e.g., row 1 excludes study "01A-3"). VE = vaccine effectiveness. Lo.CI = lower bound of the 95% confidence interval around the VE estimate. Hi.CI = higher bound of the 95% confidence interval around the VE estimate. Removal = this column indicates whether a given study contributed observations specific to this time point (if so, this is indicated by a -1).

eFigure 9. ***Leave-one-Out Analyses, Depicting the Impact of the Primary Series Against Infections at 14-42 Days.***



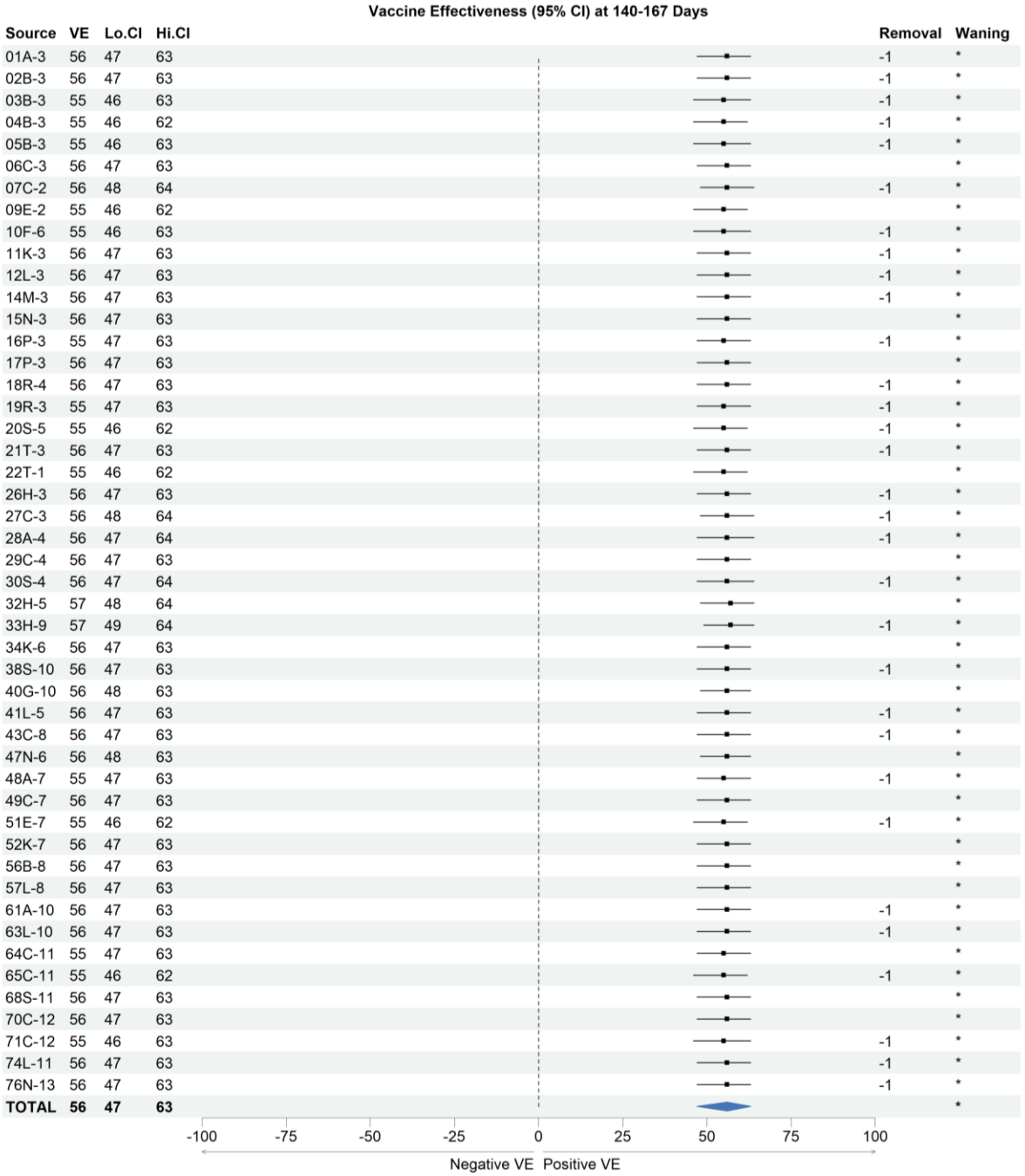
Notes. Source = individual studies from the review where each row indicates results when a specific study is excluded from the analysis (e.g., row 1 excludes study "01A-3"). VE = vaccine effectiveness. Lo.CI = lower bound of the 95% confidence interval around the VE estimate. Hi.CI = higher bound of the 95% confidence interval around the VE estimate. Removal = this column indicates whether a given study contributed observations specific to this time point (if so, this is indicated by a -1). Increase = a column indicating whether the VE at 14-42 days is significantly higher than the VE at 0-7 days (1st plot)

eFigure 10. ***Leave-one-Out Analyses, Depicting the Impact of the Primary Series Against Infections at 112-139 Days.***



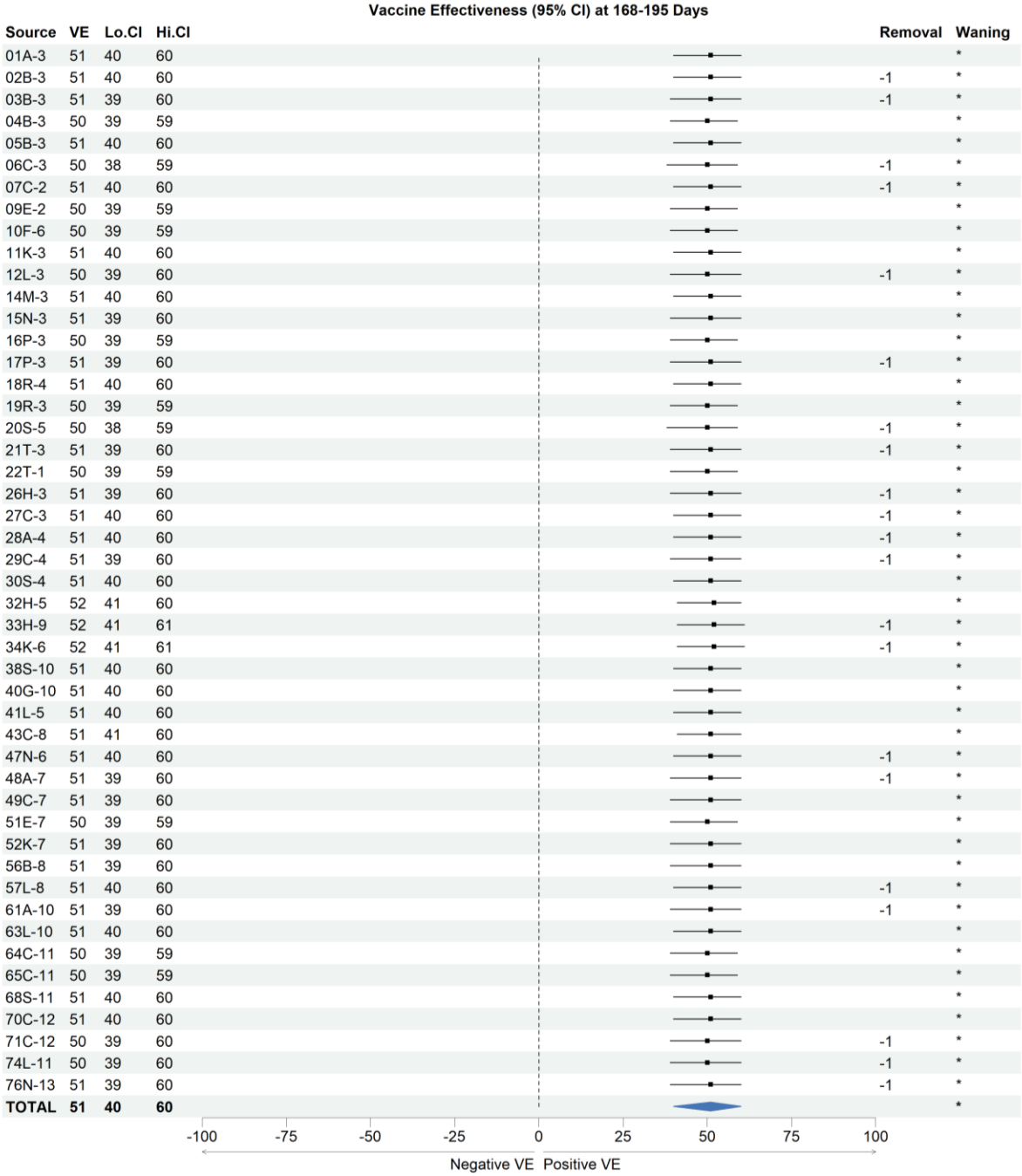
Notes. Source = individual studies from the review where each row indicates results when a specific study is excluded from the analysis (e.g., row 1 excludes study "01A-3"). VE = vaccine effectiveness. Lo.CI = lower bound of the 95% confidence interval around the VE estimate. Hi.CI = higher bound of the 95% confidence interval around the VE estimate. Removal = this column indicates whether a given study contributed observations specific to this time point (if so, this is indicated by a -1). Waning = a column indicating whether the VE at this time point is significantly lower than the VE at 14-42 days (2nd plot).

