COVID-19 VACCINATION IN SOLID ORGAN TRANSPLANT RECIPIENTS

THE EVOLUTION OF EVIDENCE ON COVID-19 VACCINATION IN SOLID ORGAN TRANSPLANT RECIPIENTS: A LIVING SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS

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TITLE: The evolution of evidence on COVID-19 vaccination in solid organ transplant recipients: a living systematic review and network meta-analysis

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LAY ABSTRACT

Solid organ transplant recipients are at a higher risk of infection from COVID-19 due to their required long-term immunosuppressive medications. Unfortunately, due to their high risk of infection, transplant recipients were excluded from the initial clinical trials investigating the effectiveness of COVID-19 vaccines. As a result, there is limited research investigating the use of COVID-19 vaccines on clinical outcomes in transplant recipients; however, new studies are being frequently conducted and published. To identify and summarize the studies conducted to date that investigated the impact of different COVID-19 vaccination strategies in transplant recipients, we systematically reviewed the literature. Furthermore, we evaluated how the research evidence and the conclusions drawn from this evidence changed over time throughout the COVID-19 pandemic.

ABSTRACT

Background: The impact of COVID-19 vaccination on clinical outcomes in solid organ transplant (SOT) recipients remains unclear. This living systematic review and network meta-analysis sought to assess the effectiveness of COVID-19 vaccination in SOT recipients and to evaluate the evolution of evidence in this population over time.

Methods: We searched six databases from inception to March 1st, 2024 for randomized controlled trials (RCTs) and observational studies evaluating different COVID-19 vaccination strategies (i.e., number of doses, type of vaccine) in SOT recipients. Based on patient-important outcomes, we performed frequentist random-effects pairwise meta-analyses and NMAs, separating RCTs and observational studies, and used the GRADE approach to assess certainty in the evidence. We compared the body evidence identified at four timepoints (October 1st, 2022, March 1st, 2023, July 1st, 2023, and March 1st, 2024).

Results: We included 6 RCTs (N=814) and 42 observational studies (N=125,101). We identified a dose-response relationship between the number of COVID-19 vaccines received and a reduction in the risk of COVID-19 infection. The evidence evaluating the number of doses on other patient-important outcomes, including mortality, hospitalization, and ICU admission, and the evidence investigating the impact of the type of COVID-19 vaccine demonstrated low to very low certainty. Across the four iterations of this living systematic review, the conclusions drawn from the evidence supported by randomized data largely remained unchanged; however, half of the conclusions drawn from the evidence supported by observational data changed in certainty or direction.

Conclusion: Throughout the COVID-19 pandemic, clinicians and SOT recipients worked with minimal evidence with variable certainty in relation to COVID-19 vaccines in this population. In the instance of future public health emergencies, clinicians and researchers should collaborate closely with patient partners to ensure there is adequate evidence in the transplant population on patient-important outcomes.

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LIST OF ABBREVIATIONS

CI: Confidence interval

GRADE: Grading of Recommendations, Assessment, Development and Evaluation

HR: Hazard ratio

ICEMAN: Instrument for assessing the Credibility of Effect Modification Analyses

ICU: Intensive care unit

MOOSE: Meta-analysis of Observational Studies in Epidemiology

NR: Not reported

OR: Odds ratio

PRISMA: Preferred Reporting Items for Systematic reviews and Meta-Analyses

PROSPERO: The International Prospective Register of Systematic Reviews

RCT: Randomized controlled trial

RD: Risk difference

ROBINS-I: Risk Of Bias In Non-randomized Studies - of Interventions

RR: Relative risk

SOT: Solid organ transplantation

USA: United States of America

DECLARATION OF ACADEMIC ACHIEVEMENT

This thesis has been prepared in fulfillment of the requirements for a Master of Science (MSc) degree in the Health Research Methodology program. Daniel Rayner prepared this thesis under the supervision of Dr. Farid Foroutan, who acted as the primary supervisor of all aspects of this research thesis. Dr. Farid Foroutan, Dr. Gordon Guyatt, and Dr. Carolina Alba served as internal thesis committee members. Dr. Shahid Husain served as the external thesis committee member.

Dr. Farid Foroutan, Dr. Natasha Aleksova, and Daniel Rayner conceived and designed the study. Dr. Natasha Aleksova, David Gou, Jairo Nunes, Si-Cheng Dai, Alexandro Chu, Dorisa Meng, and Aleesha Sheikh, and Daniel Rayner contributed to the systematic literature review screening and data extraction process. Daniel Rayner performed the data analysis and wrote the first draft of the thesis. All supervisory committee members provided feedback on the thesis proposal and thesis draft.

CHAPTER 1: Introduction

1.1 Outline

This written thesis includes my graduate research work to satisfy the requirements for a Master of Science (MSc) degree in the Health Research Methodology program. The focus of this thesis is to contribute an important study on the value of living systematic review methodology using an example of the evolution of evidence supporting COVID-19 vaccines in solid organ transplant recipients over the course of the COVID-19 pandemic. In this introductory chapter, I provide a narrative summary of the literature on solid organ transplantation, the impact of the COVID-19 pandemic on solid organ transplant recipients and living systematic review methodology.

1.2 Solid organ transplantation

Solid organ transplantation (SOT) is a medically effective treatment to improve the quality of life and survival of patients living with end-stage organ dysfunction (Black et al., 2018). In 2022, nearly 2900 solid organ transplantations were performed in Canada, of which 59% were kidney, 20% were liver, 12% were lung, 5% were heart, 2% were pancreas, and the remaining 2% were combination transplants (Canadian Institute for Health Information, 2023a; Canadian Institute for Health Information, 2023b).

Following transplantation, SOT recipients are required to strictly adhere to long-term immunosuppressive therapy, including calcineurin inhibitors, glucocorticoids, mycophenolate,

and mTOR inhibitors, to promote allograft survival and reduce their risk of donor organ rejection (Shi et al., 2020). However, this immunosuppressive regimen also increases SOT recipients' risk of infections, including viral (e.g., cytomegalovirus, Epstein-Barr virus), bacterial (e.g., urinary tract infections, pneumonia), and parasitic and fungal infections (e.g., toxoplasmosis, candidiasis) (Tarhini et al., 2023; Pappas et al., 2010; Hamandi et al., 2016; Fishman, 2017). These infections may increase SOT recipients' risk of mortality, allograft rejection, and development of malignancy (Sanromán Budiño et al., 2004).

1.3 The impact of the COVID-19 pandemic on SOT recipients

Given their need for life long immunosuppressive therapy and their frequent underlying comorbidities, including diabetes mellitus (Jenssen & Hartmann, 2019) and hypertension (Zbroch et al., 2012), SOT recipients are at a high risk of morbidity and mortality from COVID-19 (Pereira et al., 2020). Evidence from early stages of the pandemic suggests that SOT recipients are at a 3.5-fold higher risk of COVID-19-related mortality compared to their healthy counterparts (Williamson et al., 2020). Previous literature suggests that 26% to 63% (Cochran et al., 2022; Schaenman et al., 2022) of SOT recipients are hospitalized and 13% to 30% (Azzi et al., 2021) die due to COVID-19.

Despite their enhanced risk of infection, SOT recipients were excluded from the initial randomized controlled trials (RCTs) investigating the efficacy and safety of COVID-19 vaccines (Polack et al., 2020; Baden et al., 2021; Voysey et al., 2021), leading to a paucity of direct evidence evaluating their use in this population. Furthermore, previous studies have demonstrated that SOT

recipients may experience a reduced immune response due to their immunosuppressive medications (Boyarsky et al., 2021; Georgery et al., 2021; Hoffman et al., 2022; Mazzola et al., 2022). However, evidence from other immunosuppressed populations has shown that seroconversion does not strongly confer protection against the COVID-19 infection and mortality (Ollila et al., 2022), demonstrating a need for studies evaluating the impact of COVID-19 vaccination on clinical outcomes in SOT recipients.

1.4 Living systematic reviews

Systematic reviews and meta-analyses serve as means to bridge the gap between primary research evidence and clinical practice, promoting the provision of optimal health care (Sarkies et al., 2017). However, traditional systematic reviews frequently suffer from significant limitations, including their long production time and the fact that their findings can become quickly outdated with the publication of new studies (Sampson et al., 2008; Shojania et al., 2007). Living systematic reviews—reviews that are continuously updated, critically appraising and incorporating new studies as they are published—offer a novel solution to the limitations of traditional systematic reviews (Elliott et al., 2014). These living systematic reviews have been increasingly used in instances where the topic is a priority for decision-making, there is rapidly emerging and evolving evidence, and there is low certainty in the current evidence, such as the COVID-19 pandemic (Heron et al., 2023). Living systematic reviews are also an approach to reduce research waste created by outdated systematic reviews (Vandvik et al., 2016), which is a prevalent issue in the field of solid organ transplantation research (Salih et al., 2023).

1.5 Research questions

Given the paucity of evidence evaluating COVID-19 vaccines in SOT recipients in relation to clinical outcomes and the rapidly emerging evidence due to the COVID-19 pandemic, we developed a living international clinical practice guideline on COVID-19 vaccination in SOT recipients. To inform this guideline, we conducted a living systematic review and network meta-analysis evaluating different COVID-19 vaccination strategies in SOT recipients. Through our systematic review and network meta-analysis, we answered the following research questions:

(1) In SOT recipients, what is the impact of the number of COVID-19 vaccine doses on clinical outcomes?

(2) In SOT recipients, what is the impact of the type of COVID-19 vaccine on clinical outcomes?

(3) How do the conclusions drawn from the evidence evaluating COVID-19 vaccines in SOT recipients evolve over time?

CHAPTER 2: Key Methodological Considerations

2.1 Types of included studies

To answer our research questions, we chose to include both randomized and non-randomized comparative studies in our systematic review. Generally, RCTs offer the best source of evidence for evidence syntheses of interventions informing clinical practice guidelines due to the risk of confounding and other sources of bias that non-randomized studies of interventions suffer from (Sterne et al., 2016). Despite these limitations, non-randomized studies may provide evidence on the effectiveness of interventions to complement evidence from RCTs (in the paucity of randomized evidence) (Cuello-Garcia et al., 2022). Given the expected limited randomized evidence evaluating COVID-19 vaccines in the SOT population, we elected to incorporate both randomized and non-randomized studies and evaluate them in parallel. However, we restricted non-randomized studies to those reporting multivariable analyses (propensity matching, Cox proportional hazards models, logistic regression models) to minimize the risk of confounding in our analysis.

2.2 Evaluating dose-response relationships

In answering our first research question (i.e., what is the impact of the number of COVID-19 vaccine doses on clinical outcomes?), we expected to encounter instances where we would need to assess the credibility of a dose-response relationship. To assess the credibility of a dose-response relationship, we followed existing guidance from the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) Working Group (Murad et al., 2023), which involves consideration of (a) an appropriate analytical approach, (b) the likelihood of residual confounding,

(c) the likelihood of ecological bias, (d) consistency across studies, (e) and support from indirect bias. If the dose-response gradient was determined to be credible, we rated up our certainty in the evidence by one level.

2.3 Living review methodology

In answering our third research question (i.e., how do the conclusions drawn from the evidence evaluating COVID-19 vaccines in SOT recipients evolve over time?), we had to determine which metrics we would use to compare the conclusions drawn between timepoints. The GRADE approach, which is used to evaluate the certainty in the evidence, has four levels of evidence: (a) high, (b) moderate, (c) low, and (d) very low (Guyatt et al., 2008). When using the GRADE approach relative to a non-zero effect, one can make two distinct directional inferences: (a) the intervention increases the outcome compared to the comparator, (b) the intervention decreases the outcome compared to the comparator, and (c) the intervention has little to no difference on the outcome compared to the comparator. To evaluate the conclusions drawn from the evidence over multiple time periods, we assessed the changes in the certainty of the evidence and the directions of the inferences.

CHAPTER 3: Study Methods

3.1 Study design and reporting

We conducted this systematic review and network meta-analysis with guidance from the Cochrane Handbook (Higgins & Green, 2008) and we report its results in accordance with PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) and MOOSE (Meta-analysis of Observational Studies in Epidemiology) guidelines (Page et al., 2021; Stroup et al., 2000). We prospectively registered our systematic review protocol in PROSPERO (The International Prospective Register of Systematic Reviews) (CRD42022348418).

3.2 Data sources and searches

With assistance from a health research librarian with experience in solid organ transplantation, we conducted a systematic search of MEDLINE (Ovid), Embase (Ovid), CENTRAL (Ovid), the Cochrane Database of Systematic Reviews (Ovid), Clinicaltrials.gov, and the WHO COVID-19 Database. This search was repeated on a monthly basis between February 1st, 2022 and March 1st, 2024. **Appendix 1** presents the search strategies for each database. To identify additional eligible studies, we searched the reference lists of all included studies. We did not impose any restrictions based on language or publication status of the identified citations.

3.3 Study selection and data collection

We included RCTs and comparative observational (non-randomized) studies that enrolled SOT recipients and compared the impact of different COVID-19 vaccine strategies (i.e., number

of doses [3 doses vs 2 doses, 3 doses vs no vaccination, etc.], the type of COVID-19 vaccine [Moderna vs Pfizer, AstraZeneca vs Pfizer]). We included observational studies if they evaluated outcomes using multivariable analyses (Cox proportional hazards models, or logistic regression models) or propensity matching. We did not place any restrictions based on language or on publication status. If more than one study assessed the same source population, comparators, and outcomes, we included the study with the largest analyzed sample size.

Pairs of calibrated reviewers screened titles and abstracts and reviewed full-texts independently and in duplicate using Covidence (Veritas Health Innovation, Melbourne, Australia). Subsequently, paired reviewers independently extracted data using standardized pre-piloted Excel forms. We resolved disagreements between reviewers through discussion, and if necessary, a third reviewer. Collected data included study design, setting, patient characteristics (e.g., age, sex, type of SOT, management strategies of recipients, etc.), intervention and comparator characteristics, outcomes, and sources of funding. We extracted outcome data from RCTs according to the intention-to-treat principle.

3.4 Outcome measures

As part of a living international clinical practice guideline, we consulted our panel of patient partners, transplant physicians, and infectious disease specialists, who prioritized ten patient-important outcomes for assessment of benefits and harms. These outcomes included:

(1) all-cause mortality (critical)

(2) all-cause hospitalization (critical)

(3) intensive care unit (ICU) admission (critical)

(4) symptomatic COVID-19 infection (important)

(5) graft-related adverse events (important)

(6) worsening allograft function and/or allograft failure (important)

(7) mental health impact (important)

(8) quality of life (important)

(9) long COVID-19 symptoms or post-COVID-19 conditions (important)

(10) long-term impact on functioning and health status (important)

Based on the availability of the data, for the purpose of this thesis project, we assessed the following patient-important outcomes: mortality, COVID-19 infection, hospitalization, and ICU admission.

3.5 Risk of bias assessment

Pairs of calibrated reviewers independently assessed the risk of bias of eligible studies using the Cochrane Collaboration's Risk-of-Bias 2.0 tool for RCTs (Sterne et al., 2019) and the ROBINS-I (Risk Of Bias In Non-randomised Studies - of Interventions) tool for observational studies (Sterne et al., 2016). Risk of bias assessments were conducted for each eligible outcome for all included studies.

3.6 Data synthesis and data analysis

We analyzed outcomes from RCTs and observational studies separately. We calculated effect estimates in pairwise meta-analyses using DerSimonian and Laird random-effects models using the 'meta' R package. Similarly, where appropriate, we performed contrast-based,

frequentist, random-effects network meta-analyses using the 'netmeta' R package. For network meta-analyses evaluating the number of COVID-19 vaccines, network nodes represented unique numbers of doses (i.e., 4 vs 3 vs 2 vs 1 vs 0 doses).

We pooled dichotomous outcomes as odds ratios (OR) with accompanying 95% confidence intervals (CIs). For observational studies reporting point estimates and 95%CIs using relative risks (RR) or hazard ratios (HR), we converted values to OR by calculating absolute risks using formulas derived by Foroutan et al. (2020). We determined absolute effect estimates using the median baseline risk reported in the control arm (e.g., no vaccination) of the included observational studies.

All analyses were conducted in R version 4.1.2 (R Foundation for Statistical Computing, Vienna, Austria). A p-value less than 0.05 was considered significant.

3.7 Subgroup analyses

We analyzed prespecified subgroups using pairwise comparisons in instances where at least two subgroups had two or more studies. We appraised the credibility of the subgroup effects using the Instrument for assessing the Credibility of Effect Modification Analyses (ICEMAN) (Schandelmaier et al., 2020). Our prespecified subgroups were risk of bias, pregnancy status at the time of COVID-19 infection, sex, organ group (e.g., heart, lung, liver, kidney), use of mycophenolate-based immunosuppression, and number of maintenance immunosuppressive agents used. We hypothesized that the use of mycophenolate-based immunosuppression, and greater numbers of maintenance immunosuppressants used in studies would decrease the efficacy

of COVID-19 vaccines. Subgroups involving the impact of sex, organ group or pregnancy status were exploratory in nature and did not have a hypothesized direction.

3.8 Certainty of evidence

We used the GRADE approach to evaluate the certainty of the evidence in relation to a non-zero effect (Brignardello-Petersen et al., 2020). The GRADE approach for network meta-analysis involves assessment of risk of bias, inconsistency, indirectness, imprecision, publication bias, intransitivity, and incoherence. We evaluated incoherence using node splitting and intransitivity by evaluating for imbalanced distributions of potential effect modifiers across studies included in the network meta-analyses. We evaluated publication bias through visual assessment of funnel plots. In the instance of potential dose-response relationships, we assessed their credibility using established guidance (Murad et al., 2023), and if credible, we rated our certainty in the evidence up one level. We presented our synthesized results and their associated certainty in the evidence in summary of findings tables.

3.9 Living systematic review

To evaluate the evolution of evidence surrounding COVID-19 vaccines in SOT recipients over time, the aforementioned methodology was conducted using the cumulative set of studies captured by the systematic literature searches at four timepoints:

(1) Timepoint 1 - October 1st, 2022

(2) Timepoint 2 - March 1st, 2023

(3) Timepoint 3 - July 1st, 2023

(4) Timepoint 4 - March 1st, 2024

We descriptively compared the directions of the inferences drawn and the certainty of the evidence for each comparison across the four timepoints.

CHAPTER 4: Results

4.1 Summary of included studies

Our systematic literature searches up to March 1st, 2024 yielded 8,994 unique records, of which 1,056 full-texts were retrieved for further screening. Ultimately, we included 48 studies in our systematic review (6 RCTs and 42 observational studies). Three studies (6%) were pre-prints, and the remaining 45 (94%) studies were published articles. **Appendix 2** lists the studies included in our systematic review. **Appendix 3** lists examples of studies excluded during the full-text screening process. The PRISMA flowchart illustrating the study selection process is presented as **Figure 1**.

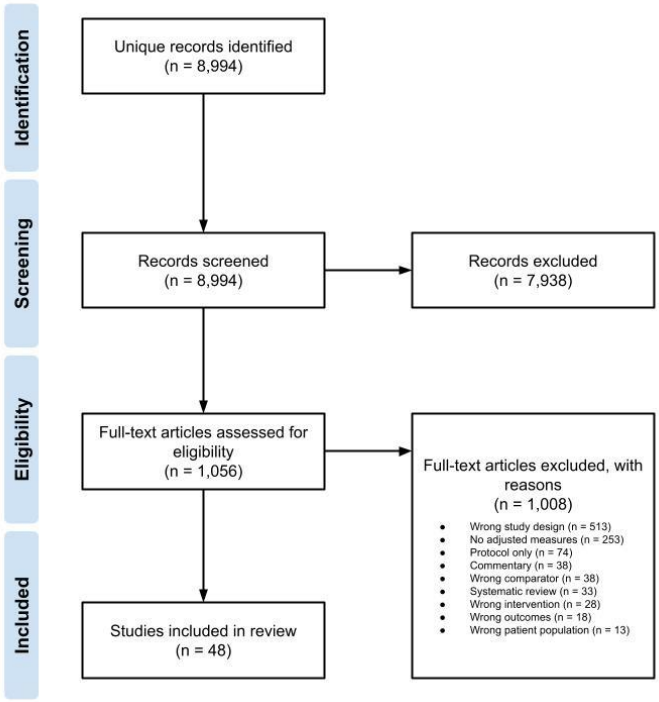

Figure 1. PRISMA flow diagram showing study selection process.

The included studies were published between August 2021 and December 2023. **Figure 2** presents the months and years of publication of the included studies.

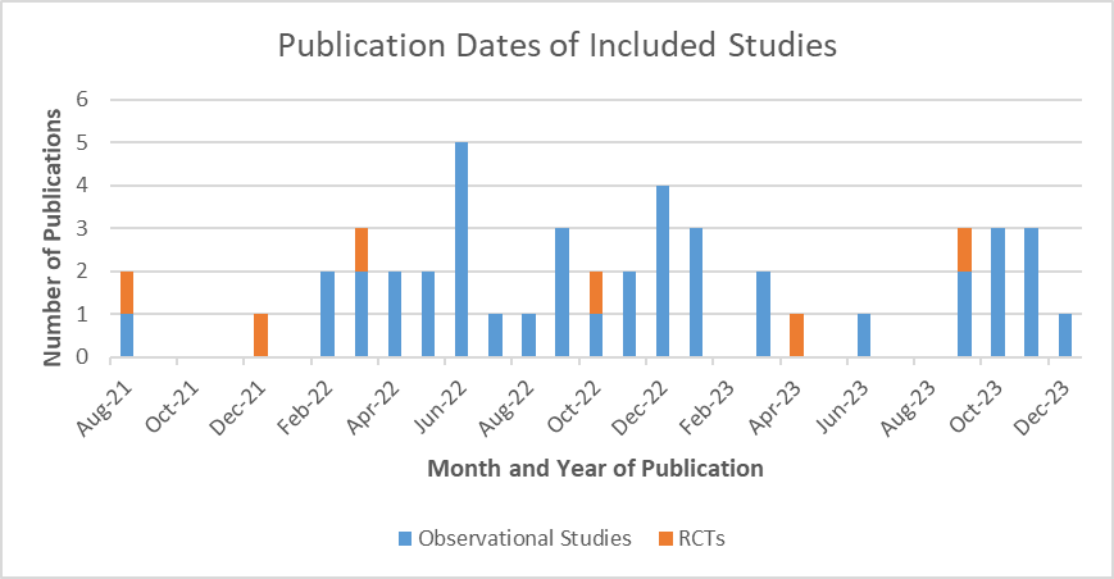

Figure 2. Stacked column chart demonstrating publication trends of the included studies.