eFigure 11. ***Leave-one-Out Analyses, Depicting the Impact of the Primary Series Against Infections at 140-167 Days.***



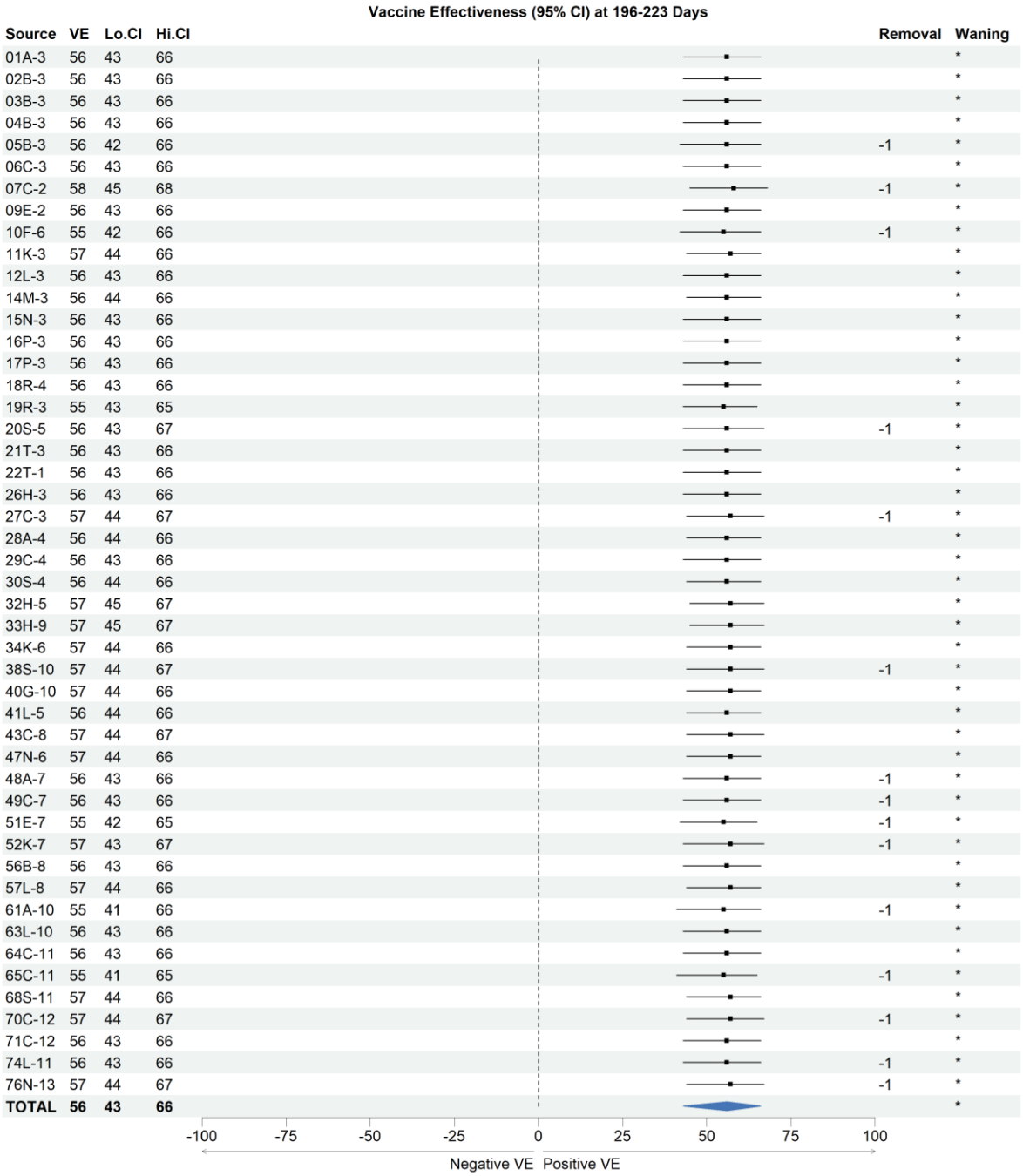
Notes. Source = individual studies from the review where each row indicates results when a specific study is excluded from the analysis (e.g., row 1 excludes study "01A-3"). VE = vaccine effectiveness. Lo.CI = lower bound of the 95% confidence interval around the VE estimate. Hi.CI = higher bound of the 95% confidence interval around the VE estimate. Removal = this column indicates whether a given study contributed observations specific to this time point (if so, this is indicated by a -1). Waning = a column indicating whether the VE at this time point is significantly lower than the VE at 14-42 days (2nd plot).

eFigure 12. ***Leave-one-Out Analyses, Depicting the Impact of the Primary Series Against Infections at 168-195 Days.***



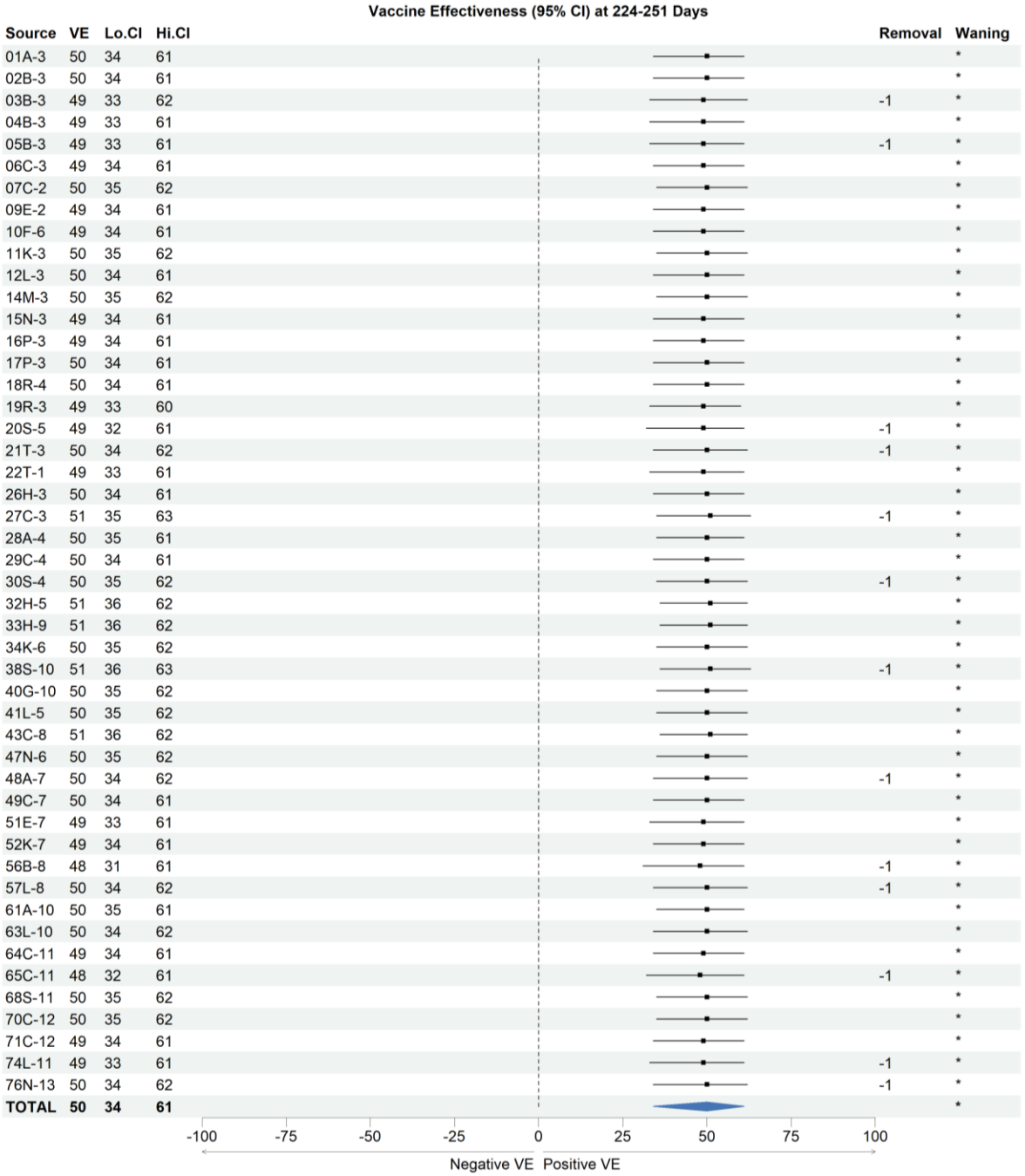
Notes. Source = individual studies from the review where each row indicates results when a specific study is excluded from the analysis (e.g., row 1 excludes study "01A-3"). VE = vaccine effectiveness. Lo.CI = lower bound of the 95% confidence interval around the VE estimate. Hi.CI = higher bound of the 95% confidence interval around the VE estimate. Removal = this column indicates whether a given study contributed observations specific to this time point (if so, this is indicated by a -1). Waning = a column indicating whether the VE at this time point is significantly lower than the VE at 14-42 days (2nd plot).

eFigure 13. ***Leave-one-Out Analyses, Depicting the Impact of the Primary Series Against Infections at 196-223 Days.***



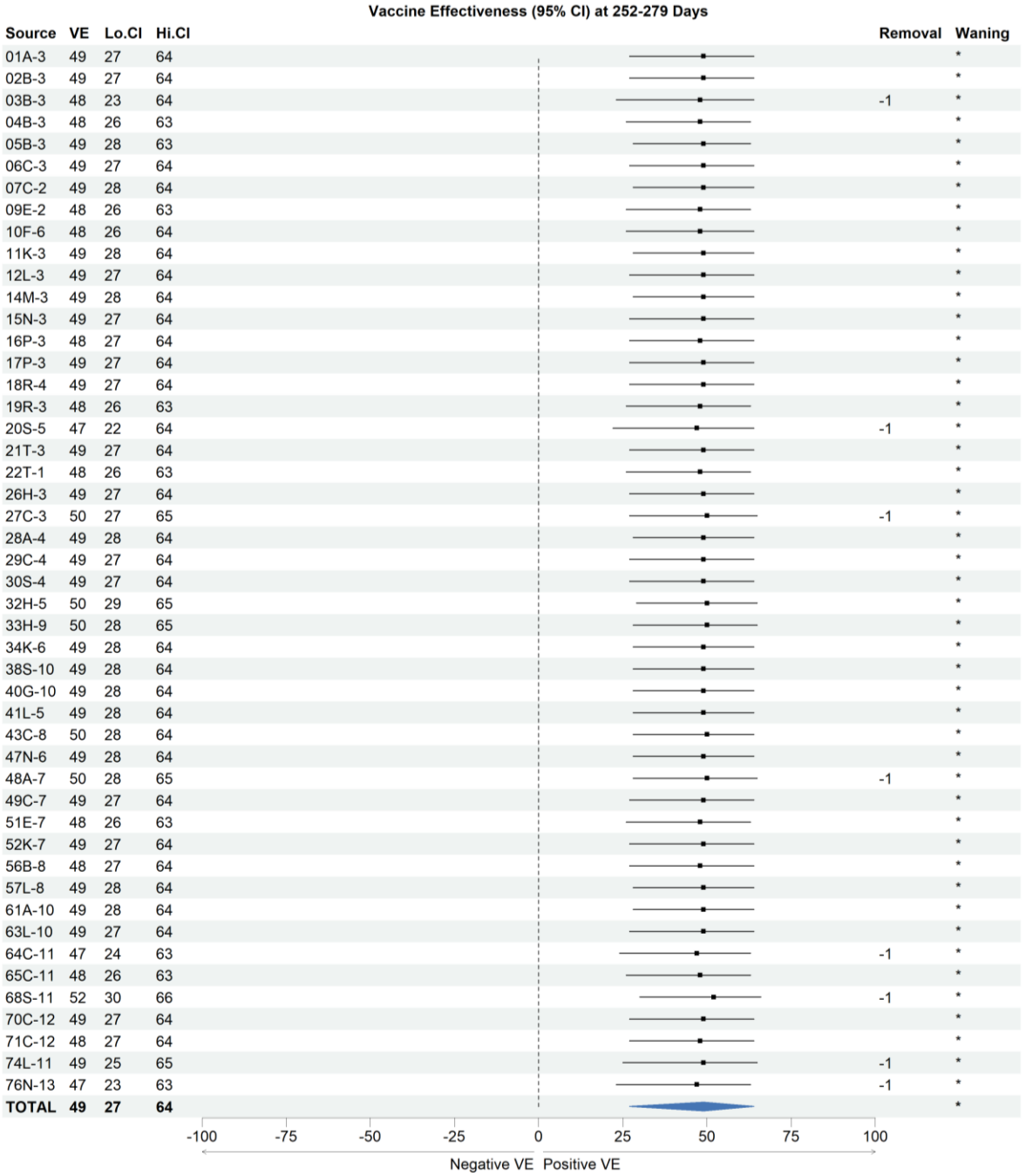
Notes. Source = individual studies from the review where each row indicates results when a specific study is excluded from the analysis (e.g., row 1 excludes study "01A-3"). VE = vaccine effectiveness. Lo.CI = lower bound of the 95% confidence interval around the VE estimate. Hi.CI = higher bound of the 95% confidence interval around the VE estimate. Removal = this column indicates whether a given study contributed observations specific to this time point (if so, this is indicated by a -1). Waning = a column indicating whether the VE at this time point is significantly lower than the VE at 14-42 days (2nd plot).

eFigure 14. ***Leave-one-Out Analyses, Depicting the Impact of the Primary Series Against Infections at 224-251 Days.***