Key characteristics of the included RCTs (n = 814 patients) are summarized in **Table 1**. Among the 6 included RCTs, the median number of participants randomized was 123 (range: 60–201). These RCTs included participants with a median of mean ages of 58.5 years (range of means: 50.7–67.0 years) and a median of 35% female patients (range of proportions: 34–58%). Three RCTs (50%) evaluated populations of mixed SOT recipients, and three RCTs (50%) evaluated only kidney transplant recipients.

Table 1. Characteristics of the included RCTs (n = 6).

Study (First Author Last Name, Year)	Country	Recruitment Period	N Randomized	Mean Age (Years)	Female (%)	Mean Time from Transplant (Years)	Transplanted Organ Group
Drenko 2023	Czech Republic	Sep 2021 – Oct 2021	125	59.5	34%	7.7	Kidney
Hall 2021	Canada	May 2021 – Jun 2021	120	67.0	34%	3.6	Mixed
Kho 2022	The Netherlands	Apr 2021 – Jul 2021	230	57.4	35%	7.0	Kidney
Natori 2023	USA	Sep 2021 – Dec 2021	60	54.2	34%	1.2	Mixed
Reindl-Schwaighofer 2022	Austria	Jun 2021 – Aug 2021	201	61.2	58%	4.8	Kidney
Speich 2022	Switzerland	Apr 2021 – Jun 2021	78	50.7	37%	NR	Mixed

Note: NR = Not reported; USA = United States of America.

Key characteristics of the included observational studies (n = 125,101 patients) are summarized in **Table 2**. Of the 42 observational studies, the median number of participants included was 618 (range: 41–18,174). These studies included participants with a median of mean ages of 54.5 years (range of means: 42.9–66.6 years) and had a median of 41% female patients (range of proportions: 4–72%). Eighteen studies (43%) assessed a mixed SOT population, followed by kidney (n = 17, 40%), liver (n = 4, 10%), lung (n = 2, 5%), and heart (n = 1, 2%) transplant recipients.

Table 2. Characteristics of the included observational studies (n = 42).

Study (First Author Last Name, Year)	Country	Recruitment Period	N Included	Mean Age (Years)	Female (%)	Mean Time from Transplant (Years)	Transplanted Organ Group
Aslam 2022	USA	Jan 2021 – Aug 2021	1904	56.9	36%	4.4	Mixed
Bonazzetti 2023	Italy	Feb 2021 – Jan 2022	614	57.3	35%	7.6	Mixed
Callaghan 2023	England	Dec 2020 – Mar 2022	12454	NR	41%	NR	Mixed
Chen 2023	Taiwan	Apr 2022 – Aug 2022	622	53.6	51%	11.4	Kidney
Collaborative 2022	United Kingdom	Dec 2020 – May 2022	8925	NR	37%	NR	Kidney
Demir 2022	Turkey	Apr 2020 – Oct 2021	164	48.7	50%	8.8	Kidney
Elhadji 2023	France	Jan 2015 – Dec 2021	10637	NR	NR	NR	Kidney
Hall 2022	Canada	Jan 2020 – Sep 2021	297	55.3	33%	6.7	Mixed
Hamm 2022	Denmark	Dec 2020 – Dec 2021	143	49.3	36%	6.2	Mixed
Hardgrave 2022	USA	Feb 2020 – Jan 2022	144	51.2	44%	NR	Mixed
Hiam 2021	Qatar	Feb 2021 – Jul 2021	782	50.4	33%	8.0	Kidney
Hod 2022	Israel	Dec 2021 – Mar 2022	447	61.5	70%	4.6	Kidney
Joerns 2022	USA	Mar 2020 – Sep 2021	54	54.5	54%	4.1	Lung
John 2022	USA	Dec 2020 – Sep 2021	1924	NR	4%	6.8	Liver
Kee 2022	Multiple	Jan 2020 – Mar 2022	657	NR	NR	NR	Kidney
Korogiannou 2023	Greece	Dec 2021 – Sep 2022	451	51.8	39%	6.6	Kidney
Kwon 2022	USA	Mar 2021 – Dec 2021	227	NR	NR	NR	Mixed
Lerner 2022	USA	Dec 2021 – May 2022	103	56.2	48%	6.1	Mixed
Llamas 2023	Mexico	Mar 2020 – Feb 2022	153	55.0	50%	4.9	Liver
Ma 2022	China	NR – Jun 2022	1881	42.9	72%	NR	Liver
Masetti 2023	Italy	Dec 2021 – Nov 2022	268	61.4	26%	12.3	Heart
Mazuecos 2022	Spain	Apr 2021 – Oct 2021	481	55.0	38%	6.0	Kidney

McEvoy 2022	Canada	Mar 2020 – Jul 2021	1793	60.2	36%	8.5	Kidney
Mikhailov 2023	Germany	Feb 2020 – Jul 2022	578	54.2	61%	8.4	Kidney
Mues 2022	USA	Dec 2020 – Jan 2022	18174	50.9	53%	NR	Mixed
Naylor 2022	Canada	Dec 2020 – Nov 2021	12842	57.7	38%	7.7	Mixed
Naylor 2024	Canada	Aug 2021 – Apr 2022	6240	62.5	39%	7.5	Mixed
Pinto-Alvarez 2022	Colombia	Mar 2021 – May 2022	6963	51.8	42%	NR	Mixed
Rasmussen 2022	Denmark	Sep 2021 – Jul 2022	800	52.9	43%	NR	Mixed
Sanayei 2023	USA	Jan 2022 – Sep 2022	323	60.8	37%	7.3	Mixed
Sandoval 2022	USA	Mar 2020 – Oct 2021	646	57.0	45%	5.1	Mixed
Sindu 2023	USA	Mar 2020 – Aug 2022	195	66.6	58%	3.1	Lung
Singh 2024	USA	Feb 2021 – Apr 2022	400	54.0	41%	1.1	Kidney
Thotsiri 2022	Thailand	Jan 2021 – Jul 2022	146	47.0	44%	4.3	Kidney
Tucker 2022	USA	Jan 2021 – Aug 2021	1668	55.1	38%	9.1	Mixed
Udomkarnjananun 2023	Thailand	Mar 2021 – Oct 2022	413	47.0	57%	5.1	Kidney
Vieira 2022	USA	Mar 2020 – Nov 2021	109	NR	NR	NR	Kidney
Vinson 2022a	USA	Dec 2020 – May 2022	12969	NR	41%	NR	Mixed
Vinson 2022b	USA	Dec 2020 – Oct 2021	15560	NR	NR	NR	Mixed
Wong 2022	Australia	Dec 2021 – Jan 2022	41	52.0	49%	8.5	Kidney
Zhang 2023	China	Dec 2022 – May 2023	930	51.0	22%	3.2	Liver
Zona 2023	USA	Apr 2020 – Apr 2022	979	56.1	58%	NR	Kidney

Note: NR = Not reported; USA = United States of America.

Risk of bias assessments conducted for each outcome are presented in **Appendix 4**. From the 6 RCTs included, 9 unique risk of bias assessments were conducted, of which all were at an overall low risk of bias. Of the 42 observational studies included, 64 unique risk of bias assessments were conducted, of which 60 were at a serious risk of bias; the remaining 4 were at a moderate risk of bias. No outcomes from observational studies were at a low risk of bias. Of those at a serious risk of bias, study limitations included a lack of adjustment for important confounders, and the potential for immortal-time bias due to the selection of participants for the study.

Appendices 5 and **6** present the forest plots and funnel plots for all pairwise meta-analyses. **Appendix 7** presents the subgroup analyses. For all timepoints, we did not observe any credible subgroup differences by organ group (e.g., heart, lung, liver, kidney). We were unable to explore effect modification by pregnancy status, sex, use of mycophenolate-based immunosuppression, or the number of maintenance immunosuppressive agents used due to an insufficient number of studies reporting data necessary to evaluate these subgroups.

Appendix 8 presents the network meta-analysis plots, network league tables, and node-splitting plots for all timepoints. **Appendix 9** presents the comparison of potential effect modifiers across pairwise comparisons to assess network transitivity in the networks. We did not observe any significant incoherence or intransitivity.

4.2 Review findings from Timepoint 1 (October 1st, 2022)

4.2.1 Summary of included studies

The systematic review capturing studies published until October 1st, 2022 identified 22 eligible studies (3 RCTs [n = 399 patients] and 19 observational studies [n = 69,892 patients]).

Among the 3 included RCTs, the median number of participants randomized was 120 (range: 78–201). These RCTs included participants with a median of mean ages of 61.2 years (range of means: 50.7–67.0 years) and a median of 37% female patients (range of proportions: 34–58%). Two RCTs (67%) evaluated populations of mixed SOT recipients, and one RCTs (33%) evaluated only kidney transplant recipients.

Across the 19 included observational studies, the median number of participants included was 657 (range: 41–18,174). These studies included participants with a median of mean ages of 55.0 years (range of means: 48.7–60.2 years) and had a median of 38% female patients (range of proportions: 4–54%). Ten studies (53%) assessed a mixed SOT population, followed by kidney (n = 7, 37%), liver (n = 1, 5%), and lung (n = 1, 5%) recipients. No study evaluated solely heart transplant recipients.

4.2.2 Number of vaccine doses

We did not identify a sufficient number of studies to conduct a network meta-analysis evaluating the number of vaccine doses using data from RCTs. One RCT evaluated the number of COVID-19 vaccine doses on patient-important outcomes. Based on randomized data, we are very uncertain on the impact of three doses on the risk of COVID-19 infection compared to two doses (**Table 3**).

Table 3. GRADE summary of findings table for number of doses (randomized data) using evidence up to October 1st, 2022.

	COVID-19 Infection	Hospitalization from COVID-19	ICU Admission from COVID-19	Mortality from COVID-19
	RD (95%CI)	RD (95%CI)	RD (95%CI)	RD (95%CI)
Baseline (Two doses)	270 per 1000	-	-	-
Three doses	-161 (-266 to 482)	-	-	-

Note: RD = Risk difference. Baseline risks were derived by taking the median reported risk in the comparator group across the included observational studies up to October 1st, 2022. The certainty and direction of the evidence is indicated by the colours below.

High certainty evidence	Moderate certainty evidence
More effective than two doses	Probably more effective than two doses
Less effective than two doses	Probably less effective than two doses

Low certainty evidence	Very low certainty evidence
May be more effective than two doses	Very uncertain on the comparison to two doses
May be less effective than two doses	

We identified a sufficient number of studies to conduct a network meta-analysis evaluating the number of COVID-19 doses received on the risk of COVID-19 infection, hospitalization from COVID-19, and mortality from COVID-19 (**Table 4**). Pairwise meta-analyses were conducted to evaluate the impact of the number of COVID-19 doses on the risk of ICU admission from COVID-19. We observed a credible dose-response relationship between increasing the number of COVID-19 vaccines received and a reduced risk of COVID-19 infection and mortality from COVID-19, but not for other patient-important outcomes (**Appendix 10**). Moderate certainty evidence demonstrates that three and two doses of any COVID-19 vaccine probably reduce the risk of COVID-19 infection and mortality from COVID-19. Low certainty evidence suggests that three doses may reduce the risk of hospitalization from COVID-19 and that one dose may have little to no difference compared to no vaccination on the risk of COVID-19 infection. There was very low certainty evidence for all other combinations of COVID-19 vaccine doses and patient-important outcomes.

Table 4. GRADE summary of findings table for number of doses (non-randomized data) using evidence up to October 1st, 2022.

	COVID-19 Infection	Hospitalization from COVID-19	ICU Admission from COVID-19	Mortality from COVID-19
	RD (95%CI)	RD (95%CI)	RD (95%CI)	RD (95%CI)
Baseline (No Vaccination)	51 per 1000	530 per 1000	122 per 1000	110 per 1000
Four doses	-	-	-	-
Three doses	-43 (-46 to -39)	-156 (-265 to -32)	-	-92 (-105 to -52)
Two doses	-27 (-33 to -19)	-82 (-174 to 17)	-61 (-102 to 44)	-40 (-64 to -5)
One dose	-13 (-26 to 7)	-50 (-230 to 131)	-	-8 (-63 to 98)

Note: RD = Risk difference. Baseline risks were derived by taking the median reported risk in the comparator group across the included observational studies up to October 1st, 2022. The certainty and direction of the evidence is indicated by the colours below.

High certainty evidence	Moderate certainty evidence
More effective than no vaccination	Probably more effective than no vaccination
Less effective than no vaccination	Probably less effective than no vaccination

Low certainty evidence	Very low certainty evidence
May be more effective than no vaccination	Very uncertain on the comparison to no vaccination
May be less effective than no vaccination	

4.2.3 Vaccine type

We did not identify a sufficient number of studies to conduct a network meta-analysis evaluating the type of vaccine using data from RCTs. Two RCTs evaluated the type of COVID-19 vaccines on patient-important outcomes; one trial compared any mRNA vaccine (Pfizer or Moderna) to the J&J vaccine and one trial compared the Moderna vaccine to the Pfizer vaccine. Based on randomized data, we are very uncertain on the impact of the type of COVID-19 vaccines on patient-important outcomes (**Table 5**).

Table 5. GRADE summary of findings table for type of vaccine (randomized data) using evidence up to October 1st, 2022.

	COVID-19 Infection	COVID-19-Related Hospitalization	COVID-19-Related ICU Admission	COVID-19-Related Mortality
	RD (95%CI)	RD (95%CI)	RD (95%CI)	RD (95%CI)
Baseline (J&J)	40 per 1000	-	20 per 1000	40 per 1000
Pfizer or Moderna	-10 (-33 to 83)	-	-10 (-19 to 81)	0 (-30 to 105)
Baseline (Pfizer)	148 per 1000	-	-	6 per 1000
Moderna	11 (-136 to 611)	-	-	1 (-6 to 92)

Note: RD = Risk difference. Baseline risks were derived by taking the median reported risk in the comparator group across the included observational studies up to October 1st, 2022. The certainty and direction of the evidence is indicated by the colours below.

High certainty evidence	Moderate certainty evidence
More effective than the reference group	Probably more effective than the reference group
Less effective than the reference group	Probably less effective than the reference group

Low certainty evidence	Very low certainty evidence
May be more effective than the reference group	Very uncertain on the comparison to the reference group
May be less effective than the reference group	

We did not identify a sufficient number of observational studies to perform a network meta-analysis evaluating the impact of the type of vaccine on patient-important outcomes. Based on pairwise comparisons, compared to Pfizer, Moderna may reduce the risk of COVID-19-related mortality. However, the impact of the type of COVID-19 vaccine on other patient-important outcomes is very uncertain (**Table 6**).

Table 6. GRADE summary of findings table for type of vaccine (non-randomized data) using evidence up to October 1st, 2022.

	COVID-19 Infection	COVID-19-Related Hospitalization	COVID-19-Related ICU Admission	COVID-19-Related Mortality
	RD (95%CI)	RD (95%CI)	RD (95%CI)	RD (95%CI)
Pfizer	148 per 1000	12 per 1000	-	6 per 1000
Moderna	-8 (-37 to 29)	-1 (-5 to 7)	-	-3 (-4 to -1)
AstraZeneca	-	-	-	-

Note: RD = Risk difference. Baseline risks were derived by taking the median reported risk in the comparator group across the included observational studies up to October 1st, 2022. The certainty and direction of the evidence is indicated by the colours below.

High certainty evidence	Moderate certainty evidence
More effective than Pfizer	Probably more effective than Pfizer
Less effective than Pfizer	Probably less effective than Pfizer

Low certainty evidence	Very low certainty evidence
May be more effective than Pfizer	Very uncertain on the comparison to Pfizer
May be less effective than Pfizer	

4.3 Review findings from Timepoint 2 (March 1st, 2023)

4.3.1 Summary of included studies

The systematic review capturing studies published until March 1st, 2023 identified 33 eligible studies (4 RCTs [n = 629 patients] and 29 observational studies [n = 102,912 patients]).

Among the 4 included RCTs, the median number of participants randomized was 161 (range: 78–230). These RCTs included participants with a median of mean ages of 59.3 years (range of means: 50.7–67.0 years) and a median of 36% female patients (range of proportions: 34–58%). Two RCTs (50%) evaluated populations of mixed SOT recipients, and two RCTs (50%) evaluated only kidney transplant recipients.

Across the 29 included observational studies, the median number of participants included was 657 (range: 41–18,174). These studies included participants with a median of mean ages of 54.5 years (range of means: 42.9–61.5 years) and had a median of 41% female patients (range of

proportions: 4–72%). Sixteen studies (55%) assessed a mixed SOT population, followed by kidney (n = 10, 35%), liver (n = 2, 7%), and lung (n = 1, 3%) recipients. No study evaluated solely heart transplant recipients.

4.3.2 Number of vaccine doses

We did not identify a sufficient number of studies to conduct a network meta-analysis evaluating the number of vaccine doses using data from RCTs. One RCT evaluated the number of COVID-19 vaccine doses on patient-important outcomes. Based on randomized data, we are very uncertain on the impact of three doses on the risk of COVID-19 infection compared to two doses (**Table 7**).

Table 7. GRADE summary of findings table for number of doses (randomized data) using evidence up to March 1st, 2023.

	COVID-19 Infection	**Hospitalization from COVID-19**	**ICU Admission from COVID-19**	**Mortality from COVID-19**
	RD (95%CI)	**RD (95%CI)**	**RD (95%CI)**	**RD (95%CI)**
Baseline (Two doses)	270 per 1000	-	-	-
Three doses	-161 (-266 to 482)	-	-	-

Note: RD = Risk difference. Baseline risks were derived by taking the median reported risk in the comparator group across the included observational studies up to March 1st, 2023. The certainty and direction of the evidence is indicated by the colours below.

High certainty evidence	**Moderate certainty evidence**
More effective than two doses	Probably more effective than two doses
Less effective than two doses	Probably less effective than two doses

Low certainty evidence	**Very low certainty evidence**
May be more effective than two doses	Very uncertain on the comparison to two doses
May be less effective than two doses	

We identified a sufficient number of studies to conduct a network meta-analysis evaluating the number of COVID-19 doses received on the risk of COVID-19 infection, hospitalization from COVID-19, and mortality from COVID-19 (**Table 8**). Pairwise meta-analyses were conducted to evaluate the impact of the number of COVID-19 doses on the risk of ICU admission from COVID-19. We observed a credible dose-response relationship between increasing the number of COVID-19 vaccines received and a reduced risk of COVID-19 infection, but not for other patient-important outcomes (**Appendix 10**). Moderate certainty evidence demonstrates that four, three, and two doses of any COVID-19 vaccine probably reduce the risk of COVID-19 infection. Low certainty evidence suggests that three doses may reduce the risk of hospitalization from COVID-19 and mortality from COVID-19. Low certainty evidence suggests that two doses may reduce the risk of ICU admission and mortality from COVID-19. There was very low certainty evidence for all other combinations of COVID-19 vaccine doses and patient-important outcomes.

Table 8. GRADE summary of findings table for number of doses (non-randomized data) using evidence up to March 1st, 2023.

	COVID-19 Infection	Hospitalization from COVID-19	ICU Admission from COVID-19	Mortality from COVID-19
	RD (95%CI)	**RD (95%CI)**	**RD (95%CI)**	**RD (95%CI)**
Baseline (No Vaccination)	51 per 1000	491 per 1000	177 per 1000	111 per 1000
Four doses	-45 (-49 to -30)	22 (-372 to 398)	-	-80 (-105 to 34)
Three doses	-41 (-46 to -33)	-213 (-343 to -24)	-	-95 (-105 to -71)
Two doses	-29 (-36 to -18)	-124 (-261 to 37)	-87 (-128 to -22)	-63 (-84 to -30)
One dose	-12 (-33 to 33)	-49 (-380 to 340)	-	-8 (-94 to 316)

Note: RD = Risk difference. Baseline risks were derived by taking the median reported risk in the comparator group across the included observational studies up to March 1st, 2023. The certainty and direction of the evidence is indicated by the colours below.

High certainty evidence	**Moderate certainty evidence**
More effective than no vaccination	Probably more effective than no vaccination
Less effective than no vaccination	Probably less effective than no vaccination

Low certainty evidence	**Very low certainty evidence**
May be more effective than no vaccination	Very uncertain on the comparison to no vaccination
May be less effective than no vaccination	

4.3.3 Vaccine type

We did not identify a sufficient number of studies to conduct a network meta-analysis evaluating the type of vaccine using data from RCTs. Three RCTs evaluated the type of COVID-19 vaccines on patient-important outcomes; two trials compared any mRNA vaccine (Pfizer or Moderna) to the J&J vaccine and one trial compared the Moderna vaccine to the Pfizer vaccine. Based on randomized data, we are very uncertain on the impact of the type of COVID-19 vaccines on patient-important outcomes (**Table 9**).

Table 9. GRADE summary of findings table for type of vaccine (randomized data) using evidence up to March 1st, 2023.

	COVID-19 Infection	COVID-19-Related Hospitalization	COVID-19-Related ICU Admission	COVID-19-Related Mortality
	RD (95%CI)	RD (95%CI)	RD (95%CI)	RD (95%CI)
Baseline (J&J)	39 per 1000	-	20 per 1000	40 per 1000
Pfizer or Moderna	-16 (-33 to 38)	-	-10 (-19 to 81)	0 (-30 to 105)
Baseline (Pfizer)	148 per 1000	-	-	6 per 1000
Moderna	11 (-136 to 611)	-	-	1 (-6 to 92)

Note: RD = Risk difference. Baseline risks were derived by taking the median reported risk in the comparator group across the included observational studies up to March 1st, 2023. The certainty and direction of the evidence is indicated by the colours below.