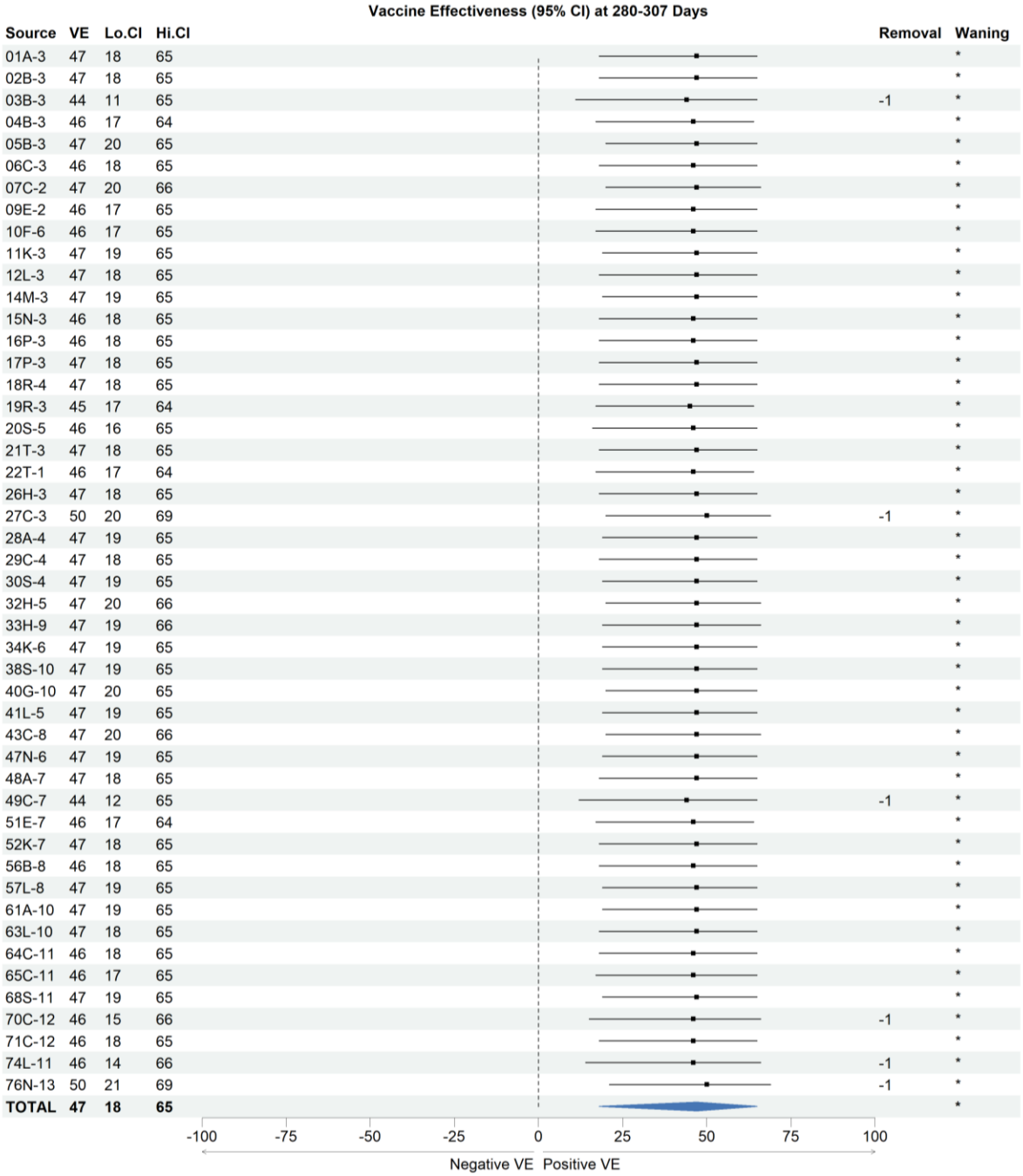
Notes. Source = individual studies from the review where each row indicates results when a specific study is excluded from the analysis (e.g., row 1 excludes study "01A-3"). VE = vaccine effectiveness. Lo.CI = lower bound of the 95% confidence interval around the VE estimate. Hi.CI = higher bound of the 95% confidence interval around the VE estimate. Removal = this column indicates whether a given study contributed observations specific to this time point (if so, this is indicated by a -1). Waning = a column indicating whether the VE at this time point is significantly lower than the VE at 14-42 days (2nd plot).

eFigure 15. ***Leave-one-Out Analyses, Depicting the Impact of the Primary Series Against Infections at 252-279 Days.***



Notes. Source = individual studies from the review where each row indicates results when a specific study is excluded from the analysis (e.g., row 1 excludes study "01A-3"). VE = vaccine effectiveness. Lo.CI = lower bound of the 95% confidence interval around the VE estimate. Hi.CI = higher bound of the 95% confidence interval around the VE estimate. Removal = this column indicates whether a given study contributed observations specific to this time point (if so, this is indicated by a -1). Waning = a column indicating whether the VE at this time point is significantly lower than the VE at 14-42 days (2nd plot).

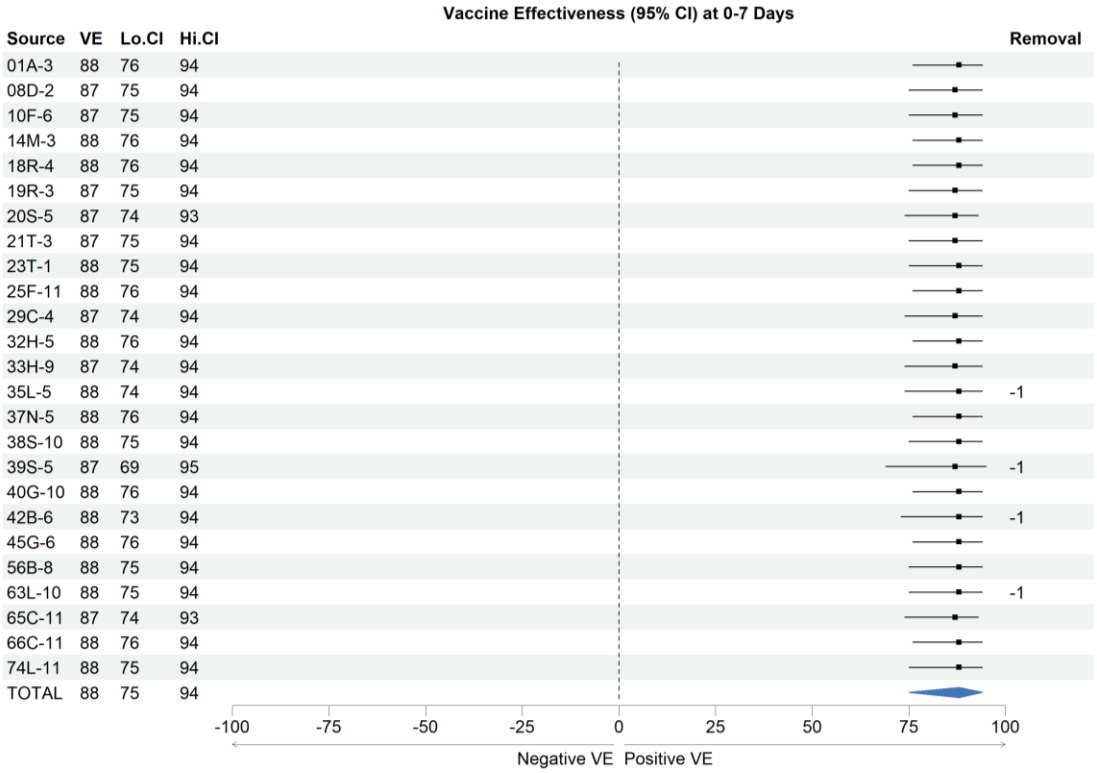
eFigure 16. ***Leave-one-Out Analyses, Depicting the Impact of the Primary Series Against Infections at 280-307 Days.***



Notes. Source = individual studies from the review where each row indicates results when a specific study is excluded from the analysis (e.g., row 1 excludes study "01A-3"). VE = vaccine effectiveness. Lo.CI = lower bound of the 95% confidence interval around the VE estimate. Hi.CI = higher bound of the 95% confidence interval around the VE estimate. Removal = this column indicates whether a given study contributed observations specific to this time point (if so, this is indicated by a -1). Waning = a column indicating whether the VE at this time point is significantly lower than the VE at 14-42 days (2nd plot).

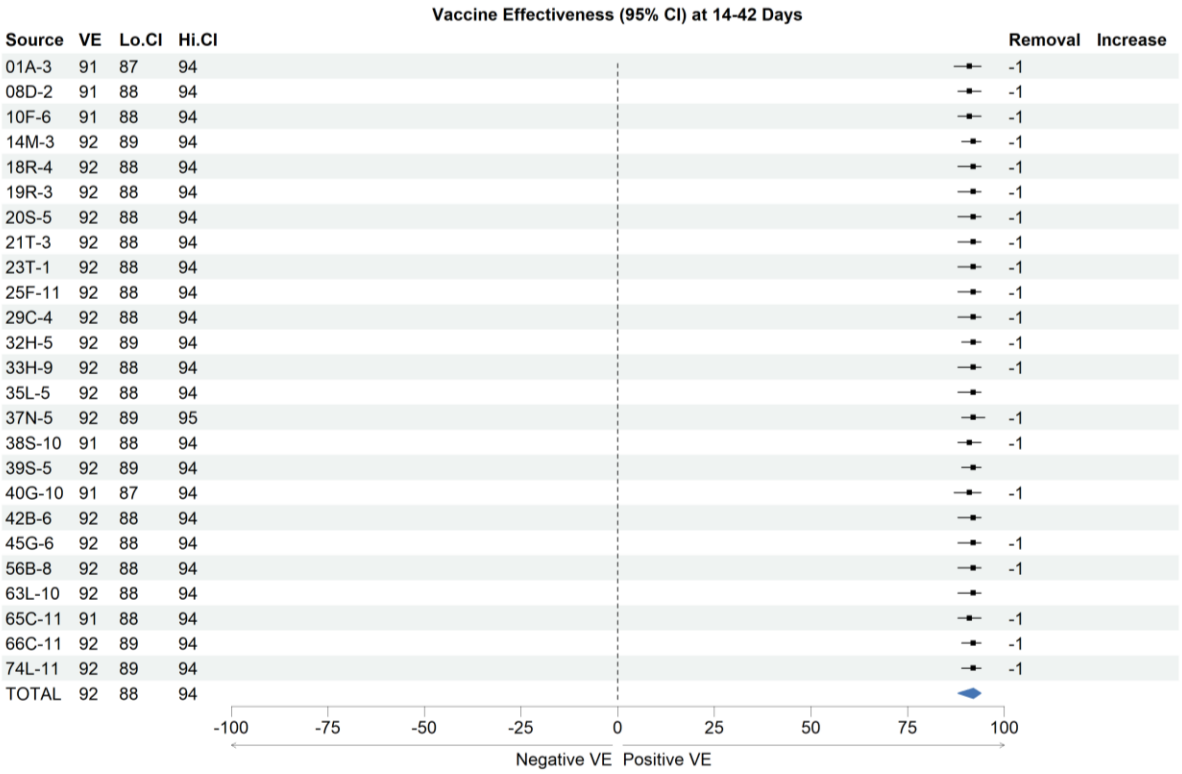
7.02. Leave-One-Out Analyses for the Primary Series Against Hospitalisations

eFigure 17. ***Leave-one-Out Analyses, Depicting the Impact of the Primary Series Against Hospitalisations at 0-7 Days.***