High certainty evidence	Moderate certainty evidence
More effective than the reference group	Probably more effective than the reference group
Less effective than the reference group	Probably less effective than the reference group

Low certainty evidence	Very low certainty evidence
May be more effective than the reference group	Very uncertain on the comparison to the reference group
May be less effective than the reference group	

We did not identify a sufficient number of observational studies to perform a network meta-analysis evaluating the impact of the type of vaccine on patient-important outcomes. Based on pairwise comparisons, compared to Pfizer, Moderna may reduce the risk of COVID-19-related mortality and AstraZeneca may increase the risk of COVID-19 infection. However, the impact of the type of COVID-19 vaccine on other patient-important outcomes is very uncertain (**Table 10**).

Table 10. GRADE summary of findings table for type of vaccine (non-randomized data) using evidence up to March 1st, 2023.

	COVID-19 Infection	COVID-19-Related Hospitalization	COVID-19-Related ICU Admission	COVID-19-Related Mortality
	RD (95%CI)	RD (95%CI)	RD (95%CI)	RD (95%CI)
Pfizer	115 per 1000	12 per 1000	-	6 per 1000
Moderna	-25 (-61 to 30)	-1 (-5 to 7)	-	-3 (-4 to -1)
AstraZeneca	41 (17 to 69)	5 (0 to 11)	-	1 (-2 to 7)

Note: RD = Risk difference. Baseline risks were derived by taking the median reported risk in the comparator group across the included observational studies up to March 1st, 2023. The certainty and direction of the evidence is indicated by the colours below.

High certainty evidence	Moderate certainty evidence
More effective than Pfizer	Probably more effective than Pfizer
Less effective than Pfizer	Probably less effective than Pfizer

Low certainty evidence	Very low certainty evidence
May be more effective than Pfizer	Very uncertain on the comparison to Pfizer
May be less effective than Pfizer	

4.4 Review findings from Timepoint 3 (July 1st, 2023)

4.4.1 Summary of included studies

The systematic review capturing studies published until July 1st, 2023 identified 38 eligible studies (5 RCTs [n = 689 patients] and 33 observational studies [n = 114,890 patients]).

Among the 5 included RCTs, the median number of participants randomized was 120 (range: 60–230). These RCTs included participants with a median of mean ages of 57.4 years (range of means: 50.7–67.0 years) and a median of 35% female patients (range of proportions: 34–58%). Three RCTs (60%) evaluated populations of mixed SOT recipients, and two RCTs (40%) evaluated only kidney transplant recipients.

Across the 33 included observational studies, the median number of participants included was 646 (range: 41–18,174). These studies included participants with a median of mean ages of 54.1 years (range of means: 42.9–61.5 years) and had a median of 41% female patients (range of

proportions: 4–72%). Sixteen studies (49%) assessed a mixed SOT population, followed by kidney (n = 13, 39%), liver (n = 2, 6%), lung (n = 1, 3%), and heart (n = 1, 3%) recipients.

4.4.2 Number of vaccine doses

We did not identify a sufficient number of studies to conduct a network meta-analysis evaluating the number of vaccine doses using data from RCTs. One RCT evaluated the number of COVID-19 vaccine doses on patient-important outcomes. Based on randomized data, we are very uncertain on the impact of three doses on the risk of COVID-19 infection compared to two doses (**Table 11**).

Table 11. GRADE summary of findings table for number of doses (randomized data) using evidence up to July 1st, 2023.

	COVID-19 Infection	**Hospitalization from COVID-19**	**ICU Admission from COVID-19**	**Mortality from COVID-19**
	RD (95%CI)	**RD (95%CI)**	**RD (95%CI)**	**RD (95%CI)**
Baseline (Two doses)	297 per 1000	-	-	-
Three doses	-175 (-293 to 479)	-	-	-

Note: RD = Risk difference. Baseline risks were derived by taking the median reported risk in the comparator group across the included observational studies up to July 1st, 2023. The certainty and direction of the evidence is indicated by the colours below.

High certainty evidence	**Moderate certainty evidence**
More effective than two doses	Probably more effective than two doses
Less effective than two doses	Probably less effective than two doses

Low certainty evidence	**Very low certainty evidence**
May be more effective than two doses	Very uncertain on the comparison to two doses
May be less effective than two doses	

We identified a sufficient number of studies to conduct a network meta-analysis evaluating the number of COVID-19 doses received on the risk of COVID-19 infection, hospitalization from COVID-19, and mortality from COVID-19 (**Table 12**). Pairwise meta-analyses were conducted to evaluate the impact of the number of COVID-19 doses on the risk of ICU admission from COVID-19. We observed a credible dose-response relationship between increasing the number of COVID-19 vaccines received and a reduced risk of COVID-19 infection, but not for other patient-important outcomes (**Appendix 10**). Moderate certainty evidence demonstrates that four, three, and two doses of any COVID-19 vaccine probably reduce the risk of COVID-19 infection. Low certainty evidence suggests that three doses may reduce the risk of hospitalization from COVID-19 and mortality from COVID-19. Low certainty evidence suggests that two doses may reduce the risk of ICU admission and mortality from COVID-19. There was very low certainty evidence for all other combinations of COVID-19 vaccine doses and patient-important outcomes.

Table 12. GRADE summary of findings table for number of doses (non-randomized data) using evidence up to July 1st, 2023.

	COVID-19 Infection	Hospitalization from COVID-19	ICU Admission from COVID-19	Mortality from COVID-19
	RD (95%CI)	RD (95%CI)	RD (95%CI)	RD (95%CI)
Baseline (No Vaccination)	51 per 1000	491 per 1000	177 per 1000	111 per 1000
Four doses	-46 (-49 to -37)	22 (-365 to 394)	-	-80 (-105 to 27)
Three doses	-41 (-45 to -34)	-218 (-336 to -59)	-	-91 (-102 to -67)
Two doses	-29 (-36 to -19)	-113 (-244 to 41)	-87 (-128 to -22)	-62 (-83 to -30)
One dose	-12 (-33 to 31)	-49 (-372 to 333)	-	-8 (-93 to 298)

Note: RD = Risk difference. Baseline risks were derived by taking the median reported risk in the comparator group across the included observational studies up to July 1st, 2023. The certainty and direction of the evidence is indicated by the colours below.

High certainty evidence	Moderate certainty evidence
More effective than no vaccination	Probably more effective than no vaccination
Less effective than no vaccination	Probably less effective than no vaccination

Low certainty evidence	Very low certainty evidence
May be more effective than no vaccination	Very uncertain on the comparison to no vaccination
May be less effective than no vaccination	

4.4.3 Vaccine type

We did not identify a sufficient number of studies to conduct a network meta-analysis evaluating the type of vaccine using data from RCTs. Four RCTs evaluated the type of COVID-19 vaccines on patient-important outcomes; three trials compared any mRNA vaccine (Pfizer or Moderna) to the J&J vaccine and one trial compared the Moderna vaccine to the Pfizer vaccine. Based on randomized data, low certainty evidence suggests that any mRNA vaccine (Pfizer or Moderna) probably has little to no difference on COVID-19 infection compared to J&J. We are very uncertain on the impact of the type of COVID-19 vaccines on patient-important outcomes (**Table 13**).

Table 13. GRADE summary of findings table for type of vaccine (randomized data) using evidence up to July 1st, 2023.

	COVID-19 Infection	COVID-19-Related Hospitalization	COVID-19-Related ICU Admission	COVID-19-Related Mortality
	RD (95%CI)	RD (95%CI)	RD (95%CI)	RD (95%CI)
Baseline (J&J)	38 per 1000	-	20 per 1000	40 per 1000
Pfizer or Moderna	-17 (-32 to 26)	-	-10 (-19 to 81)	0 (-30 to 105)
Baseline (Pfizer)	148 per 1000	-	-	6 per 1000
Moderna	11 (-136 to 611)	-	-	1 (-6 to 92)

Note: RD = Risk difference. Baseline risks were derived by taking the median reported risk in the comparator group across the included observational studies up to July 1st, 2023. The certainty and direction of the evidence is indicated by the colours below.

High certainty evidence	Moderate certainty evidence
More effective than the reference group	Probably more effective than the reference group
Less effective than the reference group	Probably less effective than the reference group

Low certainty evidence	Very low certainty evidence
May be more effective than the reference group	Very uncertain on the comparison to the reference group
May be less effective than the reference group	

We did not identify a sufficient number of observational studies to perform a network meta-analysis evaluating the impact of the type of vaccine on patient-important outcomes. Based on pairwise comparisons, compared to Pfizer, Moderna may reduce the risk of COVID-19-related mortality and AstraZeneca may increase the risk of COVID-19 infection. However, the impact of the type of COVID-19 vaccine on other patient-important outcomes is very uncertain (**Table 14**).

Table 14. GRADE summary of findings table for type of vaccine (non-randomized data) using evidence up to July 1st, 2023.

	COVID-19 Infection	COVID-19-Related Hospitalization	COVID-19-Related ICU Admission	COVID-19-Related Mortality
	RD (95%CI)	RD (95%CI)	RD (95%CI)	RD (95%CI)
Pfizer	115 per 1000	12 per 1000	-	6 per 1000
Moderna	-25 (-61 to 30)	-1 (-5 to 7)	-	-3 (-4 to -1)
AstraZeneca	41 (17 to 69)	5 (0 to 11)	-	1 (-2 to 7)

Note: RD = Risk difference. Baseline risks were derived by taking the median reported risk in the comparator group across the included observational studies up to July 1st, 2023. The certainty and direction of the evidence is indicated by the colours below.

High certainty evidence	Moderate certainty evidence
More effective than Pfizer	Probably more effective than Pfizer
Less effective than Pfizer	Probably less effective than Pfizer

Low certainty evidence	Very low certainty evidence
May be more effective than Pfizer	Very uncertain on the comparison to Pfizer
May be less effective than Pfizer	

4.5 Review findings from Timepoint 4 (March 1st, 2024)

4.5.1 Summary of included studies

The systematic review capturing studies published until March 1st, 2024 identified 48 eligible studies (6 RCTs [n = 689 patients] and 42 observational studies [n = 114,890 patients]).

Among the 6 included RCTs, the median number of participants randomized was 123 (range: 60–230). These RCTs included participants with a median of mean ages of 58.5 years (range of means: 50.7–67.0 years) and a median of 35% female patients (range of proportions: 34–58%). Three RCTs (50%) evaluated populations of mixed SOT recipients, and three RCTs (50%) evaluated only kidney transplant recipients.

Across the 42 included observational studies, the median number of participants included was 618 (range: 41–18,174). These studies included participants with a median of mean ages of 54.5 years (range of means: 42.9–66.6 years) and had a median of 41% female patients (range of

proportions: 4–72%). Eighteen studies (43%) assessed a mixed SOT population, followed by kidney (n = 17, 40%), liver (n = 4, 10%), lung (n = 2, 5%), and heart (n = 1, 2%) transplant recipients.

4.5.2 Number of vaccine doses

We did not identify a sufficient number of studies to conduct a network meta-analysis evaluating the number of vaccine doses using data from RCTs. Two RCTs evaluated the number of COVID-19 vaccine doses on patient-important outcomes; one trial evaluated three doses versus two doses and one trial evaluated four doses versus three doses. Based on randomized data, we are very uncertain on the impact of the number of COVID-19 vaccine doses on the risk of COVID-19 infection (**Table 15**).

Table 15. GRADE summary of findings table for number of doses (randomized data) using evidence up to March 1st, 2024.

	COVID-19 Infection	**Hospitalization from COVID-19**	**ICU Admission from COVID-19**	**Mortality from COVID-19**
	RD (95%CI)	**RD (95%CI)**	**RD (95%CI)**	**RD (95%CI)**
Baseline (Two doses)	297 per 1000	-	-	-
Three doses	-175 (-293 to 479)	-	-	-
Baseline (Three doses)	214 per 1000	-	-	-
Four doses	-62 (-162 to 155)	-	-	-

Note: RD = Risk difference. Baseline risks were derived by taking the median reported risk in the comparator group across the included observational studies up to March 1st, 2024. The certainty and direction of the evidence is indicated by the colours below.

High certainty evidence	**Moderate certainty evidence**
More effective than the reference group	Probably more effective than the reference group
Less effective than the reference group	Probably less effective than the reference group

Low certainty evidence	**Very low certainty evidence**
May be more effective than the reference group	Very uncertain on the comparison to the reference group
May be less effective than the reference group	

We identified a sufficient number of studies to conduct a network meta-analysis evaluating the number of COVID-19 doses received on the risk of COVID-19 infection, hospitalization from COVID-19, ICU admission from COVID-19, and mortality from COVID-19 (**Table 16**). We observed a credible dose-response relationship between increasing the number of COVID-19 vaccines received and a reduced risk of COVID-19 infection, but not for other patient-important outcomes (**Appendix 10**). Moderate certainty evidence demonstrates that four, three, and two doses of any COVID-19 vaccine probably reduce the risk of COVID-19 infection. Low certainty evidence suggests that three and two doses may reduce the risk of hospitalization from COVID-19 and mortality from COVID-19. There was very low certainty evidence for all other combinations of COVID-19 vaccine doses and patient-important outcomes.

Table 16. GRADE summary of findings table for number of doses (non-randomized data) using evidence up to March 1st, 2024.

	COVID-19 Infection	Hospitalization from COVID-19	ICU Admission from COVID-19	Mortality from COVID-19
	RD (95%CI)	RD (95%CI)	RD (95%CI)	RD (95%CI)
Baseline (No Vaccination)	54 per 1000	512 per 1000	171 per 1000	111 per 1000
Four doses	-47 (-51 to -40)	21 (-324 to 337)	-	-80 (-105 to 26)
Three doses	-43 (-48 to -35)	-232 (-318 to -122)	-43 (-104 to 57)	-87 (-99 to -66)
Two doses	-29 (-37 to -19)	-122 (-216 to -18)	-61 (-104 to 6)	-60 (-80 to -30)
One dose	-13 (-34 to 31)	-103 (-304 to 137)	-	-62 (-99 to 60)

Note: RD = Risk difference. Baseline risks were derived by taking the median reported risk in the comparator group across the included observational studies up to March 1st, 2024. The certainty and direction of the evidence is indicated by the colours below.

High certainty evidence	Moderate certainty evidence
More effective than no vaccination	Probably more effective than no vaccination
Less effective than no vaccination	Probably less effective than no vaccination

Low certainty evidence	Very low certainty evidence
May be more effective than no vaccination	Very uncertain on the comparison to no vaccination
May be less effective than no vaccination	

4.5.3 Vaccine type

We did not identify a sufficient number of studies to conduct a network meta-analysis evaluating the type of vaccine using data from RCTs. Four RCTs evaluated the type of COVID-19 vaccines on patient-important outcomes; three trials compared any mRNA vaccine (Pfizer or Moderna) to the J&J vaccine and one trial compared the Moderna vaccine to the Pfizer vaccine. Based on randomized data, low certainty evidence suggests that any mRNA vaccine (Pfizer or Moderna) probably has little to no difference on COVID-19 infection compared to J&J. We are very uncertain on the impact of the type of COVID-19 vaccines on patient-important outcomes (**Table 17**).

Table 17. GRADE summary of findings table for type of vaccine (randomized data) using evidence up to March 1st, 2024.

	COVID-19 Infection	COVID-19-Related Hospitalization	COVID-19-Related ICU Admission	COVID-19-Related Mortality
	RD (95%CI)	RD (95%CI)	RD (95%CI)	RD (95%CI)
Baseline (J&J)	38 per 1000	-	20 per 1000	40 per 1000
Pfizer or Moderna	-17 (-32 to 26)	-	-10 (-19 to 81)	0 (-30 to 105)
Baseline (Pfizer)	148 per 1000	-	-	6 per 1000
Moderna	11 (-136 to 611)	-	-	1 (-6 to 92)

Note: RD = Risk difference. Baseline risks were derived by taking the median reported risk in the comparator group across the included observational studies up to March 1st, 2024. The certainty and direction of the evidence is indicated by the colours below.

High certainty evidence	Moderate certainty evidence
More effective than the reference group	Probably more effective than the reference group
Less effective than the reference group	Probably less effective than the reference group

Low certainty evidence	Very low certainty evidence
May be more effective than the reference group	Very uncertain on the comparison to the reference group
May be less effective than the reference group	

We did not identify a sufficient number of observational studies to perform a network meta-analysis evaluating the impact of the type of vaccine on patient-important outcomes. Based on pairwise comparisons, compared to Pfizer, Moderna may reduce the risk of COVID-19-related mortality and AstraZeneca may increase the risk of COVID-19 infection. However, the impact of the type of COVID-19 vaccine on other patient-important outcomes is very uncertain (**Table 18**).

Table 18. GRADE summary of findings table for type of vaccine (non-randomized data) using evidence up to March 1st, 2024.

	COVID-19 Infection	COVID-19-Related Hospitalization	COVID-19-Related ICU Admission	COVID-19-Related Mortality
	RD (95%CI)	RD (95%CI)	RD (95%CI)	RD (95%CI)
Pfizer	115 per 1000	12 per 1000	-	6 per 1000
Moderna	-25 (-61 to 30)	-1 (-5 to 7)	-	-3 (-4 to -1)
AstraZeneca	41 (17 to 69)	5 (0 to 11)	-	1 (-2 to 7)

Note: RD = Risk difference. Baseline risks were derived by taking the median reported risk in the comparator group across the included observational studies up to March 1st, 2024. The certainty and direction of the evidence is indicated by the colours below.

High certainty evidence	Moderate certainty evidence
More effective than Pfizer	Probably more effective than Pfizer
Less effective than Pfizer	Probably less effective than Pfizer

Low certainty evidence	Very low certainty evidence
May be more effective than Pfizer	Very uncertain on the comparison to Pfizer
May be less effective than Pfizer	

4.6 Comparison of review findings across timepoints

4.6.1 Number of vaccine doses

Across the four timepoints, the conclusions drawn from the randomized evidence largely remained unchanged (**Table 19**). Seven of eight (88%) combinations of interventions and patient-important outcomes remained unchanged over the course of the living systematic review. Most (n = 6, 86%) of these intervention and outcome combinations persistently had an absence of evidence. In Timepoint 4, evidence comparing four doses and three doses of any COVID-19 vaccine was identified, albeit with very low certainty.

Table 19. Evolution of randomized evidence assessing the number of vaccine doses.

Four doses vs three doses					
Outcome	**Timepoint 1 (October 1st, 2022)**	**Timepoint 2 (March 1st, 2023)**	**Timepoint 3 (July 1st, 2023)**	**Timepoint 4 (March 1st, 2024)**	**Evolution of Evidence**
COVID-19 Infection	-	-	-	Very uncertain	Changed
COVID-19-Related Hospitalization	-	-	-	-	Unchanged
COVID-19-Related ICU Admission	-	-	-	-	Unchanged
COVID-19-Related Mortality	-	-	-	-	Unchanged
Three doses vs two doses					
Outcome	**Timepoint 1 (October 1st, 2022)**	**Timepoint 2 (March 1st, 2023)**	**Timepoint 3 (July 1st, 2023)**	**Timepoint 4 (March 1st, 2024)**	**Evolution of Evidence**
COVID-19 Infection	Very uncertain	Very uncertain	Very uncertain	Very uncertain	Unchanged
COVID-19-Related Hospitalization	-	-	-	-	Unchanged
COVID-19-Related ICU Admission	-	-	-	-	Unchanged
COVID-19-Related Mortality	-	-	-	-	Unchanged

Based on the observational studies, over half (n = 9, 56%) of the combinations of interventions and patient-important outcomes changed over the course of the living systematic review (**Table 20**). Of these nine changes, four (44%) stemmed from the identification of new studies in the previous absence of evidence, and the remaining five (56%) were a result of changes in the certainty in the evidence.

Table 20. Evolution of non-randomized evidence assessing the number of vaccine doses.

Four doses vs no vaccination					
Outcome	**Timepoint 1 (October 1st, 2022)**	**Timepoint 2 (March 1st, 2023)**	**Timepoint 3 (July 1st, 2023)**	**Timepoint 4 (March 1st, 2024)**	**Evolution of Evidence**
COVID-19 Infection	-	Probably ↓ risk	Probably ↓ risk	Probably ↓ risk	Changed
Hospitalization from COVID-19	-	Very uncertain	Very uncertain	Very uncertain	Changed
ICU Admission from COVID-19	-	-	-	-	Unchanged
Mortality from COVID-19	-	Very uncertain	Very uncertain	Very uncertain	Changed
Three doses vs no vaccination					
Outcome	**Timepoint 1 (October 1st, 2022)**	**Timepoint 2 (March 1st, 2023)**	**Timepoint 3 (July 1st, 2023)**	**Timepoint 4 (March 1st, 2024)**	**Evolution of Evidence**
COVID-19 Infection	Probably ↓ risk	Probably ↓ risk	Probably ↓ risk	Probably ↓ risk	Unchanged
Hospitalization from COVID-19	May ↓ risk	May ↓ risk	May ↓ risk	May ↓ risk	Unchanged
ICU Admission from COVID-19	-	-	-	Very uncertain	Changed
Mortality from COVID-19	Probably ↓ risk	May ↓ risk	May ↓ risk	May ↓ risk	Changed
Two doses vs no vaccination					
Outcome	**Timepoint 1 (October 1st, 2022)**	**Timepoint 2 (March 1st, 2023)**	**Timepoint 3 (July 1st, 2023)**	**Timepoint 4 (March 1st, 2024)**	**Evolution of Evidence**
COVID-19 Infection	Probably ↓ risk	Probably ↓ risk	Probably ↓ risk	Probably ↓ risk	Unchanged
Hospitalization from COVID-19	Very uncertain	Very uncertain	Very uncertain	May ↓ risk	Changed
ICU Admission from COVID-19	Very uncertain	May ↓ risk	May ↓ risk	Very uncertain	Changed
Mortality from COVID-19	Probably ↓ risk	May ↓ risk	May ↓ risk	May ↓ risk	Changed
One doses vs no vaccination					
Outcome	**Timepoint 1 (October 1st, 2022)**	**Timepoint 2 (March 1st, 2023)**	**Timepoint 3 (July 1st, 2023)**	**Timepoint 4 (March 1st, 2024)**	**Evolution of Evidence**
COVID-19 Infection	May ↓ risk	Very uncertain	Very uncertain	Very uncertain	Changed
Hospitalization from COVID-19	Very uncertain	Very uncertain	Very uncertain	Very uncertain	Unchanged
ICU Admission from COVID-19	-	-	-	-	Unchanged
Mortality from COVID-19	Very uncertain	Very uncertain	Very uncertain	Very uncertain	Unchanged

4.6.2 Vaccine type

Across the four timepoints, the conclusions drawn from the randomized evidence evaluating the type of COVID-19 vaccines also largely remained unchanged (**Table 21**). Seven of eight (88%) combinations of interventions and patient-important outcomes remained unchanged over the course of the living systematic review. Most (n = 3, 38%) of these intervention and outcome combinations persistently had an absence of evidence. The evidence evaluating mRNA vaccines versus J&J on risk of COVID-19 infection changed from very low certainty evidence to low certainty evidence suggesting mRNA vaccines may reduce risk of COVID-19 infection over the course of the living review.