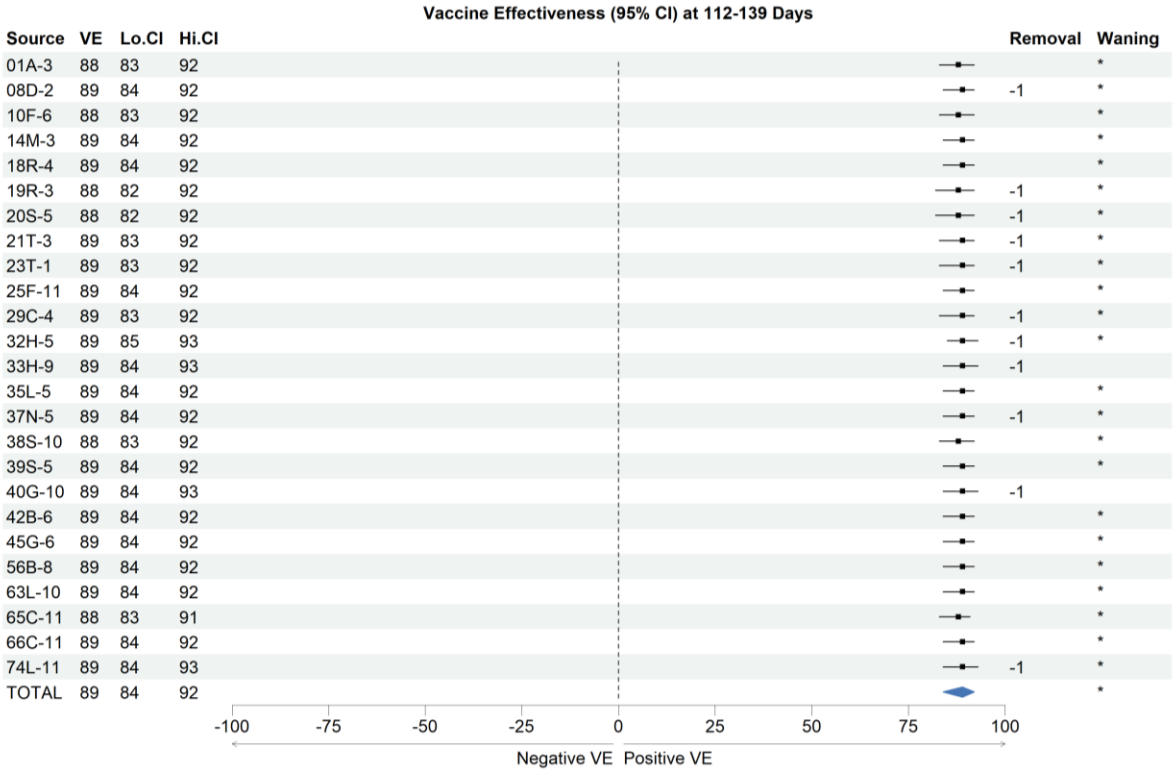
Notes. Source = individual studies from the review where each row indicates results when a specific study is excluded from the analysis (e.g., row 1 excludes study "01A-3"). VE = vaccine effectiveness. Lo.CI = lower bound of the 95% confidence interval around the VE estimate. Hi.CI = higher bound of the 95% confidence interval around the VE estimate. Removal = this column indicates whether a given study contributed observations specific to this time point (if so, this is indicated by a -1).

eFigure 18. ***Leave-one-Out Analyses, Depicting the Impact of the Primary Series Against Hospitalisations at 14-42 Days.***



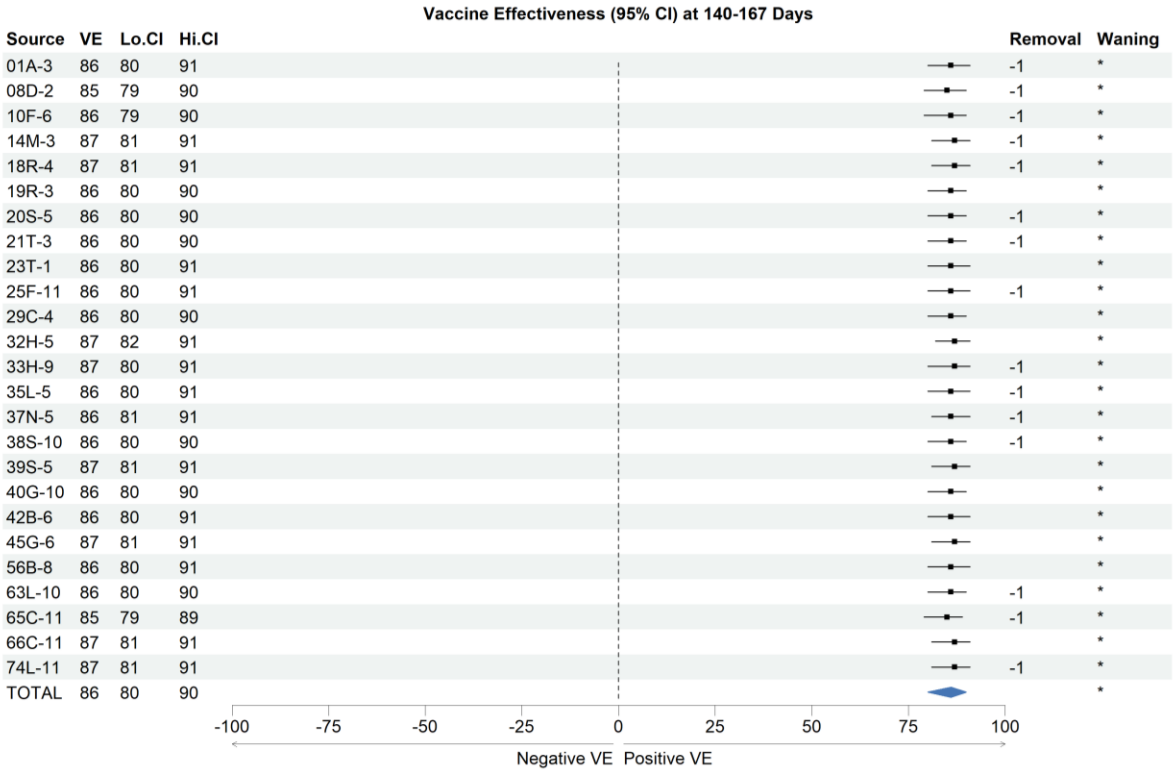
Notes. Source = individual studies from the review where each row indicates results when a specific study is excluded from the analysis (e.g., row 1 excludes study "01A-3"). VE = vaccine effectiveness. Lo.CI = lower bound of the 95% confidence interval around the VE estimate. Hi.CI = higher bound of the 95% confidence interval around the VE estimate. Removal = this column indicates whether a given study contributed observations specific to this time point (if so, this is indicated by a -1). Increase = a column indicating whether the VE at 14-42 days is significantly higher than the VE at 0-7 days (1st plot)

eFigure 19. ***Leave-one-Out Analyses, Depicting the Impact of the Primary Series Against Hospitalisations at 112-139 Days.***