Table 21. Evolution of randomized evidence assessing the type of vaccine.

mRNA vs J&J					
Outcome	**Timepoint 1 (October 1st, 2022)**	**Timepoint 2 (March 1st, 2023)**	**Timepoint 3 (July 1st, 2023)**	**Timepoint 4 (March 1st, 2024)**	**Evolution of Evidence**
COVID-19 Infection	Very uncertain	Very uncertain	May ↓ risk	May ↓ risk	Changed
COVID-19-Related Hospitalization	-	-	-	-	Unchanged
COVID-19-Related ICU Admission	Very uncertain	Very uncertain	Very uncertain	Very uncertain	Unchanged
COVID-19-Related Mortality	Very uncertain	Very uncertain	Very uncertain	Very uncertain	Unchanged
Moderna vs Pfizer					
Outcome	**Timepoint 1 (October 1st, 2022)**	**Timepoint 2 (March 1st, 2023)**	**Timepoint 3 (July 1st, 2023)**	**Timepoint 4 (March 1st, 2024)**	**Evolution of Evidence**
COVID-19 Infection	Very uncertain	Very uncertain	Very uncertain	Very uncertain	Unchanged
COVID-19-Related Hospitalization	-	-	-	-	Unchanged
COVID-19-Related ICU Admission	-	-	-	-	Unchanged
COVID-19-Related Mortality	Very uncertain	Very uncertain	Very uncertain	Very uncertain	Unchanged

Based on the observational studies, over half (n = 5, 63%) of the combinations of interventions and patient-important outcomes remained unchanged over the course of the living systematic review (**Table 22**). All three changes (37%) stemmed from the identification of new studies in the previous absence of evidence.

Table 22. Evolution of non-randomized evidence assessing the type of vaccine.

Moderna vs Pfizer					
Outcome	**Timepoint 1 (October 1st, 2022)**	**Timepoint 2 (March 1st, 2023)**	**Timepoint 3 (July 1st, 2023)**	**Timepoint 4 (March 1st, 2024)**	**Evolution of Evidence**
COVID-19 Infection	Very uncertain	Very uncertain	Very uncertain	Very uncertain	Unchanged
COVID-19-Related Hospitalization	Very uncertain	Very uncertain	Very uncertain	Very uncertain	Unchanged
COVID-19-Related ICU Admission	-	-	-	-	Unchanged
COVID-19-Related Mortality	May ↓ risk	May ↓ risk	May ↓ risk	May ↓ risk	Unchanged
AstraZeneca vs Pfizer					
Outcome	**Timepoint 1 (October 1st, 2022)**	**Timepoint 2 (March 1st, 2023)**	**Timepoint 3 (July 1st, 2023)**	**Timepoint 4 (March 1st, 2024)**	**Evolution of Evidence**
COVID-19 Infection	-	May ↑ risk	May ↑ risk	May ↑ risk	Changed
COVID-19-Related Hospitalization	-	Very uncertain	Very uncertain	Very uncertain	Changed
COVID-19-Related ICU Admission	-	-	-	-	Unchanged
COVID-19-Related Mortality	-	Very uncertain	Very uncertain	Very uncertain	Changed

CHAPTER 5: Discussion

5.1 Summary of study findings

We conducted this living systematic review and network meta-analysis to address the uncertainty regarding the clinical efficacy of COVID-19 vaccines in SOT recipients and to evaluate the evolution of the evidence over time. Incorporating evidence up to March 1st, 2024, moderate certainty evidence demonstrated that four, three, and two doses of any COVID-19 vaccine received probably reduces the risk of COVID-19 infection compared to no vaccination. A dose-response relationship between the number of COVID-19 vaccines received and risk of COVID-19 infection was observed, but this was not present for other patient-important outcomes. The evidence comparing different vaccine types on patient-important outcomes had low to very low certainty. Across the four iterations of this living systematic review, the conclusions drawn from the evidence supported by randomized data largely remained unchanged; however, half of the conclusions drawn from the evidence supported by observational data changed in certainty or direction of conclusion.

5.2 Study strengths and limitations

Strengths of our living systematic review include its comprehensive search strategy encompassing published and unpublished sources of data, and the use of standardized approaches, including GRADE (Guyatt et al., 2008) and ICEMAN (Schandelmaier et al., 2020), to assist with the interpretation of our review findings. Furthermore, this systematic review and meta-analysis is the first to comprehensively evaluate the impact of COVID-19 vaccination on patient-important outcomes in SOT recipients and to formally assess the evolution of the evidence over time. Finally,

our review is informed by guideline panel members, including patient partners, transplant clinicians, and infectious disease specialists. These panel members defined our clinical questions and prioritized patient-important outcomes, ensuring that the findings of our review are relevant to clinical practice.

Our systematic review suffers from several limitations. Unfortunately, our investigations are limited by the paucity of RCTs evaluating the effectiveness of different COVID-19 vaccination strategies in SOT recipients. These trials were designed with relatively small sample sizes, short follow-up periods, and were powered to assess immunogenicity outcomes rather than patient-important outcomes, and ultimately led to low and very low certainty evidence due to concerns related to imprecision. Given the limited quality randomized evidence, we leveraged observational studies that typically have larger sample sizes. Unfortunately, observational studies are prone to selection and confounding bias, thus limiting the certainty of the findings drawn from this body of evidence (Sterne et al., 2016). To mitigate this potential limitation, we restricted our included observational studies to those leveraging multivariable analysis or propensity matching.

Furthermore, our review was unable to compare the impact of all available COVID-19 vaccines on patient-important outcomes. Our review only identified evidence evaluating four vaccines (Moderna, Pfizer, J&J and AstraZeneca); we did not identify evidence for other World Health Organization-approved vaccines, including CoronaVac, BBIBP-CorV, and NVX-CoV2373. Moreover, our network meta-analysis evaluating the number of doses relies on the assumption that different vaccine types yield similar effects on patient-important outcomes. However, our review did not identify any high or moderate certainty evidence that the type of COVID-19 vaccine substantially influences its effect on patient-important outcomes.

Finally, our systematic review was unable to account for the time period in which the included studies took place and the country they were conducted in. The baseline infection rate at the beginning of the COVID-19 pandemic and during the post-vaccination era were likely substantially different. Likewise, baseline infection rates likely differed between countries over the course of the pandemic. The changing charactersitcs of the SARS-CoV-2 virus, combined with the refinements made to COVID-19 vaccines over the course of the pandemic likely affected the relationship between the various COVID-19 vaccine strategies and clinical outcomes.

5.3 Relation to previous work and implications for future research

Previous systematic reviews have highlighted the dose-response relationship between the number of COVID-19 vaccine doses and enhanced seroconversion in SOT recipients (Alotaibi et al., 2023; Efros et al., 2022). Our review supports these previous findings—we identified a dose-response relationship between the number of COVID-19 vaccines received and the risk of COVID-19 infection. However, such a relationship was not confirmed for other patient-important outcomes, including hospitalization, ICU admission, and mortality due to COVID-19. This lack of dose response for mortality may be related to the less virulent strain of SARS-CoV-2 and the impact of previous COVID-19 infections during the time period in which fourth doses were available.

Our systematic review was unable to evaluate the impact of mycophenolate-based immunosuppression on COVID-19 vaccination responsiveness and patient-important outcomes. Previous systematic reviews have identified mycophenolate use as a predictor of nonresponse following COVID-19 vaccination (Meshram et al., 2022; Manothummetha et al., 2022).

Conversely, one small RCT found no significant difference in seroconversion and risk of COVID-19 infection between continuing or discontinuing antimetabolite therapy around the time of vaccination (Kho et al., 2023). Future research is needed to assess the potential modulating relationship of mycophenolate-based immunosuppressive therapies on the efficacy of COVID-19 vaccination towards patient-important outcomes.

Over the course of the COVID-19 pandemic, several national and international transplant organizations, including the American Society of Transplantation (AST), the Canadian Society of Transplantation (CST), the American Society of Transplant Surgeons (ASTS), and the International Society for Heart and Lung Transplantation (ISHLT) developed recommendations related to COVID-19 vaccination in solid organ transplant recipients (ISHLT/AST/ASTS, 2022; Canadian Society of Transplantation, 2023; American Society of Transplantation, 2023). All organizations strongly recommend vaccination against SARS-CoV-2 in transplant recipients. Furthermore, they recommend that transplant recipients receive 3 doses of an mRNA vaccine as their "primary series." These recommendations are consistent with our review's findings; across all timepoints, our review found a credible dose-response relationship between increasing the number of COVID-19 vaccines received and a reduction in the risk of COVID-19 infection. Furthermore, our review identified low certainty evidence that mRNA vaccines may reduce the risk of infection compared to non-mRNA vaccines, such as J&J and AstraZeneca. However, our review also identified low certainty observational evidence suggesting that vaccination with Moderna may reduce the risk of COVID-19 mortality compared to vaccination with Pfizer. Transplant organizations did not develop any recommendations regarding the type of mRNA vaccine during the pandemic. This decision may have been due to the paucity of evidence

comparing these COVID-19 vaccines, combined with the availability of certain vaccines in their jurisdiction at the time.

Overall, it remains difficult to assess the impact of COVID-19 vaccination on patient-important outcomes in SOT recipients due to the inherent limitations of observational studies and the limited randomized evidence throughout the course of the pandemic. Should future public health emergencies occur, clinicians and researchers should collaborate closely with patient partners to ensure there is not a paucity of research on patient-important outcomes.

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CHAPTER 7: Appendices

Appendix 1. Systematic database search strategies.

MEDLINE	
Ovid MEDLINE(R) ALL <1946 to March 01, 2024>	
#	**Searches**
1	((covid or covid-19 or covid19 or SARS-COV-2 or coronavirus or 2019-nCoV or SARS2 or 2019nCoV or SARSCOV2 or SARS-COV2 or nCov-19 or nCov19 or cov19 or cov2019 or cov-19 or cov-2019) and (vaccine$ or vaccinating or vaccination$1 or immunization$ or immuniz$ or "herd immunity" or "anti adj vaccination")).mp.
2	((exp vaccines/ or exp vaccinations/ or vaccination refusal/ or anti-vaccination movement/ or immunization programs/ or mass vaccination/ or vaccination coverage/ or Immunity, Herd/) and (COVID-19/ or SARS-CoV-2/)) or exp COVID-19 vaccines/
3	mRNA 1273.mp.
4	Elasomeran.mp.
5	TAK-919.mp.
6	TAK919.mp.
7	M-1273.mp.
8	M1273.mp.
9	EPK39PL4R4.af.
10	Ad26COVS1.mp.
11	JNJ-78436735.mp.
12	JNJ78436735.mp.
13	JT2NS6183B.af.
14	BNT162.mp.
15	BNT162b2.mp.
16	BNT-162B2.mp.
17	Pidacmeran.mp.
18	BNT-162C2.mp.
19	BNT-162.mp.
20	BNT162C2.mp.
21	BNT-162B1.mp.
22	BNT162B1.mp.
23	BNT-162A1.mp.
24	BNT162A1.mp.
25	Tozinameran.mp.
26	ChAdOx1 nCoV-19.mp.
27	Covishield.mp.
28	AZD1222.mp.
29	AZD-1222.mp.
30	B5S3K2V0G8.af.
31	ChAdOx1-S.mp.
32	Vaxzevria.mp.
33	Ad26-COV2-S.mp.
34	BBIBP-CorV.mp.
35	Covilo.mp.
36	CoronaVac.mp.
37	COVAXIN.mp.
38	NVX-CoV2373.mp.
39	Covovax.mp.
40	Nuvaxovid.mp.
41	Sputnik V.mp.
42	Gam-COVID-Vac.mp.
43	Ad5-nCoV.mp.
44	CoV2 preS dTM.mp.

45	SCB-2019.mp.
46	(Vero Cell adj5 vaccin*).mp.
47	(CHO Cell adj5 vaccin*).mp.
48	CVnCoV.mp.
49	CV07050101.mp.
50	EpiVacCorona.mp.
51	Aurora-CoV.mp.
52	"Soberana 01".mp.
53	FINLAY-FR-1.mp.
54	"Soberana 02".mp.
55	FINLAY-FR-2.mp.
56	PastoCovac.mp.
57	Soberana Plus.mp.
58	FINLAY-FR-1A.mp.
59	(cilgavimab adj2 tixagevimab).mp.
60	(azd 1061 adj2 azd 8895).mp.
61	azd 7442.mp.
62	azd7442.mp.
63	(azd1061 adj2 azd8895).mp.
64	evusheld.mp.
65	or/1-64
66	[Solid Organ Transplantation]
67	Organ Transplantation/
68	exp Heart Transplantation/
69	Kidney Transplantation/
70	Liver Transplantation/
71	exp Lung Transplantation/
72	Pancreas Transplantation/
73	Transplant Recipients/
74	Transplantation/
75	Immunocompromised Host/
76	(Immunocompromi?ed adj2 host?).mp.
77	(Immunocompromi?ed adj2 patient*).mp.
78	(immunosuppressed adj2 host?).mp.
79	(immunosuppressed adj2 patient*).mp.
80	Transplant*.mp.
81	(organ? adj2 transplant*).mp.
82	(organ? adj2 graft*).mp.
83	(organ? adj2 allograft*).mp.
84	(organ? adj2 allotransplant*).mp.
85	(organ? adj2 heterograft*).mp.
86	(organ? adj2 heterotransplant*).mp.
87	(organ? adj2 homotransplant*).mp.
88	(organ? adj2 homograft*).mp.
89	(heart? adj2 transplant*).mp.
90	(heart? adj2 graft*).mp.
91	(heart? adj2 allograft*).mp.
92	(heart? adj2 allotransplant*).mp.
93	(heart? adj2 heterograft*).mp.
94	(heart? adj2 heterotransplant*).mp.
95	(heart? adj2 homotransplant*).mp.
96	(heart? adj2 homograft*).mp.
97	(cardiac adj2 transplant*).mp.
98	(cardiac adj2 graft*).mp.
99	(cardiac adj2 allograft*).mp.
100	(cardiac adj2 allotransplant*).mp.
101	(cardiac adj2 heterograft*).mp.
102	(cardiac adj2 heterotransplant*).mp.
103	(cardiac adj2 homotransplant*).mp.

104	(cardiac adj2 homograft*).mp.
105	(cardiothoracic adj2 transplant*).mp.
106	(cardiothoracic adj2 graft*).mp.
107	(cardiothoracic adj2 allograft*).mp.
108	(cardiothoracic adj2 allotransplant*).mp.
109	(cardiothoracic adj2 heterograft*).mp.
110	(cardiothoracic adj2 heterotransplant*).mp.
111	(cardiothoracic adj2 homotransplant*).mp.
112	(cardiothoracic adj2 homograft*).mp.
113	(cardiopulmonary adj2 transplant*).mp.
114	(cardiopulmonary adj2 graft*).mp.
115	(cardiopulmonary adj2 allograft*).mp.
116	(cardiopulmonary adj2 allotransplant*).mp.
117	(cardiopulmonary adj2 heterograft*).mp.
118	(cardiopulmonary adj2 heterotransplant*).mp.
119	(cardiopulmonary adj2 homotransplant*).mp.
120	(cardiopulmonary adj2 homograft*).mp.
121	(liver? adj2 transplant*).mp.
122	(liver? adj2 graft*).mp.
123	(liver? adj2 allograft*).mp.
124	(liver? adj2 allotransplant*).mp.
125	(liver? adj2 heterograft*).mp.
126	(liver? adj2 heterotransplant*).mp.
127	(liver? adj2 homotransplant*).mp.
128	(liver? adj2 homograft*).mp.
129	(hepat* adj2 transplant*).mp.
130	(hepat* adj2 graft*).mp.
131	(hepat* adj2 allograft*).mp.
132	(hepat* adj2 allotransplant*).mp.
133	(hepat* adj2 heterograft*).mp.
134	(hepat* adj2 heterotransplant*).mp.
135	(hepat* adj2 homotransplant*).mp.
136	(hepat* adj2 homograft*).mp.
137	(pancrea* adj2 transplant*).mp.
138	(pancrea* adj2 graft*).mp.
139	(pancrea* adj2 allograft*).mp.
140	(pancrea* adj2 allotransplant*).mp.
141	(pancrea* adj2 heterograft*).mp.
142	(pancrea* adj2 heterotransplant*).mp.
143	(pancrea* adj2 homotransplant*).mp.
144	(pancrea* adj2 homograft*).mp.
145	(lung? adj2 transplant*).mp.
146	(lung? adj2 graft*).mp.
147	(lung? adj2 allograft*).mp.
148	(lung? adj2 allotransplant*).mp.
149	(lung? adj2 heterograft*).mp.
150	(lung? adj2 heterotransplant*).mp.
151	(lung? adj2 homotransplant*).mp.
152	(lung? adj2 homograft*).mp.
153	(thoracic adj2 transplant*).mp.
154	(thoracic adj2 graft*).mp.
155	(thoracic adj2 allograft*).mp.
156	(thoracic adj2 allotransplant*).mp.
157	(thoracic adj2 heterograft*).mp.
158	(thoracic adj2 heterotransplant*).mp.
159	(thoracic adj2 homotransplant*).mp.
160	(thoracic adj2 homograft*).mp.
161	(pulmonary adj2 transplant*).mp.
162	(pulmonary adj2 graft*).mp.

163	(pulmonary adj2 allograft*).mp.
164	(pulmonary adj2 allotransplant*).mp.
165	(pulmonary adj2 heterograft*).mp.
166	(pulmonary adj2 heterotransplant*).mp.
167	(pulmonary adj2 homotransplant*).mp.
168	(pulmonary adj2 homograft*).mp.
169	(kidney? adj2 transplant*).mp.
170	(kidney? adj2 graft*).mp.
171	(kidney? adj2 allograft*).mp.
172	(kidney? adj2 allotransplant*).mp.
173	(kidney? adj2 heterograft*).mp.
174	(kidney? adj2 heterotransplant*).mp.
175	(kidney? adj2 homotransplant*).mp.
176	(kidney? adj2 homograft*).mp.
177	(renal adj2 transplant*).mp.
178	(renal adj2 graft*).mp.
179	(renal adj2 allograft*).mp.
180	(renal adj2 allotransplant*).mp.
181	(renal adj2 heterograft*).mp.
182	(renal adj2 heterotransplant*).mp.
183	(renal adj2 homotransplant*).mp.
184	(renal adj2 homograft*).mp.
185	or/67-184
186	65 and 185
187	animals/ not (animals/ and humans/)
188	186 not 187
189	limit 188 to ("all infant (birth to 23 months)" or "all child (0 to 18 years)")
190	limit 188 to "all adult (19 plus years)"
191	188 not 189
192	190 or 191
193	remove duplicates from 192
CENTRAL	
EBM Reviews - Cochrane Central Register of Controlled Trials	
#	**Searches**
1	((covid or covid-19 or covid19 or SARS-COV-2 or coronavirus or 2019-nCoV or SARS2 or 2019nCoV or SARSCOV2 or SARS-COV2 or nCov-19 or nCov19 or cov19 or cov2019 or cov-19 or cov-2019) and (vaccine$ or vaccinating or vaccination$1 or immunization$ or immuniz$ or "herd immunity" or "anti adj vaccination")).mp.
2	((exp vaccines/ or exp vaccinations/ or vaccination refusal/ or anti-vaccination movement/ or immunization programs/ or mass vaccination/ or vaccination coverage/ or Immunity, Herd/) and (COVID-19/ or SARS-CoV-2/)) or exp COVID-19 vaccines/
3	mRNA 1273.mp.
4	Elasomeran.mp.
5	TAK-919.mp.
6	TAK919.mp.
7	M-1273.mp.
8	M1273.mp.
9	EPK39PL4R4.af.
10	Ad26COVS1.mp.
11	JNJ-78436735.mp.
12	JNJ78436735.mp.
13	JT2NS6183B.af.
14	BNT162.mp.
15	BNT162b2.mp.
16	BNT-162B2.mp.
17	Pidacmeran.mp.
18	BNT-162C2.mp.
19	BNT-162.mp.
20	BNT162C2.mp.
21	BNT-162B1.mp.