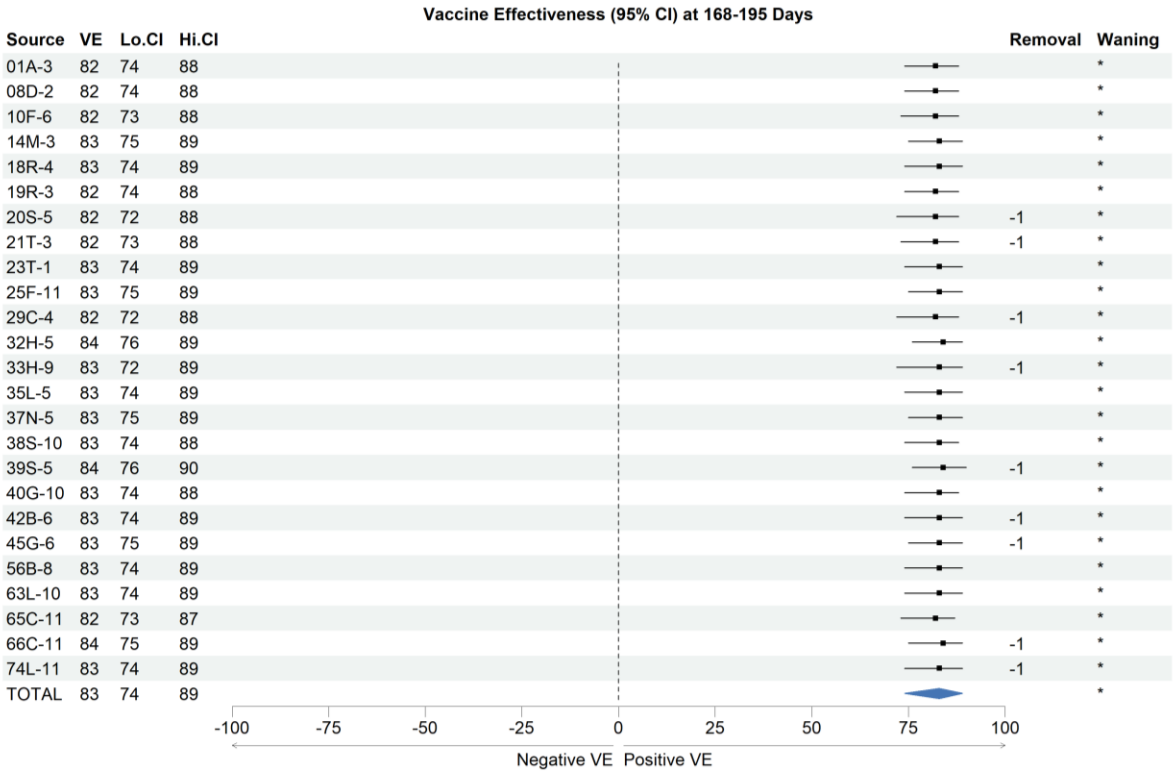
Notes. Source = individual studies from the review where each row indicates results when a specific study is excluded from the analysis (e.g., row 1 excludes study "01A-3"). VE = vaccine effectiveness. Lo.CI = lower bound of the 95% confidence interval around the VE estimate. Hi.CI = higher bound of the 95% confidence interval around the VE estimate. Removal = this column indicates whether a given study contributed observations specific to this time point (if so, this is indicated by a -1). Waning = a column indicating whether the VE at this time point is significantly lower than the VE at 14-42 days (2nd plot).

eFigure 20. ***Leave-one-Out Analyses, Depicting the Impact of the Primary Series Against Hospitalisations at 140-167 Days.***



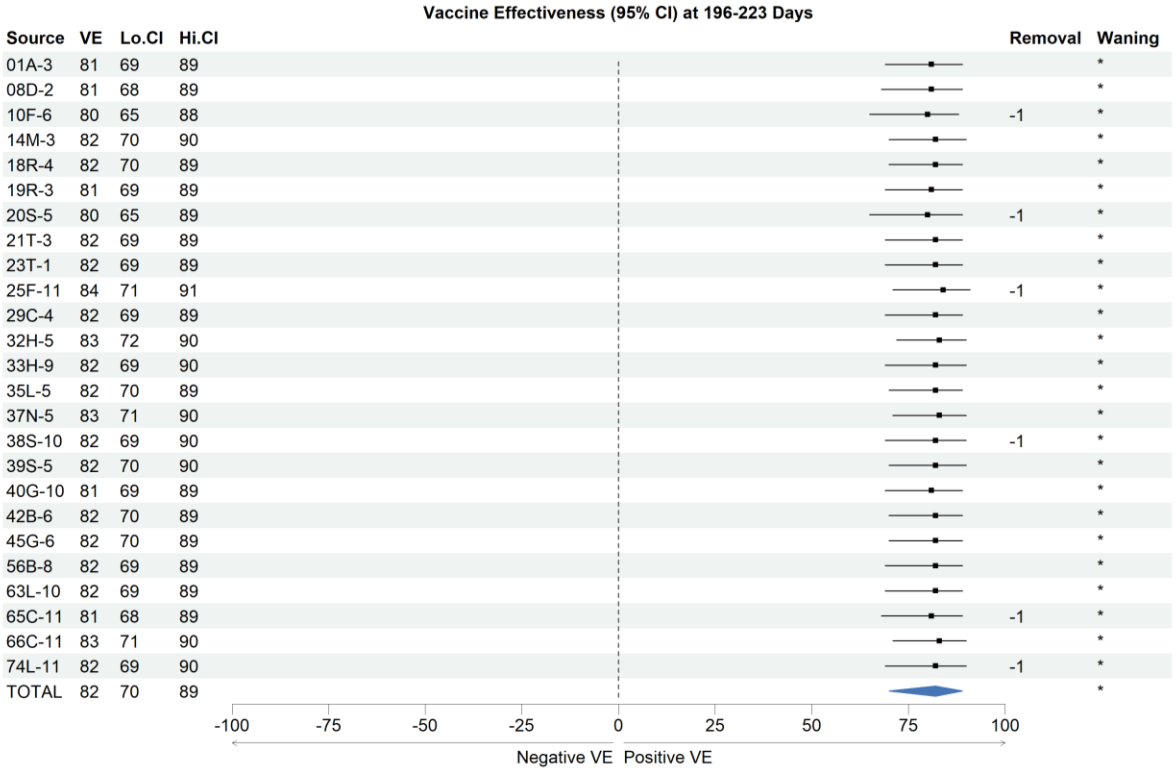
Notes. Source = individual studies from the review where each row indicates results when a specific study is excluded from the analysis (e.g., row 1 excludes study "01A-3"). VE = vaccine effectiveness. Lo.CI = lower bound of the 95% confidence interval around the VE estimate. Hi.CI = higher bound of the 95% confidence interval around the VE estimate. Removal = this column indicates whether a given study contributed observations specific to this time point (if so, this is indicated by a -1). Waning = a column indicating whether the VE at this time point is significantly lower than the VE at 14-42 days (2nd plot).

eFigure 211. ***Leave-one-Out Analyses, Depicting the Impact of the Primary Series Against Hospitalisations at 168-195 Days.***