22	BNT162B1.mp.
23	BNT-162A1.mp.
24	BNT162A1.mp.
25	Tozinameran.mp.
26	ChAdOx1 nCoV-19.mp.
27	Covishield.mp.
28	AZD1222.mp.
29	AZD-1222.mp.
30	B5S3K2V0G8.af.
31	ChAdOx1-S.mp.
32	Vaxzevria.mp.
33	Ad26-COV2-S.mp.
34	BBIBP-CorV.mp.
35	Covilo.mp.
36	CoronaVac.mp.
37	COVAXIN.mp.
38	NVX-CoV2373.mp.
39	Covovax.mp.
40	Nuvaxovid.mp.
41	Sputnik V.mp.
42	Gam-COVID-Vac.mp.
43	Ad5-nCoV.mp.
44	CoV2 preS dTM.mp.
45	SCB-2019.mp.
46	(Vero Cell adj5 vaccin*).mp.
47	(CHO Cell adj5 vaccin*).mp.
48	CVnCoV.mp.
49	CV07050101.mp.
50	EpiVacCorona.mp.
51	Aurora-CoV.mp.
52	"Soberana 01".mp.
53	FINLAY-FR-1.mp.
54	"Soberana 02".mp.
55	FINLAY-FR-2.mp.
56	PastoCovac.mp.
57	Soberana Plus.mp.
58	FINLAY-FR-1A.mp.
59	(cilgavimab adj2 tixagevimab).mp.
60	(azd 1061 adj2 azd 8895).mp.
61	azd 7442.mp.
62	azd7442.mp.
63	(azd1061 adj2 azd8895).mp.
64	evusheld.mp.
65	or/1-64
66	Organ Transplantation/
67	exp Heart Transplantation/
68	Kidney Transplantation/
69	Liver Transplantation/
70	exp Lung Transplantation/
71	Pancreas Transplantation/
72	Transplant Recipients/
73	Transplantation/
74	Immunocompromised Host/
75	(Immunocompromi?ed adj2 host?).mp.
76	(Immunocompromi?ed adj2 patient*).mp.
77	(immunosuppressed adj2 host?).mp.
78	(immunosuppressed adj2 patient*).mp.
79	Transplant*.mp.
80	(organ? adj2 transplant*).mp.

81	(organ? adj2 graft*).mp.
82	(organ? adj2 allograft*).mp.
83	(organ? adj2 allotransplant*).mp.
84	(organ? adj2 heterograft*).mp.
85	(organ? adj2 heterotransplant*).mp.
86	(organ? adj2 homotransplant*).mp.
87	(organ? adj2 homograft*).mp.
88	(heart? adj2 transplant*).mp.
89	(heart? adj2 graft*).mp.
90	(heart? adj2 allograft*).mp.
91	(heart? adj2 allotransplant*).mp.
92	(heart? adj2 heterograft*).mp.
93	(heart? adj2 heterotransplant*).mp.
94	(heart? adj2 homotransplant*).mp.
95	(heart? adj2 homograft*).mp.
96	(cardiac adj2 transplant*).mp.
97	(cardiac adj2 graft*).mp.
98	(cardiac adj2 allograft*).mp.
99	(cardiac adj2 allotransplant*).mp.
100	(cardiac adj2 heterograft*).mp.
101	(cardiac adj2 heterotransplant*).mp.
102	(cardiac adj2 homotransplant*).mp.
103	(cardiac adj2 homograft*).mp.
104	(cardiothoracic adj2 transplant*).mp.
105	(cardiothoracic adj2 graft*).mp.
106	(cardiothoracic adj2 allograft*).mp.
107	(cardiothoracic adj2 allotransplant*).mp.
108	(cardiothoracic adj2 heterograft*).mp.
109	(cardiothoracic adj2 heterotransplant*).mp.
110	(cardiothoracic adj2 homotransplant*).mp.
111	(cardiothoracic adj2 homograft*).mp.
112	(cardiopulmonary adj2 transplant*).mp.
113	(cardiopulmonary adj2 graft*).mp.
114	(cardiopulmonary adj2 allograft*).mp.
115	(cardiopulmonary adj2 allotransplant*).mp.
116	(cardiopulmonary adj2 heterograft*).mp.
117	(cardiopulmonary adj2 heterotransplant*).mp.
118	(cardiopulmonary adj2 homotransplant*).mp.
119	(cardiopulmonary adj2 homograft*).mp.
120	(liver? adj2 transplant*).mp.
121	(liver? adj2 graft*).mp.
122	(liver? adj2 allograft*).mp.
123	(liver? adj2 allotransplant*).mp.
124	(liver? adj2 heterograft*).mp.
125	(liver? adj2 heterotransplant*).mp.
126	(liver? adj2 homotransplant*).mp.
127	(liver? adj2 homograft*).mp.
128	(hepat* adj2 transplant*).mp.
129	(hepat* adj2 graft*).mp.
130	(hepat* adj2 allograft*).mp.
131	(hepat* adj2 allotransplant*).mp.
132	(hepat* adj2 heterograft*).mp.
133	(hepat* adj2 heterotransplant*).mp.
134	(hepat* adj2 homotransplant*).mp.
135	(hepat* adj2 homograft*).mp.
136	(pancrea* adj2 transplant*).mp.
137	(pancrea* adj2 graft*).mp.
138	(pancrea* adj2 allograft*).mp.
139	(pancrea* adj2 allotransplant*).mp.

140	(pancrea* adj2 heterograft*).mp.
141	(pancrea* adj2 heterotransplant*).mp.
142	(pancrea* adj2 homotransplant*).mp.
143	(pancrea* adj2 homograft*).mp.
144	(lung? adj2 transplant*).mp.
145	(lung? adj2 graft*).mp.
146	(lung? adj2 allograft*).mp.
147	(lung? adj2 allotransplant*).mp.
148	(lung? adj2 heterograft*).mp.
149	(lung? adj2 heterotransplant*).mp.
150	(lung? adj2 homotransplant*).mp.
151	(lung? adj2 homograft*).mp.
152	(thoracic adj2 transplant*).mp.
153	(thoracic adj2 graft*).mp.
154	(thoracic adj2 allograft*).mp.
155	(thoracic adj2 allotransplant*).mp.
156	(thoracic adj2 heterograft*).mp.
157	(thoracic adj2 heterotransplant*).mp.
158	(thoracic adj2 homotransplant*).mp.
159	(thoracic adj2 homograft*).mp.
160	(pulmonary adj2 transplant*).mp.
161	(pulmonary adj2 graft*).mp.
162	(pulmonary adj2 allograft*).mp.
163	(pulmonary adj2 allotransplant*).mp.
164	(pulmonary adj2 heterograft*).mp.
165	(pulmonary adj2 heterotransplant*).mp.
166	(pulmonary adj2 homotransplant*).mp.
167	(pulmonary adj2 homograft*).mp.
168	(kidney? adj2 transplant*).mp.
169	(kidney? adj2 graft*).mp.
170	(kidney? adj2 allograft*).mp.
171	(kidney? adj2 allotransplant*).mp.
172	(kidney? adj2 heterograft*).mp.
173	(kidney? adj2 heterotransplant*).mp.
174	(kidney? adj2 homotransplant*).mp.
175	(kidney? adj2 homograft*).mp.
176	(renal adj2 transplant*).mp.
177	(renal adj2 graft*).mp.
178	(renal adj2 allograft*).mp.
179	(renal adj2 allotransplant*).mp.
180	(renal adj2 heterograft*).mp.
181	(renal adj2 heterotransplant*).mp.
182	(renal adj2 homotransplant*).mp.
183	(renal adj2 homograft*).mp.
184	or/66-183
185	65 and 184
186	remove duplicates from 185
Embase	
Embase <1974 to 2024 March 01>	
#	**Searches**
1	((covid or covid-19 or covid19 or SARS-COV-2 or coronavirus or 2019-nCoV or SARS2 or 2019nCoV or SARSCOV2 or SARS-COV2 or nCov-19 or nCov19 or cov19 or cov2019 or cov-19 or cov-2019) and (vaccine$ or vaccinating or vaccination$1 or immunization$ or immuniz$ or "herd immunity" or "anti adj vaccination")).mp.
2	(exp coronavirus disease 2019/ or severe acute respiratory syndrome coronavirus 2/ or covid-19.mp. or SARS-COV-2.mp.) and (exp vaccine/ or exp vaccination/ or exp vaccination reaction/ or vaccination refusal/ or exp anti-vaccination movement/ or exp immunization/ or mass immunization/ or vaccination coverage/ or herd immunity/)
3	exp SARS-CoV-2 vaccine/
4	cilgavimab plus tixagevimab/
5	mRNA 1273.mp.

6	Elasomeran.mp.
7	TAK-919.mp.
8	TAK919.mp.
9	M-1273.mp.
10	M1273.mp.
11	EPK39PL4R4.af.
12	Ad26COVS1.mp.
13	JNJ-78436735.mp.
14	JNJ78436735.mp.
15	JT2NS6183B.af.
16	BNT162.mp.
17	BNT162b2.mp.
18	BNT-162B2.mp.
19	Pidacmeran.mp.
20	BNT-162C2.mp.
21	BNT-162.mp.
22	BNT162C2.mp.
23	BNT-162B1.mp.
24	BNT162B1.mp.
25	BNT-162A1.mp.
26	BNT162A1.mp.
27	Tozinameran.mp.
28	ChAdOx1 nCoV-19.mp.
29	Covishield.mp.
30	AZD1222.mp.
31	AZD-1222.mp.
32	B5S3K2V0G8.af.
33	ChAdOx1-S.mp.
34	Vaxzevria.mp.
35	Ad26-COV2-S.mp.
36	BBIBP-CorV.mp.
37	Covilo.mp.
38	CoronaVac.mp.
39	COVAXIN.mp.
40	NVX-CoV2373.mp.
41	Covovax.mp.
42	Nuvaxovid.mp.
43	Sputnik V.mp.
44	Gam-COVID-Vac.mp.
45	Ad5-nCoV.mp.
46	CoV2 preS dTM.mp.
47	SCB-2019.mp.
48	(Vero Cell adj5 vaccin*).mp.
49	(CHO Cell adj5 vaccin*).mp.
50	CVnCoV.mp.
51	CV07050101.mp.
52	EpiVacCorona.mp.
53	Aurora-CoV.mp.
54	"Soberana 01".mp.
55	FINLAY-FR-1.mp.
56	"Soberana 02".mp.
57	FINLAY-FR-2.mp.
58	PastoCovac.mp.
59	Soberana Plus.mp.
60	FINLAY-FR-1A.mp.
61	(cilgavimab adj2 tixagevimab).mp.
62	(azd 1061 adj2 azd 8895).mp.
63	azd 7442.mp.
64	azd7442.mp.

65	(azd1061 adj2 azd8895).mp.
66	evusheld.mp.
67	or/1-66
68	[Solid Organ Transplantation]
69	organ transplantation/
70	exp heart transplantation/
71	exp hypophysis transplantation/
72	exp intestine transplantation/
73	exp kidney transplantation/
74	exp liver transplantation/
75	exp lung transplantation/
76	exp pancreas transplantation/
77	parathyroid transplantation/
78	spleen transplantation/
79	exp thymus transplantation/
80	graft recipient/
81	immunocompromised patient/
82	(Immunocompromi?ed adj2 host?).mp.
83	(Immunocompromi?ed adj2 patient*).mp.
84	(immunosuppressed adj2 host?).mp.
85	(immunosuppressed adj2 patient*).mp.
86	Transplant*.mp.
87	(organ? adj2 transplant*).mp.
88	(organ? adj2 graft*).mp.
89	(organ? adj2 allograft*).mp.
90	(organ? adj2 allotransplant*).mp.
91	(organ? adj2 heterograft*).mp.
92	(organ? adj2 heterotransplant*).mp.
93	(organ? adj2 homotransplant*).mp.
94	(organ? adj2 homograft*).mp.
95	(heart? adj2 transplant*).mp.
96	(heart? adj2 graft*).mp.
97	(heart? adj2 allograft*).mp.
98	(heart? adj2 allotransplant*).mp.
99	(heart? adj2 heterograft*).mp.
100	(heart? adj2 heterotransplant*).mp.
101	(heart? adj2 homotransplant*).mp.
102	(heart? adj2 homograft*).mp.
103	(cardiac adj2 transplant*).mp.
104	(cardiac adj2 graft*).mp.
105	(cardiac adj2 allograft*).mp.
106	(cardiac adj2 allotransplant*).mp.
107	(cardiac adj2 heterograft*).mp.
108	(cardiac adj2 heterotransplant*).mp.
109	(cardiac adj2 homotransplant*).mp.
110	(cardiac adj2 homograft*).mp.
111	(cardiothoracic adj2 transplant*).mp.
112	(cardiothoracic adj2 graft*).mp.
113	(cardiothoracic adj2 allograft*).mp.
114	(cardiothoracic adj2 allotransplant*).mp.
115	(cardiothoracic adj2 heterograft*).mp.
116	(cardiothoracic adj2 heterotransplant*).mp.
117	(cardiothoracic adj2 homotransplant*).mp.
118	(cardiothoracic adj2 homograft*).mp.
119	(cardiopulmonary adj2 transplant*).mp.
120	(cardiopulmonary adj2 graft*).mp.
121	(cardiopulmonary adj2 allograft*).mp.
122	(cardiopulmonary adj2 allotransplant*).mp.
123	(cardiopulmonary adj2 heterograft*).mp.

124	(cardiopulmonary adj2 heterotransplant*).mp.
125	(cardiopulmonary adj2 homotransplant*).mp.
126	(cardiopulmonary adj2 homograft*).mp.
127	(liver? adj2 transplant*).mp.
128	(liver? adj2 graft*).mp.
129	(liver? adj2 allograft*).mp.
130	(liver? adj2 allotransplant*).mp.
131	(liver? adj2 heterograft*).mp.
132	(liver? adj2 heterotransplant*).mp.
133	(liver? adj2 homotransplant*).mp.
134	(liver? adj2 homograft*).mp.
135	(hepat* adj2 transplant*).mp.
136	(hepat* adj2 graft*).mp.
137	(hepat* adj2 allograft*).mp.
138	(hepat* adj2 allotransplant*).mp.
139	(hepat* adj2 heterograft*).mp.
140	(hepat* adj2 heterotransplant*).mp.
141	(hepat* adj2 homotransplant*).mp.
142	(hepat* adj2 homograft*).mp.
143	(pancrea* adj2 transplant*).mp.
144	(pancrea* adj2 graft*).mp.
145	(pancrea* adj2 allograft*).mp.
146	(pancrea* adj2 allotransplant*).mp.
147	(pancrea* adj2 heterograft*).mp.
148	(pancrea* adj2 heterotransplant*).mp.
149	(pancrea* adj2 homotransplant*).mp.
150	(pancrea* adj2 homograft*).mp.
151	(lung? adj2 transplant*).mp.
152	(lung? adj2 graft*).mp.
153	(lung? adj2 allograft*).mp.
154	(lung? adj2 allotransplant*).mp.
155	(lung? adj2 heterograft*).mp.
156	(lung? adj2 heterotransplant*).mp.
157	(lung? adj2 homotransplant*).mp.
158	(lung? adj2 homograft*).mp.
159	(thoracic adj2 transplant*).mp.
160	(thoracic adj2 graft*).mp.
161	(thoracic adj2 allograft*).mp.
162	(thoracic adj2 allotransplant*).mp.
163	(thoracic adj2 heterograft*).mp.
164	(thoracic adj2 heterotransplant*).mp.
165	(thoracic adj2 homotransplant*).mp.
166	(thoracic adj2 homograft*).mp.
167	(pulmonary adj2 transplant*).mp.
168	(pulmonary adj2 graft*).mp.
169	(pulmonary adj2 allograft*).mp.
170	(pulmonary adj2 allotransplant*).mp.
171	(pulmonary adj2 heterograft*).mp.
172	(pulmonary adj2 heterotransplant*).mp.
173	(pulmonary adj2 homotransplant*).mp.
174	(pulmonary adj2 homograft*).mp.
175	(kidney? adj2 transplant*).mp.
176	(kidney? adj2 graft*).mp.
177	(kidney? adj2 allograft*).mp.
178	(kidney? adj2 allotransplant*).mp.
179	(kidney? adj2 heterograft*).mp.
180	(kidney? adj2 heterotransplant*).mp.
181	(kidney? adj2 homotransplant*).mp.
182	(kidney? adj2 homograft*).mp.

183	(renal adj2 transplant*).mp.
184	(renal adj2 graft*).mp.
185	(renal adj2 allograft*).mp.
186	(renal adj2 allotransplant*).mp.
187	(renal adj2 heterograft*).mp.
188	(renal adj2 heterotransplant*).mp.
189	(renal adj2 homotransplant*).mp.
190	(renal adj2 homograft*).mp.
191	or/69-190
192	67 and 191
193	(exp animals/ or exp animal experimentation/ or nonhuman/) not ((exp animals/ or exp animal experimentation/ or nonhuman/) and exp human/)
194	192 not 193
195	limit 194 to (embryo <first trimester> or infant <to one year> or child <unspecified age> or preschool child <1 to 6 years> or school child <7 to 12 years> or adolescent <13 to 17 years>)
196	limit 194 to (adult <18 to 64 years> or aged <65+ years>)
197	194 not 195
198	196 or 197
199	remove duplicates from 198
Cochrane Database of Systematic Reviews	
EBM Reviews - Cochrane Database of Systematic Reviews <2005 to March 1, 2024>	
#	**Searches**
1	((covid or covid-19 or covid19 or SARS-COV-2 or coronavirus or 2019-nCoV or SARS2 or 2019nCoV or SARSCOV2 or SARS-COV2 or nCov-19 or nCov19 or cov19 or cov2019 or cov-19 or cov-2019) and (vaccine$ or vaccinating or vaccination$1 or immunization$ or immuniz$ or "herd immunity" or "anti adj vaccination")).ti,ab.
2	mRNA 1273.ti,ab.
3	Elasomeran.ti,ab.
4	TAK-919.ti,ab.
5	TAK919.ti,ab.
6	M-1273.ti,ab.
7	M1273.ti,ab.
8	EPK39PL4R4.af.
9	Ad26COVS1.ti,ab.
10	JNJ-78436735.ti,ab.
11	JNJ78436735.ti,ab.
12	JT2NS6183B.af.
13	BNT162.ti,ab.
14	BNT162b2.ti,ab.
15	BNT-162B2.ti,ab.
16	Pidacmeran.ti,ab.
17	BNT-162C2.ti,ab.
18	BNT-162.ti,ab.
19	BNT162C2.ti,ab.
20	BNT-162B1.ti,ab.
21	BNT162B1.ti,ab.
22	BNT-162A1.ti,ab.
23	BNT162A1.ti,ab.
24	Tozinameran.ti,ab.
25	ChAdOx1 nCoV-19.ti,ab.
26	Covishield.ti,ab.
27	AZD1222.ti,ab.
28	AZD-1222.ti,ab.
29	B5S3K2V0G8.af.
30	ChAdOx1-S.ti,ab.
31	Vaxzevria.ti,ab.
32	Ad26-COV2-S.ti,ab.
33	BBIBP-CorV.ti,ab.
34	Covilo.ti,ab.
35	CoronaVac.ti,ab.

36	COVAXIN.ti,ab.
37	NVX-CoV2373.ti,ab.
38	Covovax.ti,ab.
39	Nuvaxovid.ti,ab.
40	Sputnik V.ti,ab.
41	Gam-COVID-Vac.ti,ab.
42	Ad5-nCoV.ti,ab.
43	CoV2 preS dTM.ti,ab.
44	SCB-2019.ti,ab.
45	(Vero Cell adj5 vaccin*).ti,ab.
46	(CHO Cell adj5 vaccin*).ti,ab.
47	CVnCoV.ti,ab.
48	CV07050101.ti,ab.
49	EpiVacCorona.ti,ab.
50	Aurora-CoV.ti,ab.
51	"Soberana 01".ti,ab.
52	FINLAY-FR-1.ti,ab.
53	"Soberana 02".ti,ab.
54	FINLAY-FR-2.ti,ab.
55	PastoCovac.ti,ab.
56	Soberana Plus.ti,ab.
57	FINLAY-FR-1A.ti,ab.
58	(cilgavimab adj2 tixagevimab).ti,ab.
59	(azd 1061 adj2 azd 8895).ti,ab.
60	azd 7442.ti,ab.
61	azd7442.ti,ab.
62	(azd1061 adj2 azd8895).ti,ab.
63	evusheld.ti,ab.
64	or/1-63
65	(organ? adj2 transplant*).ti,ab.
66	(organ? adj2 graft*).ti,ab.
67	(organ? adj2 allograft*).ti,ab.
68	(organ? adj2 allotransplant*).ti,ab.
69	(organ? adj2 heterograft*).ti,ab.
70	(organ? adj2 heterotransplant*).ti,ab.
71	(organ? adj2 homotransplant*).ti,ab.
72	(organ? adj2 homograft*).ti,ab.
73	(heart? adj2 transplant*).ti,ab.
74	(heart? adj2 graft*).ti,ab.
75	(heart? adj2 allograft*).ti,ab.
76	(heart? adj2 allotransplant*).ti,ab.
77	(heart? adj2 heterograft*).ti,ab.
78	(heart? adj2 heterotransplant*).ti,ab.
79	(heart? adj2 homotransplant*).ti,ab.
80	(heart? adj2 homograft*).ti,ab.
81	(cardiac adj2 transplant*).ti,ab.
82	(cardiac adj2 graft*).ti,ab.
83	(cardiac adj2 allograft*).ti,ab.
84	(cardiac adj2 allotransplant*).ti,ab.
85	(cardiac adj2 heterograft*).ti,ab.
86	(cardiac adj2 heterotransplant*).ti,ab.
87	(cardiac adj2 homotransplant*).ti,ab.
88	(cardiac adj2 homograft*).ti,ab.
89	(cardiothoracic adj2 transplant*).ti,ab.
90	(cardiothoracic adj2 graft*).ti,ab.
91	(cardiothoracic adj2 allograft*).ti,ab.
92	(cardiothoracic adj2 allotransplant*).ti,ab.
93	(cardiothoracic adj2 heterograft*).ti,ab.
94	(cardiothoracic adj2 heterotransplant*).ti,ab.

95	(cardiothoracic adj2 homotransplant*).ti,ab.
96	(cardiothoracic adj2 homograft*).ti,ab.
97	(cardiopulmonary adj2 transplant*).ti,ab.
98	(cardiopulmonary adj2 graft*).ti,ab.
99	(cardiopulmonary adj2 allograft*).ti,ab.
100	(cardiopulmonary adj2 allotransplant*).ti,ab.
101	(cardiopulmonary adj2 heterograft*).ti,ab.
102	(cardiopulmonary adj2 heterotransplant*).ti,ab.
103	(cardiopulmonary adj2 homotransplant*).ti,ab.
104	(cardiopulmonary adj2 homograft*).ti,ab.
105	(liver? adj2 transplant*).ti,ab.
106	(liver? adj2 graft*).ti,ab.
107	(liver? adj2 allograft*).ti,ab.
108	(liver? adj2 allotransplant*).ti,ab.
109	(liver? adj2 heterograft*).ti,ab.
110	(liver? adj2 heterotransplant*).ti,ab.
111	(liver? adj2 homotransplant*).ti,ab.
112	(liver? adj2 homograft*).ti,ab.
113	(hepat* adj2 transplant*).ti,ab.
114	(hepat* adj2 graft*).ti,ab.
115	(hepat* adj2 allograft*).ti,ab.
116	(hepat* adj2 allotransplant*).ti,ab.
117	(hepat* adj2 heterograft*).ti,ab.
118	(hepat* adj2 heterotransplant*).ti,ab.
119	(hepat* adj2 homotransplant*).ti,ab.
120	(hepat* adj2 homograft*).ti,ab.
121	(pancrea* adj2 transplant*).ti,ab.
122	(pancrea* adj2 graft*).ti,ab.
123	(pancrea* adj2 allograft*).ti,ab.
124	(pancrea* adj2 allotransplant*).ti,ab.
125	(pancrea* adj2 heterograft*).ti,ab.
126	(pancrea* adj2 heterotransplant*).ti,ab.
127	(pancrea* adj2 homotransplant*).ti,ab.
128	(pancrea* adj2 homograft*).ti,ab.
129	(lung? adj2 transplant*).ti,ab.
130	(lung? adj2 graft*).ti,ab.
131	(lung? adj2 allograft*).ti,ab.
132	(lung? adj2 allotransplant*).ti,ab.
133	(lung? adj2 heterograft*).ti,ab.
134	(lung? adj2 heterotransplant*).ti,ab.
135	(lung? adj2 homotransplant*).ti,ab.
136	(lung? adj2 homograft*).ti,ab.
137	(thoracic adj2 transplant*).ti,ab.
138	(thoracic adj2 graft*).ti,ab.
139	(thoracic adj2 allograft*).ti,ab.
140	(thoracic adj2 allotransplant*).ti,ab.
141	(thoracic adj2 heterograft*).ti,ab.
142	(thoracic adj2 heterotransplant*).ti,ab.
143	(thoracic adj2 homotransplant*).ti,ab.
144	(thoracic adj2 homograft*).ti,ab.
145	(pulmonary adj2 transplant*).ti,ab.
146	(pulmonary adj2 graft*).ti,ab.
147	(pulmonary adj2 allograft*).ti,ab.
148	(pulmonary adj2 allotransplant*).ti,ab.
149	(pulmonary adj2 heterograft*).ti,ab.
150	(pulmonary adj2 heterotransplant*).ti,ab.
151	(pulmonary adj2 homotransplant*).ti,ab.
152	(pulmonary adj2 homograft*).ti,ab.
153	(kidney? adj2 transplant*).ti,ab.

154	(kidney? adj2 graft*).ti,ab.
155	(kidney? adj2 allograft*).ti,ab.
156	(kidney? adj2 allotransplant*).ti,ab.
157	(kidney? adj2 heterograft*).ti,ab.
158	(kidney? adj2 heterotransplant*).ti,ab.
159	(kidney? adj2 homotransplant*).ti,ab.
160	(kidney? adj2 homograft*).ti,ab.
161	(renal adj2 transplant*).ti,ab.
162	(renal adj2 graft*).ti,ab.
163	(renal adj2 allograft*).ti,ab.
164	(renal adj2 allotransplant*).ti,ab.
165	(renal adj2 heterograft*).ti,ab.
166	(renal adj2 heterotransplant*).ti,ab.
167	(renal adj2 homotransplant*).ti,ab.
168	(renal adj2 homograft*).ti,ab.
169	(Immunocompromi?ed adj2 host?).ti,ab.
170	(Immunocompromi?ed adj2 patient*).ti,ab.
171	(immunosuppressed adj2 host?).ti,ab.
172	(immunosuppressed adj2 patient*).ti,ab.
173	Transplant*.ti,ab.
174	or/65-173
175	64 and 174
Clinicaltrials.gov	
#	**Searches**
1	Condition: COVID-19 AND transplant Other terms: (vaccine OR vaccines OR vaccination OR vaccinations OR immunization OR immunizations OR immunize OR evusheld OR cilgavimab OR tixagevimab)
WHO Covid-19 database (up to June 2023)	
#	**Searches**
1	(tw:(transplant*)) AND (tw:((vaccine OR vaccines OR vaccination OR vaccinations OR immunization OR immunizations OR immunize OR evusheld OR cilgavimab OR tixagevimab)))

Appendix 2. List of studies included in the systematic review.

List of included randomized studies (n = 6)

Study (First Author Last Name, Year)	Reference
Drenko 2023	Drenko, P., Kacer, M., Kielberger, L., Vlas, T., Topolcan, O., Kucera, R., & Reischig, T. (2023). Safety and efficacy of one and two booster doses of SARS-CoV-2 mRNA vaccines in kidney transplant recipients: A randomized clinical trial. Transplant infectious disease, 25(5), e14150. https://doi.org/10.1111/tid.14150
Hall 2021	Hall, V. G., Ferreira, V. H., Ku, T., Ierullo, M., Majchrzak-Kita, B., Chaparro, C., Selzner, N., Schiff, J., McDonald, M., Tomlinson, G., Kulasingam, V., Kumar, D., & Humar, A. (2021). Randomized Trial of a Third Dose of mRNA-1273 Vaccine in Transplant Recipients. The New England journal of medicine, 385(13), 1244–1246. https://doi.org/10.1056/NEJMc2111462
Kho 2022	Kho, M. M. L., Messchendorp, A. L., Frölke, S. C., Imhof, C., Koomen, V. J., Malahe, S. R. K., Vart, P., Geers, D., de Vries, R. D., GeurtsvanKessel, C. H., Baan, C. C., van der Molen, R. G., Diavatopoulos, D. A., Remmerswaal, E. B. M., van Baarle, D., van Binnendijk, R., den Hartog, G., de Vries, A. P. J., Gansevoort, R. T., Bemelman, F. J., … RECOVAC collaborators (2023). Alternative strategies to increase the immunogenicity of COVID-19 vaccines in kidney transplant recipients not responding to two or three doses of an mRNA vaccine (RECOVAC): a randomised clinical trial. The Lancet. Infectious diseases, 23(3), 307–319. https://doi.org/10.1016/S1473-3099(22)00650-8
Natori 2023	Natori, Y., Martin, E., Mattiazzi, A., Arosemena, L., Ortigosa-Goggins, M., Shobana, S., Roth, D., Kupin, W. L., Burke, G. W., Ciancio, G., Morsi, M., Phancao, A., Munagala, M. R., Butrous, H., Manickavel, S., Sinha, N., Sota, K., Pallikkuth, S., Bini, J., Simkins, J., … Guerra, G. (2023). A Pilot Single-Blinded, Randomized, Controlled Trial Comparing BNT162b2 vs. JNJ-78436735 Vaccine as the Third Dose After Two Doses of BNT162b2 Vaccine in Solid Organ Transplant Recipients. Transplant international, 36, 10938. https://doi.org/10.3389/ti.2023.10938
Reindl-Schwaighofer 2022	Reindl-Schwaighofer, R., Heinzel, A., Mayrdorfer, M., Jabbour, R., Hofbauer, T. M., Merrelaar, A., Eder, M., Regele, F., Doberer, K., Spechtl, P., Aschauer, C., Koblischke, M., Paschen, C., Eskandary, F., Hu, K., Öhler, B., Bhandal, A., Kleibenböck, S., Jagoditsch, R. I., Reiskopf, B., … Oberbauer, R. (2022). Comparison of SARS-CoV-2 Antibody Response 4 Weeks After Homologous vs Heterologous Third Vaccine Dose in Kidney Transplant Recipients: A Randomized Clinical Trial. JAMA internal medicine, 182(2), 165–171. https://doi.org/10.1001/jamainternmed.2021.7372
Speich 2022	Speich, B., Chammartin, F., Abela, I. A., Amico, P., Stoeckle, M. P., Eichenberger, A. L., Hasse, B., Braun, D. L., Schuurmans, M. M., Müller, T. F., Tamm, M., Audigé, A., Mueller, N. J., Rauch, A., Günthard, H. F., Koller, M. T., Trkola, A., Briel, M., Kusejko, K., Bucher, H. C., … Swiss HIV Cohort Study and the Swiss Transplant Cohort Study (2022). Antibody Response in Immunocompromised Patients After the Administration of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Vaccine BNT162b2 or mRNA-1273: A Randomized Controlled Trial. Clinical infectious diseases, 75(1), e585–e593. https://doi.org/10.1093/cid/ciac169

List of included non-randomized studies (n = 42)

Study (First Author Last Name, Year)	Reference
Aslam 2022	Aslam, S., Liu, J., Sigler, R., Syed, R. R., Tu, X. M., Little, S. J., & De Gruttola, V. (2022). Coronavirus disease 2019 vaccination is protective of clinical disease in solid organ transplant recipients. Transplant infectious disease, 24(2), e13788. https://doi.org/10.1111/tid.13788
Bonazzetti 2023	Bonazzetti, C., Tazza, B., Gibertoni, D., Pasquini, Z., Caroccia, N., Fanì, F., Fornaro, G., Pascale, R., Rinaldi, M., Miani, B., Gamberini, C., Morelli, M. C., Tamé, M., Busutti, M., Comai, G., Potena, L., Borgese, L., Salvaterra, E., Lazzarotto, T., Scudeller, L., … CONTRAST Study Group (2023). Relationship Between Immune Response to Severe Acute Respiratory Syndrome Coronavirus 2 Vaccines and Development of Breakthrough Infection in Solid Organ Transplant Recipients: The CONTRAST Cohort. Clinical infectious diseases, 76(10), 1761–1767. https://doi.org/10.1093/cid/ciad016
Callaghan 2023	Callaghan, C. J., Curtis, R. M. K., Mumford, L., Whitaker, H., Pettigrew, G., Gardiner, D., Marson, L., Thorburn, D., White, S., Parmar, J., Ushiro-Lumb, I., Manas, D., Ravanan, R., & NHS Blood and Transplant Organ and Tissue Donation and Transplantation Clinical Team (2023). Vaccine Effectiveness Against the SARS-CoV-2 B.1.1.529 Omicron Variant in Solid Organ and Islet Transplant Recipients in England: A National Retrospective Cohort Study. Transplantation, 107(5), 1124–1135. https://doi.org/10.1097/TP.0000000000004535
Chen 2023	Chen, C. C., Hsu, M. K., Huang, Y. J., Lai, M. J., Wu, S. W., Lin, M. H., Hung, H. S., Lin, Y. C., Huang, Y. T., Lee, Y. F., Tsai, M. K., & Lee, C. Y. (2023). Protective Effect of Vaccine Doses and Antibody Titers Against SARS-CoV-2 Infection in Kidney Transplant Recipients. Transplant international, 36, 11196. https://doi.org/10.3389/ti.2023.11196
Collaborative 2022	OpenSAFELY Collaborative, Parker, E. P. K., Horne, E. M. F., Hulme, W. J., Tazare, J., Zheng, B., Carr, E. J., Loud, F., Lyon, S., Mahalingasivam, V., MacKenna, B., Mehrkar, A., Scanlon, M., Santhakumaran, S., Steenkamp, R., Goldacre, B., Sterne, J. A. C., Nitsch, D., Tomlinson, L. A., & LH&W NCS (or CONVALESCENCE) Collaborative (2023). Comparative effectiveness of two- and three-dose COVID-19 vaccination schedules involving AZD1222 and BNT162b2 in people with kidney disease: a linked OpenSAFELY and UK Renal Registry cohort study. The Lancet regional health. Europe, 30, 100636. https://doi.org/10.1016/j.lanepe.2023.100636
Demir 2022	Demir, E., Dheir, H., Safak, S., Serra Artan, A., Sipahi, S., & Turkmen, A. (2022). Differences in clinical outcomes of COVID-19 among vaccinated and unvaccinated kidney transplant recipients. Vaccine, 40(24), 3313–3319. https://doi.org/10.1016/j.vaccine.2022.04.066
Elhadji 2023	Leye, E., Delory, T., Karoui, K. E., Espagnacq, M., Khlat, M., Le Coeur, S., Lapidus, N., Hejblum, G. (2023). Direct and indirect impact of the COVID-19 pandemic on the survival of kidney transplant recipients: a national observational study in France. medRxiv. https://doi.org/10.1101/2023.04.05.23288113
Hall 2022	Hall, V. G., Al-Alahmadi, G., Solera, J. T., Marinelli, T., Cardinal, H., Prasad, G. V. R., De Serres, S. A., Isaac, D., Mainra, R., Lamarche, C., Sapir-Pichhadze, R., Gilmour, S., Matelski, J., Humar, A., & Kumar, D. (2022). Outcomes of SARS-CoV-2 Infection in Unvaccinated Compared With Vaccinated Solid Organ Transplant Recipients: A Propensity Matched Cohort Study. Transplantation, 106(8), 1622–1628. https://doi.org/10.1097/TP.0000000000004178
Hamm 2022	Hamm, S. R., Rezahosseini, O., Møller, D. L., Loft, J. A., Poulsen, J. R., Knudsen, J. D., Pedersen, M. S., Schønning, K., Harboe, Z. B., Rasmussen, A., Sørensen, S. S., & Nielsen, S. D. (2022). Incidence and severity of SARS-CoV-2 infections in liver and kidney transplant recipients in the post-vaccination era: Real-life data from Denmark. American journal of transplantation, 22(11), 2637–2650. https://doi.org/10.1111/ajt.17141
Hardgrave 2022	Hardgrave, H., Wells, A., Nigh, J., Klutts, G., Krinock, D., Osborn, T., Bhusal, S., Rude, M. K., Burdine, L., & Giorgakis, E. (2022). COVID-19 Mortality in Vaccinated vs. Unvaccinated Liver & Kidney Transplant Recipients: A Single-Center United States Propensity Score Matching Study on Historical Data. Vaccines, 10(11), 1921. https://doi.org/10.3390/vaccines10111921
Hiam 2021	Chemaitelly, H., AlMukdad, S., Joy, J. P., Ayoub, H. H., Yassine, H. M., Benslimane, F. M., Al Khatib, H. A., Tang, P., Hasan, M. R., Coyle, P., Al Kanaani, Z., Al Kuwari, E., Jeremijenko, A., Hassan Kaleeckal, A., Latif, A. N., Shaik, R. M., Abdul Rahim, H. F., Nasrallah, G. K., Al Kuwari, M. G., …, Al Khal, A. (2021). SARS-CoV-2 vaccine effectiveness in immunosuppressed kidney transplant recipients. medRxiv. https://doi.org/10.1101/2021.08.07.21261578
Hod 2022	Hod, T., Ben-David, A., Mor, E., Olmer, L., Halperin, R., Indenbaum, V., Beckerman, P., Doolman, R., Asraf, K., Atari, N., Benjamini, O., Lustig, Y., Grossman, E., Mandelboim, M., & Rahav, G. (2023). Humoral Response to the Fourth BNT162b2 Vaccination and Link Between the Fourth Dose, Omicron Infection, and Disease Severity in Renal Transplant Recipients. Transplantation, 107(1), 192–203. https://doi.org/10.1097/TP.0000000000004383
Joerns 2022	Joerns, J., Bollineni, S., Mahan, L. D., Mohanka, M. R., Lawrence, A., Timofte, I., Torres, F., La Hoz, R. M., Zhang, S., Kershaw, C. D., Kaza, V., Terada, L. S., & Banga, A. (2022). High-dose Mycophenolate Use at Vaccination Is Independently Associated With Breakthrough COVID-19 Among Lung Transplant Patients. Transplantation, 106(5), e271–e274. https://doi.org/10.1097/TP.0000000000004089
John 2022	John, B. V., Deng, Y., Khakoo, N. S., Taddei, T. H., Kaplan, D. E., & Dahman, B. (2022). Coronavirus Disease 2019 Vaccination Is Associated With Reduced Severe Acute Respiratory Syndrome Coronavirus 2 Infection and Death in Liver Transplant Recipients. Gastroenterology, 162(2), 645–647.e2. https://doi.org/10.1053/j.gastro.2021.11.001
Kee 2022	Kee, T., Jeong, J. C., Arakama, M. H., Khishgee, T., Tan, M. H., Tiwari, V., Begum, N. A. S., Hustrini, N. M., Jalalonmuhali, M. B., Tan, S. Y., Tan, J., Kim, Y., Mingyao, B. M., Sran, H. K., Ahmad, G. (2022). Impact of COVID-19 Era, Nation's Economic Status, Vaccination Status, Vaccine Doses and New COVID-19 Therapeutics on Mortality From COVID-19 Infections in Kidney Transplant Recipients From Asia: An Asian Society of Transplantation Research Group (ASTREGO). Transplantation, 106(9):S395-S395.
Korogiannou 2023	Korogiannou, M., Vallianou, K., Xagas, E., Rokka, E., Soukouli, I., Boletis, I. N., & Marinaki, S. (2023). Disease Course, Management and Outcomes in Kidney Transplant Recipients with SARS-CoV-2 Infection during the Omicron-Variant Wave: A Single-Center Experience. Vaccines, 11(3), 632. https://doi.org/10.3390/vaccines11030632
Kwon 2022	Kwon, J. H., Tenforde, M. W., Gaglani, M., Talbot, H. K., Ginde, A. A., McNeal, T., Ghamande, S., Douin, D. J., Casey, J. D., Mohr, N. M., Zepeski, A., Shapiro, N. I., Gibbs, K. W., Files, D. C., Hager, D. N., Shehu, A., Prekker, M. E., Caspers, S. D., Exline, M. C., Botros, M., … Self, W. H. (2022). mRNA Vaccine Effectiveness Against Coronavirus Disease 2019 Hospitalization Among Solid Organ Transplant Recipients. The Journal of infectious diseases, 226(5), 797–807. https://doi.org/10.1093/infdis/jiac118
Lerner 2022	Lerner, A. H., Arvanitis, P., Vieira, K., Klein, E. J., & Farmakiotis, D. (2022). mRNA Vaccination Decreases COVID-19-Associated Morbidity and Mortality Among Organ Transplant Recipients: A Contemporary Cohort Study. Open forum infectious diseases, 9(10), ofac503. https://doi.org/10.1093/ofid/ofac503
Llamas 2023	Azamar-Llamas, D., Arenas-Martinez, J. S., Olivas-Martinez, A., Jimenez, J. V., Kauffman-Ortega, E., García-Carrera, C. J., Papacristofilou-Riebeling, B., Rivera-López, F. E., & García-Juárez, I. (2024). Impact of COVID-19 vaccination on liver transplant recipients. Experience in a reference center in Mexico. PloS one, 19(3), e0301198. https://doi.org/10.1371/journal.pone.0301198