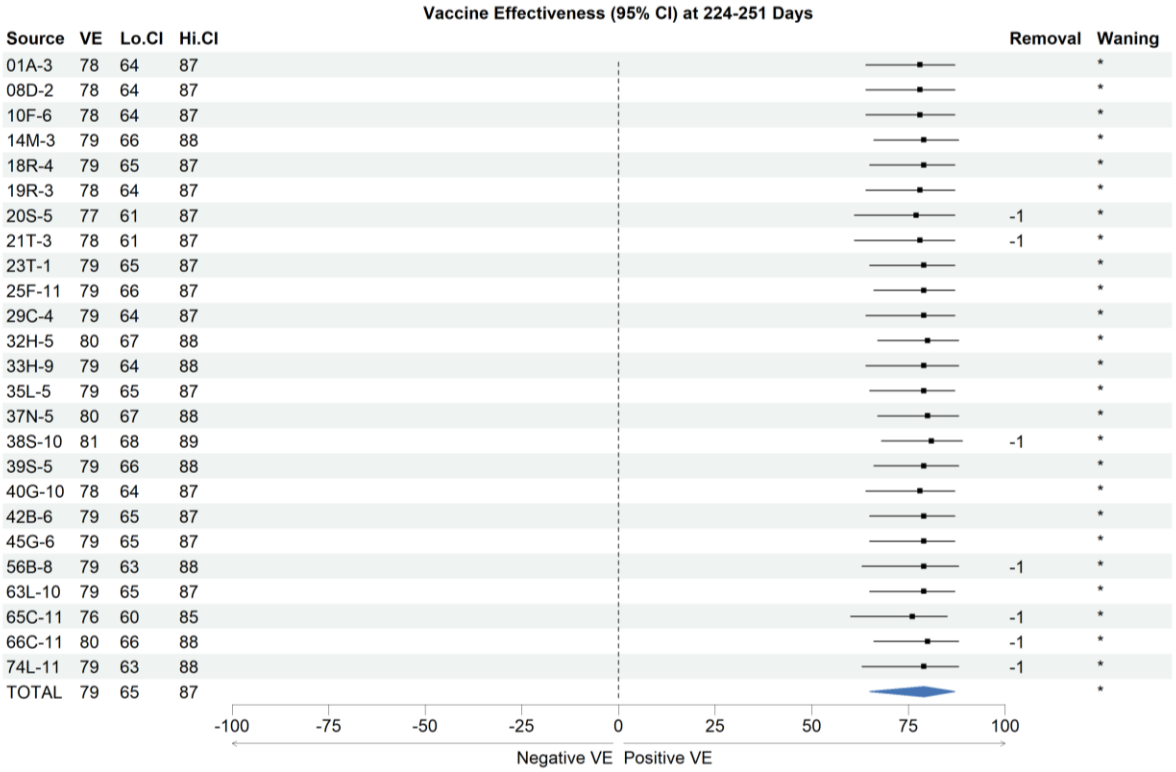
Notes. Source = individual studies from the review where each row indicates results when a specific study is excluded from the analysis (e.g., row 1 excludes study "01A-3"). VE = vaccine effectiveness. Lo.CI = lower bound of the 95% confidence interval around the VE estimate. Hi.CI = higher bound of the 95% confidence interval around the VE estimate. Removal = this column indicates whether a given study contributed observations specific to this time point (if so, this is indicated by a -1). Waning = a column indicating whether the VE at this time point is significantly lower than the VE at 14-42 days (2nd plot).

eFigure 222. ***Leave-one-Out Analyses, Depicting the Impact of the Primary Series Against Hospitalisations at 196-223 Days.***



Notes. Source = individual studies from the review where each row indicates results when a specific study is excluded from the analysis (e.g., row 1 excludes study "01A-3"). VE = vaccine effectiveness. Lo.CI = lower bound of the 95% confidence interval around the VE estimate. Hi.CI = higher bound of the 95% confidence interval around the VE estimate. Removal = this column indicates whether a given study contributed observations specific to this time point (if so, this is indicated by a -1). Waning = a column indicating whether the VE at this time point is significantly lower than the VE at 14-42 days (2nd plot).

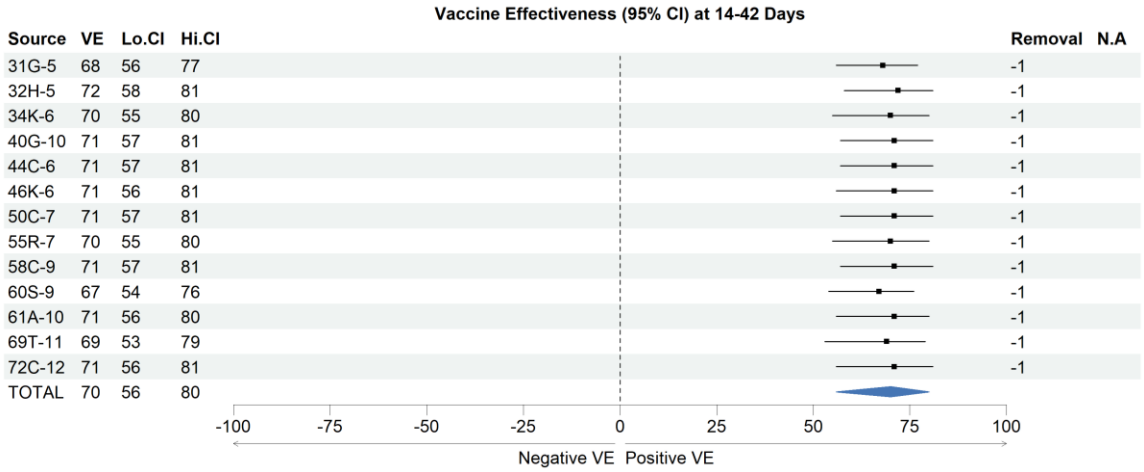
eFigure 233. ***Leave-one-Out Analyses, Depicting the Impact of the Primary Series Against Hospitalisations at 224-251 Days.***



Notes. Source = individual studies from the review where each row indicates results when a specific study is excluded from the analysis (e.g., row 1 excludes study "01A-3"). VE = vaccine effectiveness. Lo.CI = lower bound of the 95% confidence interval around the VE estimate. Hi.CI = higher bound of the 95% confidence interval around the VE estimate. Removal = this column indicates whether a given study contributed observations specific to this time point (if so, this is indicated by a -1). Waning = a column indicating whether the VE at this time point is significantly lower than the VE at 14-42 days (2nd plot).

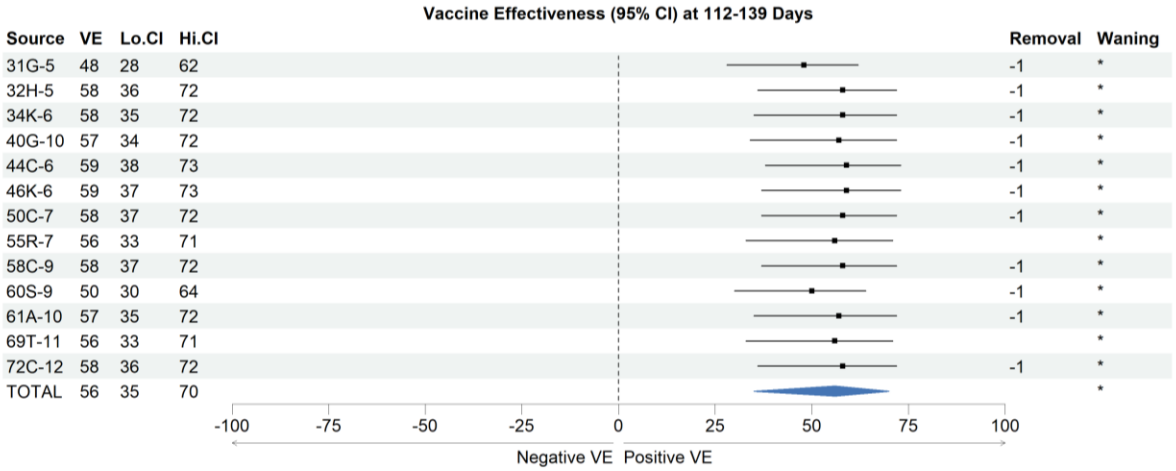
7.03. Leave-One-Out Analyses for the First Booster Dose Against Infections

eFigure 244. ***Leave-one-Out Analyses, Depicting the Impact of the Booster Against Infections at 14-42 Days.***



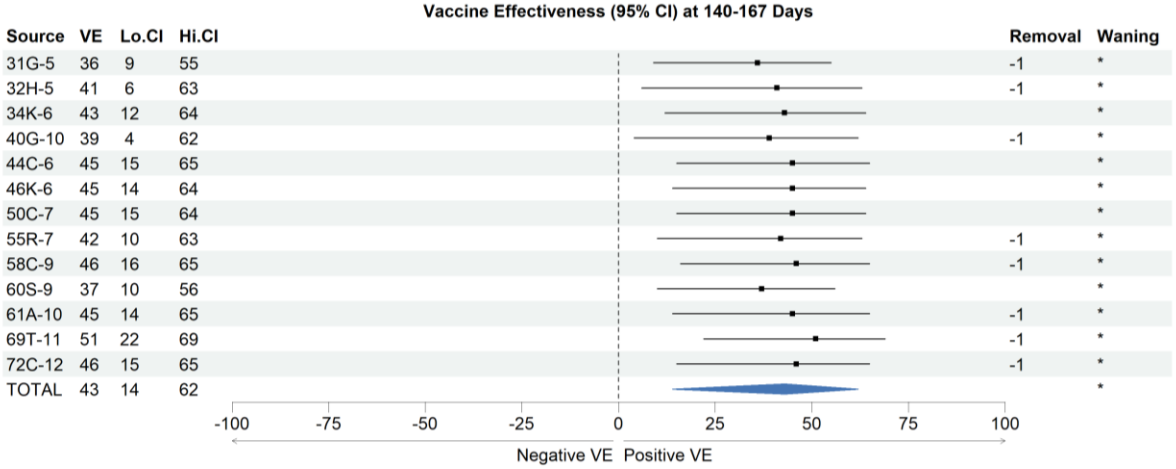
Notes. Source = individual studies from the review where each row indicates results when a specific study is excluded from the analysis (e.g., row 1 excludes study "31G-5"). VE = vaccine effectiveness. Lo.CI = lower bound of the 95% confidence interval around the VE estimate. Hi.CI = higher bound of the 95% confidence interval around the VE estimate. Removal = this column indicates whether a given study contributed observations specific to this time point (if so, this is indicated by a -1). N.A. = Not applicable; this column indicates that this time point cannot be evaluated against the previous one (0-13 days) because no data is available at this earlier time point.