Ma 2022	Ma, E., Ai, J., Zhang, Y., Zheng, J., Gao, X., Xu, J., Yin, H., Fu, Z., Xing, H., Li, L., Sun, L., Huang, H., Zhang, Q., Xu, L., Jin, Y., Chen, R., Lv, G., Zhu, Z., Zhang, W., & Wang, Z. (2022). Omicron infections profile and vaccination status among 1881 liver transplant recipients: a multi-centre retrospective cohort. Emerging microbes & infections, 11(1), 2636–2644. https://doi.org/10.1080/22221751.2022.2136535
Masetti 2023	Masetti, M., Scuppa, M. F., Aloisio, A., Giovannini, L., Borgese, L., Manno, S., Tazza, B., Pascale, R., Bonazzetti, C., Caroccia, N., Sabatino, M., Spitaleri, G., Viale, P., Giannella, M., & Potena, L. (2023). Effect of a Fourth Dose of mRNA Vaccine and of Immunosuppression in Preventing SARS-CoV-2 Breakthrough Infections in Heart Transplant Patients. Microorganisms, 11(3), 755. https://doi.org/10.3390/microorganisms11030755
Mazuecos 2022	Mazuecos, A., Villanego, F., Zarraga, S., López, V., Oppenheimer, F., Llinàs-Mallol, L., Hernández, A. M., Rivas, A., Ruiz-Fuentes, M. C., Toapanta, N. G., Jiménez, C., Cabello, S., Beneyto, I., Aladrén, M. J., Rodríguez-Benot, A., Canal, C., Molina, M., Pérez-Flores, I., Saura, I. M., Gavela, E., … Spanish Society of Nephrology COVID-19 Group (2022). Breakthrough Infections Following mRNA SARS-CoV-2 Vaccination in Kidney Transplant Recipients. Transplantation, 106(7), 1430–1439. https://doi.org/10.1097/TP.0000000000004119
McEvoy 2022	McEvoy, C. M., Lee, A., Misra, P. S., Lebovic, G., Wald, R., & Yuen, D. A. (2022). Real-world Impact of 2-dose SARS-CoV-2 Vaccination in Kidney Transplant Recipients. Transplantation, 106(5), e279–e280. https://doi.org/10.1097/TP.0000000000004081
Mikhailov 2023	Mikhailov, M., Budde, K., Halleck, F., Eleftheriadis, G., Naik, M. G., Schrezenmeier, E., Bachmann, F., Choi, M., Duettmann, W., von Hoerschelmann, E., Koch, N., Liefeldt, L., Lücht, C., Straub-Hohenbleicher, H., Waiser, J., Weber, U., Zukunft, B., & Osmanodja, B. (2023). COVID-19 Outcomes in Kidney Transplant Recipients in a German Transplant Center. Journal of clinical medicine, 12(18), 6103. https://doi.org/10.3390/jcm12186103
Mues 2022	Mues, K. E., Kirk, B., Patel, D. A., Gelman, A., Chavers, S., Talarico, C., Esposito, D. B., Martin, D., Mansi, J., Chen, X., Gatto, N. M., de Velde, N. V. (2022). Real-world comparative effectiveness of mRNA-1273 and BNT162b2 vaccines among immunocompromised adults in the United States. medRxiv. https://doi.org/10.1101/2022.05.13.22274960
Naylor 2022	Naylor, K. L., Kim, S. J., Smith, G., McArthur, E., Kwong, J. C., Dixon, S. N., Treleaven, D., & Knoll, G. A. (2022). Effectiveness of first, second, and third COVID-19 vaccine doses in solid organ transplant recipients: A population-based cohort study from Canada. American journal of transplantation, 22(9), 2228–2236. https://doi.org/10.1111/ajt.17095
Naylor 2024	Naylor, K. L., Knoll, G. A., Smith, G., McArthur, E., Kwong, J. C., Dixon, S. N., Treleaven, D., & Kim, S. J. (2024). Effectiveness of a Fourth COVID-19 mRNA Vaccine Dose Against the Omicron Variant in Solid Organ Transplant Recipients. Transplantation, 108(1), 294–302. https://doi.org/10.1097/TP.0000000000004766
Pinto-Alvarez 2022	Pinto-Álvarez, M., Fernández-Niño, J. A., Arregocés-Castillo, L., Rojas-Botero, M. L., Palacios, A. F., Galvis-Pedraza, M., & Ruiz-Gomez, F. (2023). Real-world Evidence of COVID-19 Vaccines Effectiveness in Solid-organ Transplant Recipient Population in Colombia: A Study Nested in the Esperanza Cohort. Transplantation, 107(1), 216–224. https://doi.org/10.1097/TP.0000000000004411
Rasmussen 2022	Rasmussen, L. D., Lebech, A. M., Øvrehus, A., Poulsen, B. K., Christensen, H. R., Nielsen, H., Johansen, I. S., Omland, L. H., Wiese, L., Helleberg, M., Storgaard, M., Dalager-Pedersen, M., Rasmussen, T. A., Benfield, T., Petersen, T. S., Andersen, Å. B., Gram, M. A., Stegger, M., Edslev, S. M., & Obel, N. (2023). Experience with sotrovimab treatment of SARS-CoV-2-infected patients in Denmark. British journal of clinical pharmacology, 89(6), 1820–1833. https://doi.org/10.1111/bcp.15644
Sanayei 2023	Sanayei, A. M., Montalvan, A., Faria, I., Ochalla, J., Pavlakis, M., Blair, B. M., Alonso, C. D., Curry, M., & Saberi, B. (2023). Tixagevimab-Cilgavimab Decreases the Rate of SARS-CoV-2 Infection Among Solid Organ Transplant Recipients. Transplantation proceedings, 55(8), 1784–1792. https://doi.org/10.1016/j.transproceed.2023.07.011
Sandoval 2022	Sandoval, M., Nguyen, D. T., Huang, H. J., Yi, S. G., Ghobrial, R. M., Gaber, A. O., & Graviss, E. A. (2022). COVID-19 mortality may be reduced among fully vaccinated solid organ transplant recipients. PloS one, 17(12), e0279222. https://doi.org/10.1371/journal.pone.0279222
Sindu 2023	Sindu, D., Razia, D., Bay, C., Padiyar, J., Grief, K., Buddhdev, B., Arjuna, A., Abdelrazek, H., Mohamed, H., McAnally, K., Omar, A., Walia, R., Schaheen, L., & Tokman, S. (2024). Evolving impact of the COVID-19 pandemic on lung transplant recipients: A single-center experience. The Journal of heart and lung transplantation, 43(3), 442–452. https://doi.org/10.1016/j.healun.2023.10.010
Singh 2024	Singh, P., Von Stein, L., McGowan, M., Nolan, A., Ross, A., Kaur, M., Maxwell, M., Ma, J., Peng, J., & Pesavento, T. (2024). Comparison of outcomes in vaccinated versus unvaccinated COVID-19 kidney transplant recipients, a single center retrospective study-Is the taboo justified?. Clinical transplantation, 38(1), e15187. https://doi.org/10.1111/ctr.15187
Thotsiri 2022	Thotsiri, S., Sittiudomsuk, R., Sutharattanapong, N., Kantachuvesiri, S., & Wiwattanathum, P. (2022). The Effect of a Booster Dose mRNA Vaccine on COVID-19 Infection in Kidney Transplant Recipients after Inactivated or Viral Vector Vaccine Immunization. Vaccines, 10(10), 1690. https://doi.org/10.3390/vaccines10101690
Tucker 2022	Tucker, M., Azar, M. M., Cohen, E., Gan, G., Deng, Y., Foppiano Palacios, C., & Malinis, M. (2022). Evaluating clinical effectiveness of SARS-CoV-2 vaccine in solid organ transplant recipients: A propensity score matched analysis. Transplant infectious disease, 24(4), e13876. https://doi.org/10.1111/tid.13876
Udomkarnjananun 2023	Udomkarnjananun, S., Kerr, S. J., Banjongjit, A., Phonphok, K., Larpparisuth, N., Vongwiwatana, A., Noppakun, K., Lumpaopong, A., Supaporn, T., Pongskul, C., Avihingsanon, Y., & Townamchai, N. (2023). Outcomes of COVID-19 in kidney transplant recipients in the vaccination Era: A national multicenter cohort from Thailand. Heliyon, 9(12), e22811. https://doi.org/10.1016/j.heliyon.2023.e22811
Vieira 2022	Vieira K., Klein E., Lerner A., Farmakioits D. (2022). High Case Fatality Rate Among Fully Vaccinated Kidney Transplant Recipients with Breakthrough Covid-19 During the Delta Surge. American Journal of Transplantation, 22(Supplement 3):440
Vinson 2022a	Vinson, A. J., Anzalone, A. J., Sun, J., Dai, R., Agarwal, G., Lee, S. B., French, E., Olex, A., Ison, M. G., Mannon, R. B., & N3C consortium (2022). The risk and consequences of breakthrough SARS-CoV-2 infection in solid organ transplant recipients relative to non-immunosuppressed controls. American journal of transplantation, 22(10), 2418–2432. https://doi.org/10.1111/ajt.17117
Vinson 2022b	Vinson A.J., Anzalone A., Dai R., French E., Olex A., Sun J., Agarwal G., Lee S., Mannon R.B. (2022). Role of Vaccination in the COVID-19 Nationwide Cohort (N3C) of Solid Organ Transplant Recipients. American Journal of Transplantation, 22(Supplement 3):407
Wong 2022	Wong, G., Rowlandson, M., Sabanayagam, D., Ginn, A. N., Kable, K., Sciberras, F., Au, E., Draper, J., Arnott, A., Sintchenko, V., Dwyer, D. E., Chen, S. C. A., & Kok, J. (2022). COVID-19 Infection With the Omicron SARS-CoV-2 Variant in a Cohort of Kidney and Kidney Pancreas Transplant Recipients: Clinical Features, Risk Factors, and Outcomes. Transplantation, 106(9), 1860–1866. https://doi.org/10.1097/TP.0000000000004203
Zhang 2023	Zhang, W., Wang, R., Jin, P., Yu, X., Wang, W., Zhang, Y., Bai, X., & Liang, T. (2024). Clinical characteristics and outcomes of liver transplant recipients infected by Omicron during the opening up of the dynamic zero-coronavirus disease policy in China: A prospective, observational study. American journal of transplantation, 24(4), 631–640. https://doi.org/10.1016/j.ajt.2023.09.022
Zona 2023	Zona, E. E., Gibes, M. L., Jain, A. S., Danobeitia, J. S., Garonzik-Wang, J., Smith, J. A., Mandelbrot, D. A., & Parajuli, S. (2024). Sequelae of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infection among Kidney Transplant Recipients: A Large Single-Center Experience. Critical care research and practice, 2024, 7140548. https://doi.org/10.1155/2024/7140548

Appendix 3. Examples of studies excluded during the full-text screening phase.

Study (First Author Last Name, Year)	Reference
Exclusion reason: No adjusted measures	
Softeland 2024	Søfteland, J. M., Li, H., Magnusson, J. M., Leach, S., Friman, V., Gisslén, M., Felldin, M., Schult, A., Karason, K., Baid-Agrawal, S., Wallquist, C., & Nyberg, F. (2024). COVID-19 Outcomes and Vaccinations in Swedish Solid Organ Transplant Recipients 2020-2021: A Nationwide Multi-Register Comparative Cohort Study. Viruses, 16(2), 271. https://doi.org/10.3390/v16020271
Exclusion reason: Systematic review	
Efros 2022	Efros, O., Anteby, R., Halfon, M., Meisel, E., Klang, E., & Soffer, S. (2022). Efficacy and Safety of Third Dose of the COVID-19 Vaccine among Solid Organ Transplant Recipients: A Systemic Review and Meta-Analysis. Vaccines, 10(1), 95. https://doi.org/10.3390/vaccines10010095
Exclusion reason: Wrong study design	
Yin 2022	Yin, S., Ma, M., Zhong, Q., Lin, T., & Song, T. (2022). Renal Complications in Kidney Transplant Recipients After Whole-virus Inactivated COVID-19 Vaccination. Transplantation, 106(11), e510–e511. https://doi.org/10.1097/TP.0000000000004330
Exclusion reason: Wrong outcomes	
Ferreira 2023	Ferreira, V. H., Ierullo, M., Mavandadnejad, F., Kurtesi, A., Hu, Q., Hardy, W. R., Hall, V. G., Pinzon, N., Yotis, D., Gingras, A. C., Belga, S., Shalhoub, S., Hébert, M. J., Humar, A., Kabbani, D., & Kumar, D. (2023). Omicron BA.4/5 Neutralization and T-Cell Responses in Organ Transplant Recipients After Booster Messenger RNA Vaccine: A Multicenter Cohort Study. Clinical infectious diseases, 77(2), 229–236. https://doi.org/10.1093/cid/ciad175
Exclusion reason: Wrong intervention	
Benotmane 2022	Benotmane, I., Velay, A., Gautier-Vargas, G., Olagne, J., Obrecht, A., Cognard, N., Heibel, F., Braun-Parvez, L., Keller, N., Martzloff, J., Perrin, P., Pszczolinski, R., Moulin, B., Fafi-Kremer, S., Thaunat, O., & Caillard, S. (2022). Breakthrough COVID-19 cases despite prophylaxis with 150 mg of tixagevimab and 150 mg of cilgavimab in kidney transplant recipients. American journal of transplantation, 22(11), 2675–2681. https://doi.org/10.1111/ajt.17121
Exclusion reason: Wrong comparator	
Charmetant 2022	Charmetant, X., Espi, M., Benotmane, I., Barateau, V., Heibel, F., Buron, F., Gautier-Vargas, G., Delafosse, M., Perrin, P., Koenig, A., Cognard, N., Levi, C., Gallais, F., Manière, L., Rossolillo, P., Soulier, E., Pierre, F., Ovize, A., Morelon, E., Defrance, T., … Thaunat, O. (2022). Infection or a third dose of mRNA vaccine elicits neutralizing antibody responses against SARS-CoV-2 in kidney transplant recipients. Science translational medicine, 14(636), eabl6141. https://doi.org/10.1126/scitranslmed.abl6141
Exclusion reason: Wrong patient population	
Mohanraj 2022	Mohanraj, D., Baldwin, S., Singh, S., Gordon, A., & Whitelegg, A. (2022). Cellular and humoral responses to SARS-CoV-2 vaccination in immunosuppressed patients. Cellular immunology, 373, 104501. https://doi.org/10.1016/j.cellimm.2022.104501
Exclusion reason: Commentary	
Toniutto 2021	Toniutto, P., Aghemo, A., Grossi, P., Burra, P., & Permanent Transplant Commission of the Italian Association for the Study of the Liver (2021). Clinical update on the efficacy of anti-SARS-CoV-2 mRNA vaccines in patients on the waiting list for liver transplantation and in liver transplant recipients. Digestive and liver disease, 53(10), 1232–1234. https://doi.org/10.1016/j.dld.2021.07.019
Exclusion reason: Protocol only	
Bouwmans 2022	Bouwmans, P., Messchendorp, A. L., Sanders, J. S., Hilbrands, L., Reinders, M. E. J., Vart, P., Bemelman, F. J., Abrahams, A. C., van den Dorpel, M. A., Ten Dam, M. A., de Vries, A. P. J., Rispens, T., Steenhuis, M., Gansevoort, R. T., Hemmelder, M. H., & RECOVAC Collaborators (2022). Long-term efficacy and safety of SARS-CoV-2 vaccination in patients with chronic kidney disease, on dialysis or after kidney transplantation: a national prospective observational cohort study. BMC nephrology, 23(1), 55. https://doi.org/10.1186/s12882-022-02680-3

Appendix 4. Risk of bias assessments of included studies.

Risk of bias assessments of included RCTs using Cochrane's RoB 2.0 tool

Study (First Author Last Name, Year)	Domain 1	Domain 2	Domain 3	Domain 4	Domain 5	Overall Risk of Bias
Outcome: COVID-19 infection						
Drenko 2023	Low	Some concerns	Low	Low	Some concerns	**Low**
Hall 2021	Low	Low	Low	Low	Low	**Low**
Kho 2022	Low	Some concerns	Low	Some concerns	Low	**Low**
Natori 2023	Low	Some concerns	Low	Low	Low	**Low**
Reindl-Schwaighofer 2022	Some concerns	Low	Low	Low	Some concerns	**Low**
Speich 2022	Low	Some concerns	Low	Low	Low	**Low**
Outcome: ICU Admission						
Reindl-Schwaighofer 2022	Some concerns	Low	Low	Low	Some concerns	**Low**
Outcome: Mortality						
Reindl-Schwaighofer 2022	Some concerns	Low	Low	Low	Low	**Low**
Speich 2022	Low	Some concerns	Low	Low	Low	**Low**

Note: Domain 1 = Bias arising from the randomization process; **Domain 2** = Bias due to deviations from the intended intervention; **Domain 3** = Bias due to missing outcome data; **Domain 4** = Bias in measurement of the outcome; **Domain 5** = Bias in selection of the reported results.

Risk of bias assessments of included observational studies using ROBINS-I

Study (First Author Last Name, Year)	Domain 1	Domain 2	Domain 3	Domain 4	Domain 5	Domain 6	Domain 7	Overall Risk of Bias
Outcome: COVID-19 Infection								
Aslam 2022	Serious	Low	Moderate	Low	Low	Low	Moderate	**Serious**
Bonazzetti 2023	Serious	Low	Moderate	Low	Low	Low	Moderate	**Serious**
Chen 2023	Serious	Low	Low	Low	Low	Low	Moderate	**Serious**
Collaborative 2022	Serious	Low	Low	Low	Moderate	Low	Moderate	**Serious**
Hiam 2021	Serious	Low	Moderate	Low	Low	Low	Moderate	**Serious**
Hod 2022	Moderate	Low	Low	Low	Low	Low	Moderate	**Moderate**
Joerns 2022	Serious	Low	Moderate	Low	Low	Low	Moderate	**Serious**
John 2022	Serious	Low	Moderate	Low	Low	Low	Moderate	**Serious**
Ma 2022	Serious	Low	Moderate	Low	Low	Low	Moderate	**Serious**
Masetti 2023	Serious	Low	Low	Low	Moderate	Low	Moderate	**Serious**
McEvoy 2022	Serious	Low	Serious	Low	Low	Moderate	Moderate	**Serious**
Mues 2022	Serious	Low	Low	Low	Low	Low	Moderate	**Serious**
Naylor 2022	Serious	Low	Moderate	Low	Low	Low	Moderate	**Serious**
Naylor 2024	Serious	Low	Low	Low	Low	Low	Moderate	**Serious**
Pinto-Alvarez 2022	Serious	Low	Moderate	Low	Low	Low	Moderate	**Serious**
Sanayei 2023	Serious	Low	Low	Low	Low	Low	Moderate	**Serious**
Singh 2024	Serious	Low	Low	Low	Low	Low	Moderate	**Serious**
Tucker 2022	Moderate	Low	Moderate	Low	Low	Low	Moderate	**Moderate**
Vinson 2022a	Moderate	Low	Moderate	Low	Low	Low	Moderate	**Moderate**
Outcome: Hospitalization								
Chen 2023	Serious	Low	Low	Low	Low	Low	Moderate	**Serious**
Collaborative 2022	Serious	Low	Low	Low	Moderate	Low	Moderate	**Serious**
Demir 2022	Serious	Serious	Moderate	Low	Low	Low	Moderate	**Serious**
Hall 2022	Moderate	Serious	Moderate	Low	Low	Low	Moderate	**Serious**
Hamm 2022	Serious	Serious	Moderate	Low	Low	Low	Moderate	**Serious**
Hardgrave 2022	Serious	Serious	Low	Low	Low	Low	Moderate	**Serious**
Korogiannou 2023	Serious	Serious	Low	Low	Moderate	Low	Moderate	**Serious**
Kwon 2022	Serious	Serious	Moderate	Low	Low	Low	Moderate	**Serious**
Mikhailov 2023	Serious	Low	Low	Low	Low	Low	Moderate	**Serious**
Mues 2022	Serious	Low	Moderate	Low	Low	Low	Moderate	**Serious**
Pinto-Alvarez 2022	Serious	Low	Moderate	Low	Low	Low	Moderate	**Serious**
Rasmussen 2022	Serious	Serious	Low	Low	Low	Low	Moderate	**Serious**
Sindu 2024	Serious	Low	Low	Low	Low	Low	Moderate	**Serious**
Vinson 2022a	Moderate	Serious	Moderate	Low	Low	Low	Moderate	**Serious**
Vinson 2022b	Moderate	Serious	Moderate	Low	Low	Low	Moderate	**Serious**
Wong 2022	Serious	Serious	Low	Low	Low	Low	Moderate	**Serious**
Zhang 2023	Serious	Low	Low	Low	Low	Low	Moderate	**Serious**
Zona 2023	Serious	Low	Low	Low	Low	Low	Moderate	**Serious**
Outcome: ICU Admission								
Demir 2022	Serious	Serious	Moderate	Low	Low	Low	Moderate	**Serious**
Llamas 2023	Serious	Low	Low	Low	Low	Low	Moderate	**Serious**
Mikhailov 2023	Serious	Low	Low	Low	Low	Low	Moderate	**Serious**
Sandoval 2022	Serious	Serious	Low	Low	Low	Low	Moderate	**Serious**
Sindu 2023	Serious	Low	Low	Low	Low	Low	Moderate	**Serious**
Outcome: Mortality								
Callaghan 2023	Serious	Serious	Low	Low	Low	Low	Moderate	**Serious**
Collaborative 2022	Serious	Low	Low	Low	Moderate	Low	Moderate	**Serious**
Demir 2022	Serious	Serious	Moderate	Low	Low	Low	Moderate	**Serious**

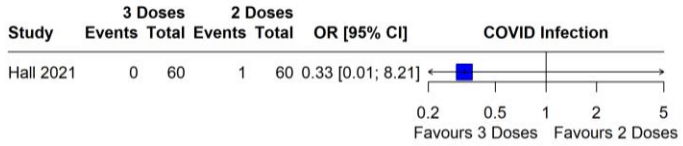
Elhadji 2023	Serious	Low	Moderate	Low	Moderate	Low	Moderate	**Serious**
Hall 2022	Moderate	Serious	Moderate	Low	Low	Low	Low	**Serious**
Hardgrave 2022	Serious	Serious	Low	Low	Low	Low	Low	**Serious**
John 2022	Serious	Low	Low	Low	Moderate	Low	Moderate	**Serious**
Kee 2022	Serious	Serious	Low	Low	Low	Low	Moderate	**Serious**
Lerner 2022	Moderate	Serious	Low	Low	Low	Low	Low	**Serious**
Llamas 2023	Serious	Low	Low	Low	Low	Low	Moderate	**Serious**
Mazuecos 2022	Serious	Low	Moderate	Low	Low	Low	Moderate	**Serious**
Mikhailov 2023	Serious	Low	Low	Low	Low	Low	Moderate	**Serious**
Pinto-Alvarez 2022	Serious	Low	Low	Low	Low	Low	Moderate	**Serious**
Rasmussen 2022	Serious	Serious	Low	Low	Low	Low	Moderate	**Serious**
Sandoval 2022	Serious	Serious	Moderate	Low	Low	Low	Moderate	**Serious**
Sindu 2023	Serious	Low	Low	Low	Low	Low	Moderate	**Serious**
Thotsiri 2022	Serious	Serious	Moderate	Low	Low	Low	Moderate	**Serious**
Tucker 2022	Moderate	Low	Moderate	Low	Low	Low	Moderate	**Moderate**
Udomkarnjananun 2023	Serious	Low	Low	Low	Low	Low	Moderate	**Serious**
Vieira 2022	Serious	Serious	Moderate	Low	Low	Low	Moderate	**Serious**
Vinson 2022a	Moderate	Serious	Moderate	Low	Low	Low	Moderate	**Serious**
Vinson 2022b	Moderate	Serious	Moderate	Low	Low	Low	Moderate	**Serious**

Note: Domain 1 = Bias due to confounding; **Domain 2** = Bias in the selection of participants into the study; **Domain 3** = Bias in classification of interventions; **Domain 4** = Bias due to deviations from intended interventions; **Domain 5** = Bias due to missing outcome data; D**omain 6** = Bias in measurement of the outcome; **Domain 7** = Bias in the selection of the reported result.

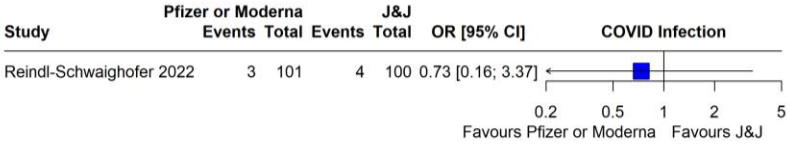
Appendix 5. Pairwise forest plots.