eFigure 255. ***Leave-one-Out Analyses, Depicting the Impact of the Booster Against Infections at 112-139 Days.***



Notes. Source = individual studies from the review where each row indicates results when a specific study is excluded from the analysis (e.g., row 1 excludes study "31G-5"). VE = vaccine effectiveness. Lo.CI = lower bound of the 95% confidence interval around the VE estimate. Hi.CI = higher bound of the 95% confidence interval around the VE estimate. Removal = this column indicates whether a given study contributed observations specific to this time point (if so, this is indicated by a -1). Waning = a column indicating whether the VE at this time point is significantly lower than the VE at 14-42 days (2nd plot).

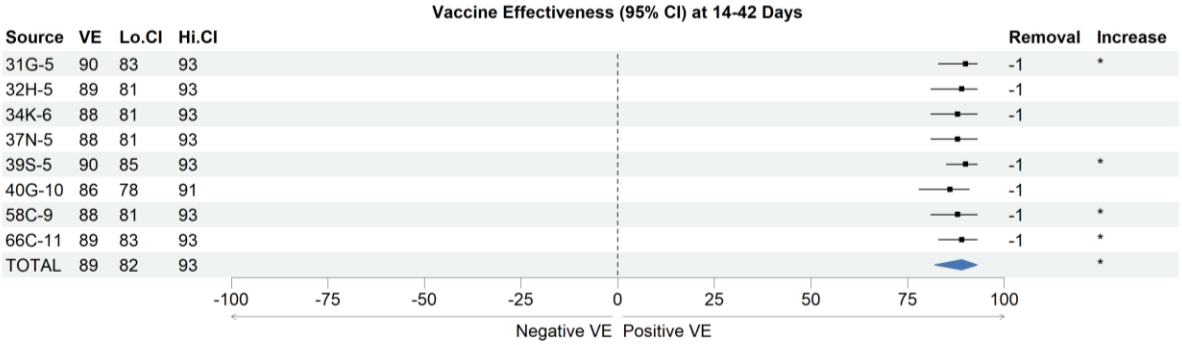
eFigure 266. ***Leave-one-Out Analyses, Depicting the Impact of the Booster Against Infections at 140-167 Days.***



Notes. Source = individual studies from the review where each row indicates results when a specific study is excluded from the analysis (e.g., row 1 excludes study "31G-5"). VE = vaccine effectiveness. Lo.CI = lower bound of the 95% confidence interval around the VE estimate. Hi.CI = higher bound of the 95% confidence interval around the VE estimate. Removal = this column indicates whether a given study contributed observations specific to this time point (if so, this is indicated by a -1). Waning = a column indicating whether the VE at this time point is significantly lower than the VE at 14-42 days (2nd plot).

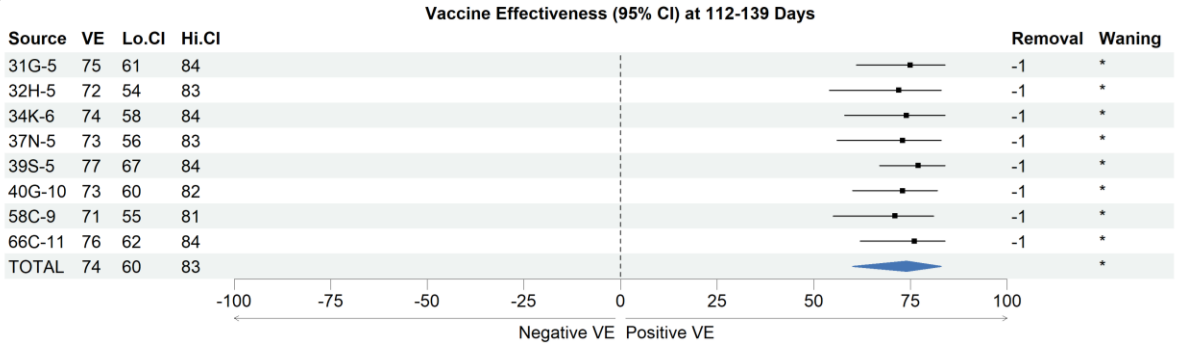
7.04. Leave-One-Out Analyses for the First Booster Dose Against Hospitalizations

eFigure 277. ***Leave-one-Out Analyses, Depicting the Impact of the Booster Against Hospitalisations at 14-42 Days.***



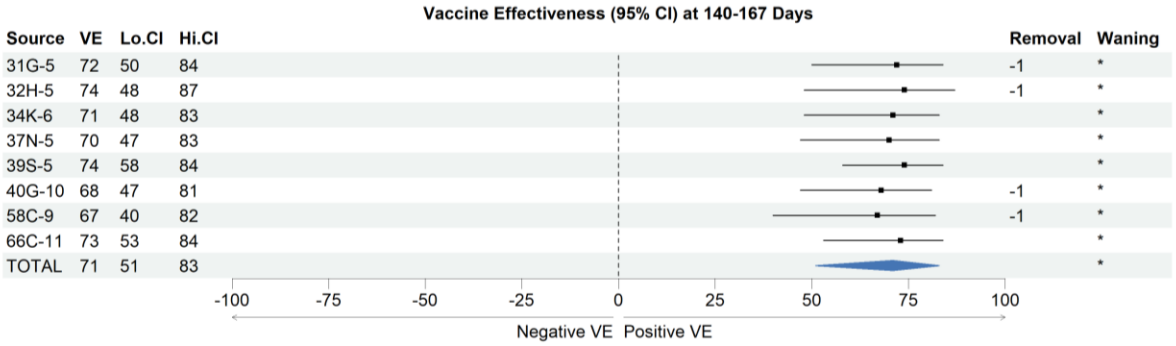
Notes. Source = individual studies from the review where each row indicates results when a specific study is excluded from the analysis (e.g., row 1 excludes study "31G-5"). VE = vaccine effectiveness. Lo.CI = lower bound of the 95% confidence interval around the VE estimate. Hi.CI = higher bound of the 95% confidence interval around the VE estimate. Removal = this column indicates whether a given study contributed observations specific to this time point (if so, this is indicated by a -1). Increase = a column indicating whether the VE at 14-42 days is significantly higher than the VE at 0-7 days

eFigure 288. ***Leave-one-Out Analyses, Depicting the Impact of the Booster Against Hospitalisations at 112-139 Days.***



Notes. Source = individual studies from the review where each row indicates results when a specific study is excluded from the analysis (e.g., row 1 excludes study "31G-5"). VE = vaccine effectiveness. Lo.CI = lower bound of the 95% confidence interval around the VE estimate. Hi.CI = higher bound of the 95% confidence interval around the VE estimate. Removal = this column indicates whether a given study contributed observations specific to this time point (if so, this is indicated by a -1). Waning = a column indicating whether the VE at this time point is significantly lower than the VE at 14-42 days (2nd plot).

eFigure 299. ***Leave-one-Out Analyses, Depicting the Impact of the Booster Against Hospitalisations at 140-167 Days.***



Notes. Source = individual studies from the review where each row indicates results when a specific study is excluded from the analysis (e.g., row 1 excludes study "31G-5"). VE = vaccine effectiveness. Lo.CI = lower bound of the 95% confidence interval around the VE estimate. Hi.CI = higher bound of the 95% confidence interval around the VE estimate. Removal = this column indicates whether a given study contributed observations specific to this time point (if so, this is indicated by a -1). Waning = a column indicating whether the VE at this time point is significantly lower than the VE at 14-42 days (2nd plot).