Timepoint 1 (October 1st, 2022)

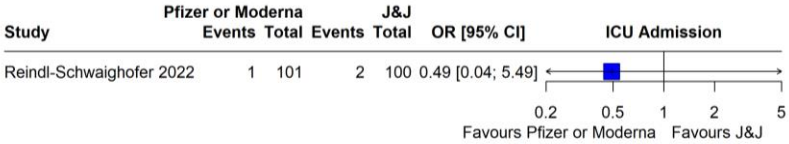
Randomized evidence evaluating three versus two doses on COVID-19 infection



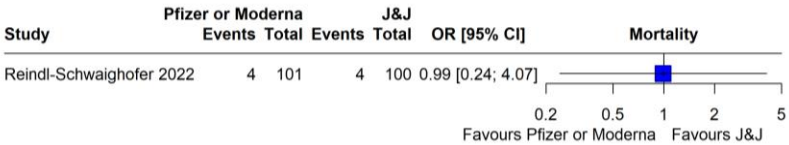
Randomized evidence evaluating mRNA versus J&J vaccines on COVID-19 infection



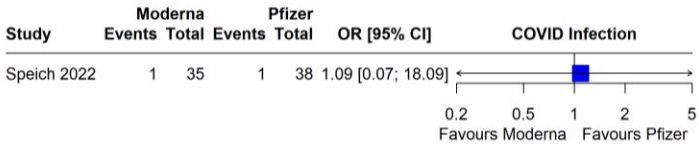
Randomized evidence evaluating mRNA versus J&J vaccines on ICU admission



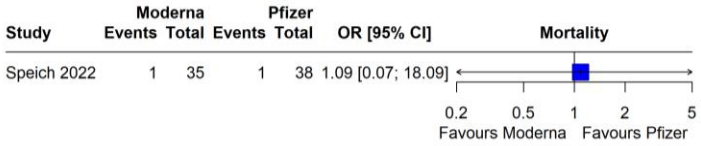
Randomized evidence evaluating mRNA versus J&J vaccines on mortality



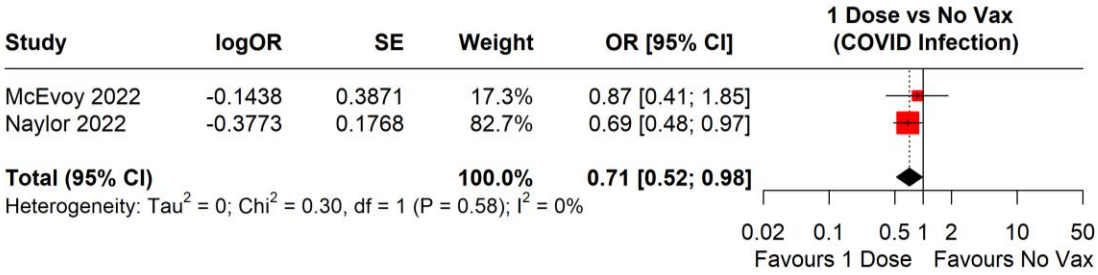
Randomized evidence evaluating Moderna versus Pfizer vaccines on COVID-19 infection



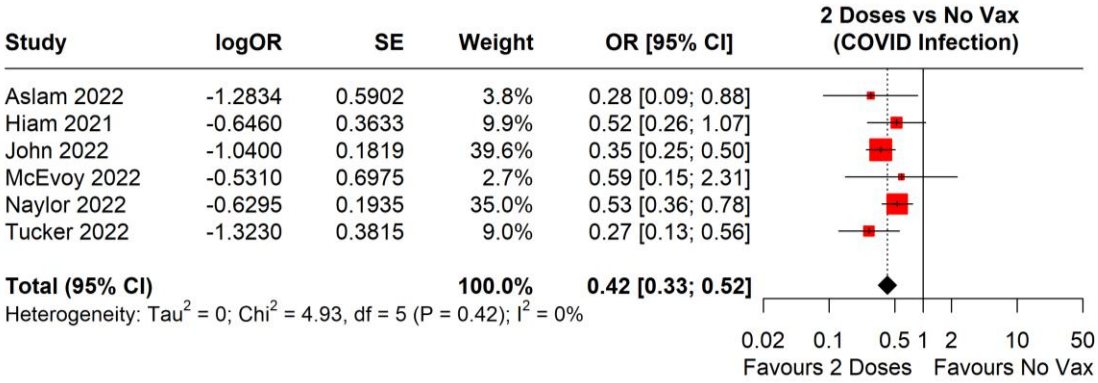
Randomized evidence evaluating Moderna versus Pfizer vaccines on mortality



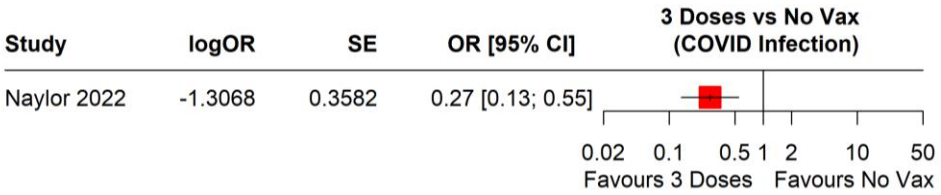
Observational evidence evaluating one dose versus no vaccination on COVID-19 infection



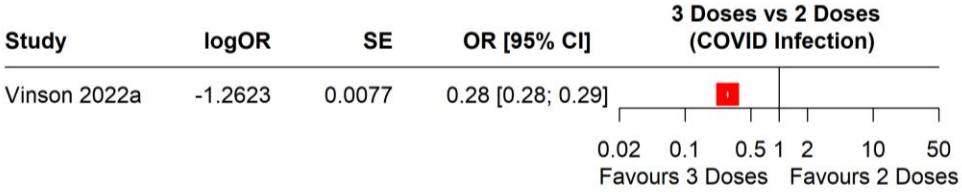
Observational evidence evaluating two doses versus no vaccination on COVID-19 infection



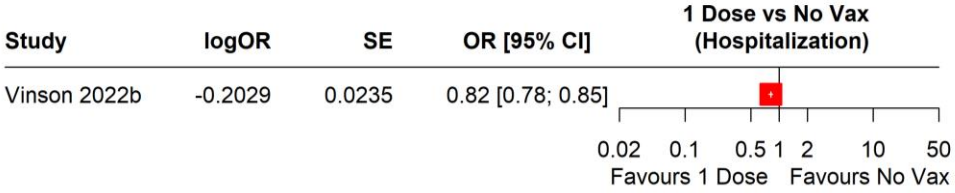
Observational evidence evaluating three doses versus no vaccination on COVID-19 infection



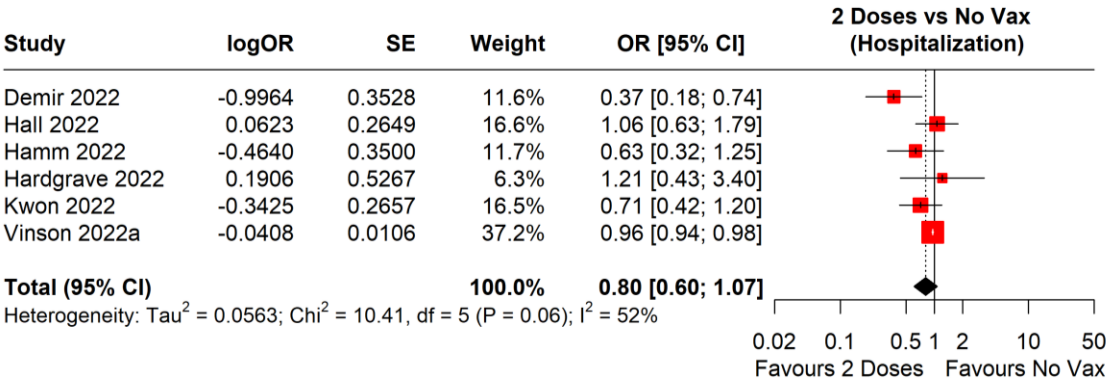
Observational evidence evaluating three versus two doses on COVID-19 infection



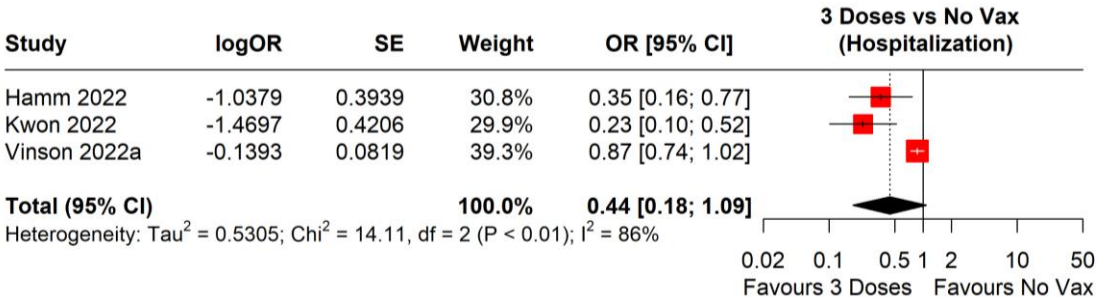
Observational evidence evaluating one dose versus no vaccination on hospitalization from COVID-19



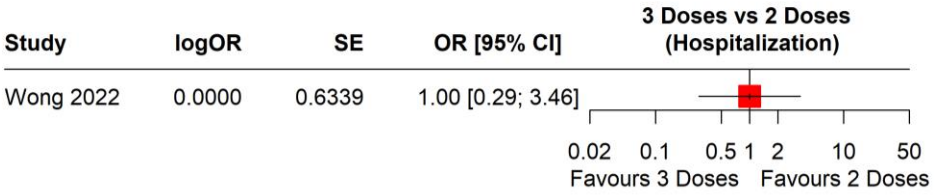
Observational evidence evaluating two doses versus no vaccination on hospitalization from COVID-19



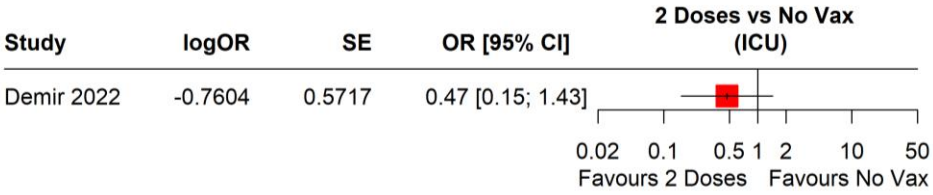
Observational evidence evaluating three doses versus no vaccination on hospitalization from COVID-19



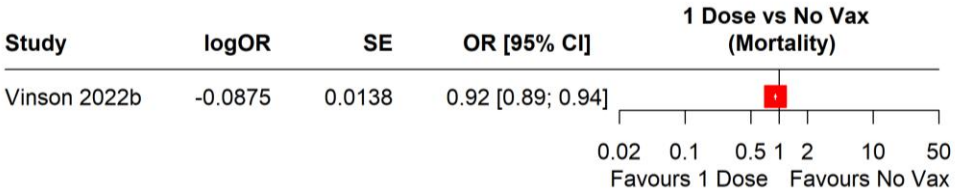
Observational evidence evaluating three versus two doses on hospitalization from COVID-19



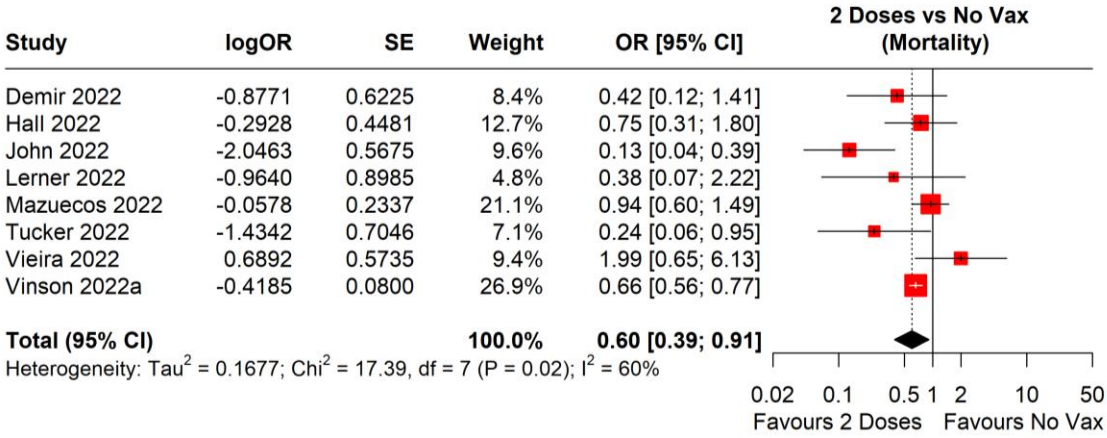
Observational evidence evaluating two doses versus no vaccination on ICU admission from COVID-19



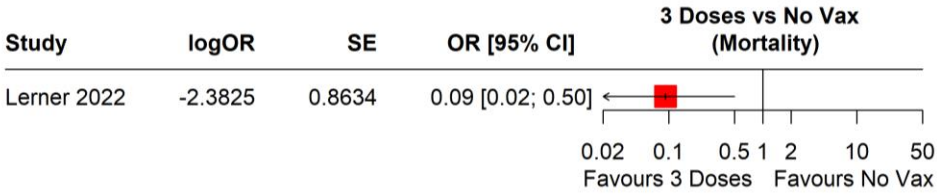
Observational evidence evaluating one dose versus no vaccination on mortality from COVID-19



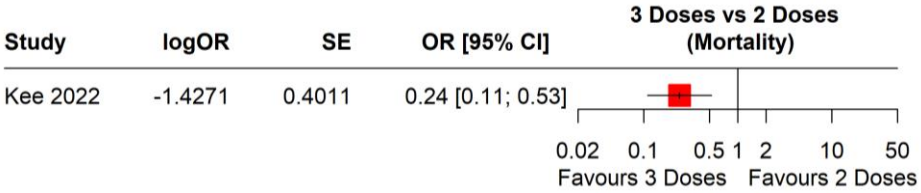
Observational evidence evaluating two doses versus no vaccination on mortality from COVID-19



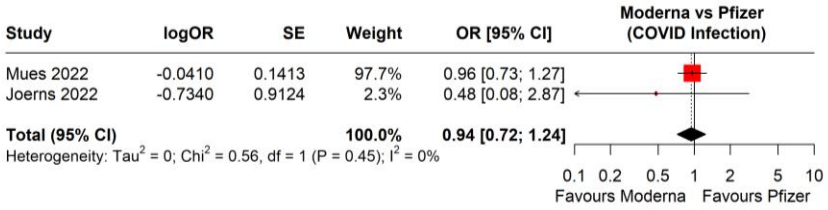
Observational evidence evaluating three doses versus no vaccination on mortality from COVID-19



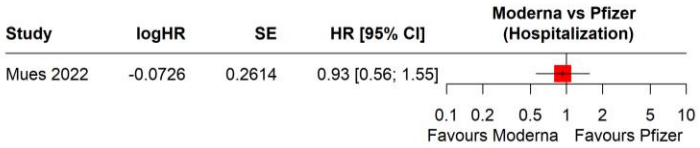
Observational evidence evaluating three versus two doses on mortality from COVID-19



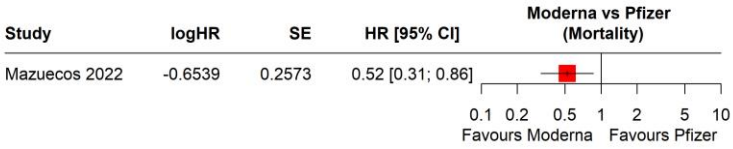
Observational evidence evaluating Moderna vs Pfizer vaccines on COVID-19 infection



Observational evidence evaluating Moderna vs Pfizer vaccines on COVID-19 hospitalization

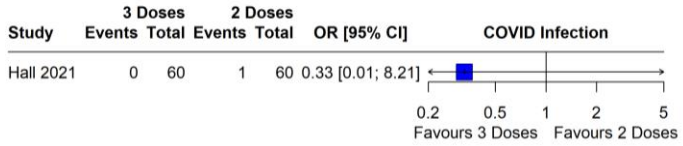


Observational evidence evaluating Moderna vs Pfizer vaccines on COVID-19 mortality

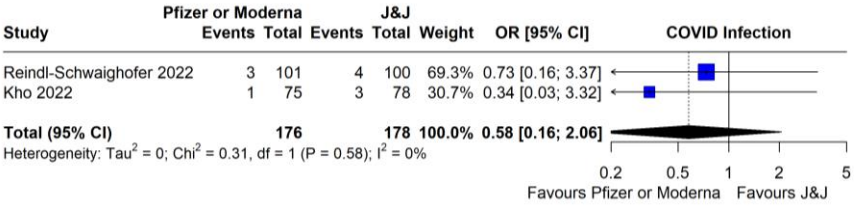


Timepoint 2 (March 1st, 2023)

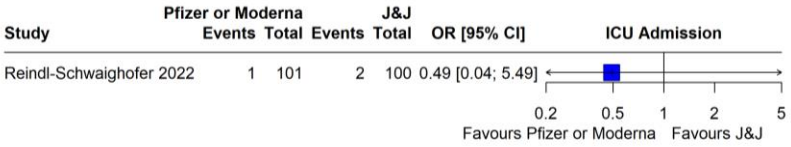
Randomized evidence evaluating three versus two doses on COVID-19 infection



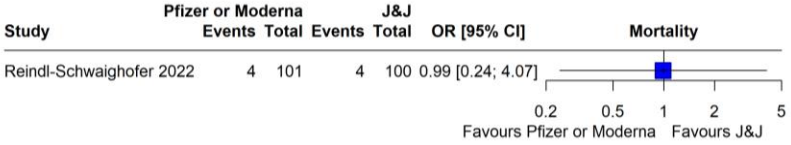
Randomized evidence evaluating mRNA versus J&J vaccines on COVID-19 infection



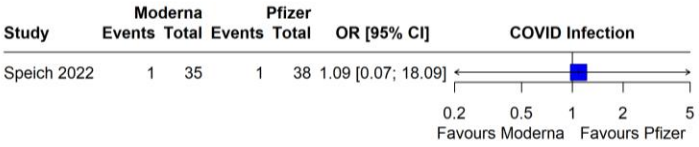
Randomized evidence evaluating mRNA versus J&J vaccines on ICU admission



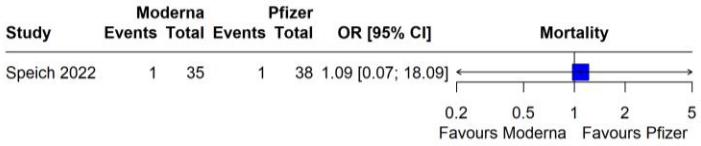
Randomized evidence evaluating mRNA versus J&J vaccines on mortality



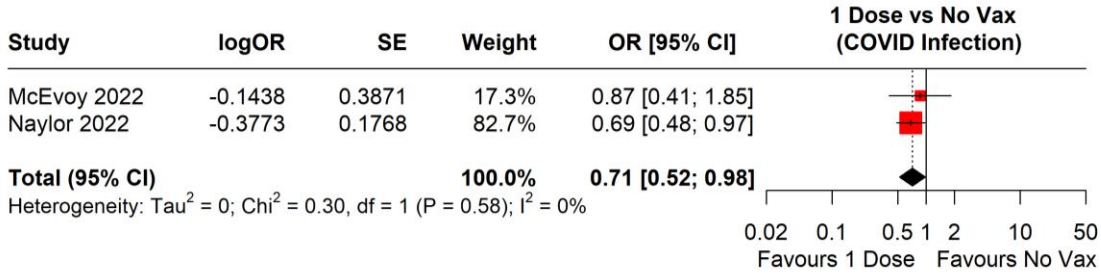
Randomized evidence evaluating Moderna versus Pfizer vaccines on COVID-19 infection



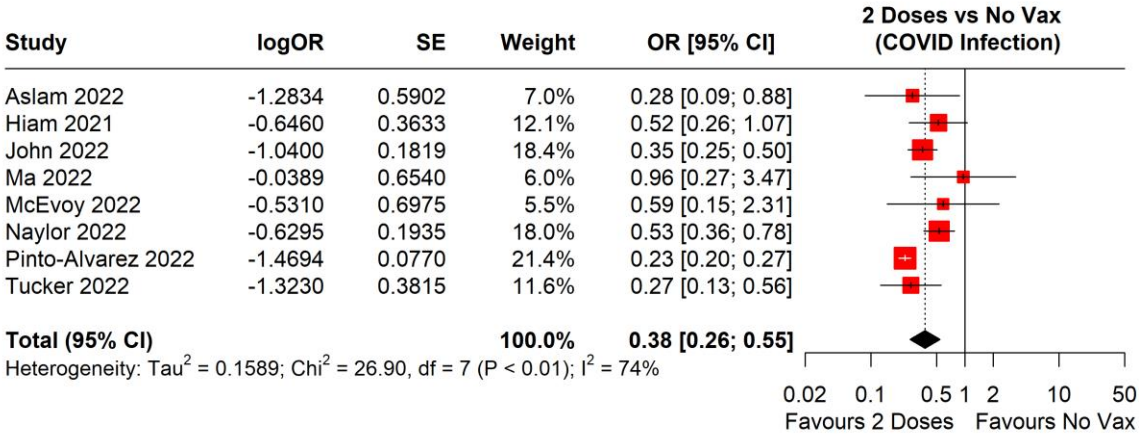
Randomized evidence evaluating Moderna versus Pfizer vaccines on mortality



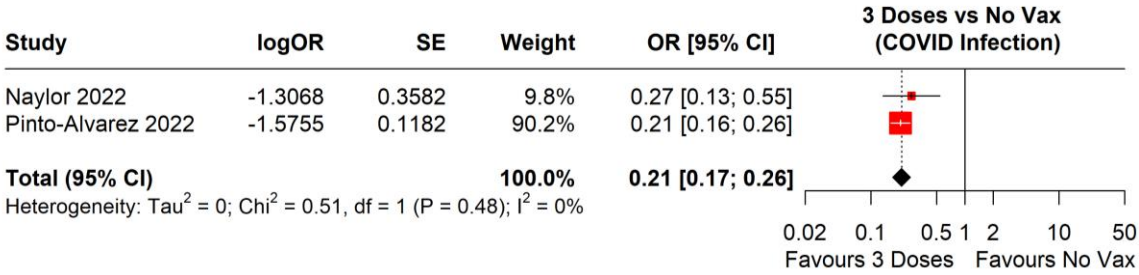
Observational evidence evaluating one dose versus no vaccination on COVID-19 infection



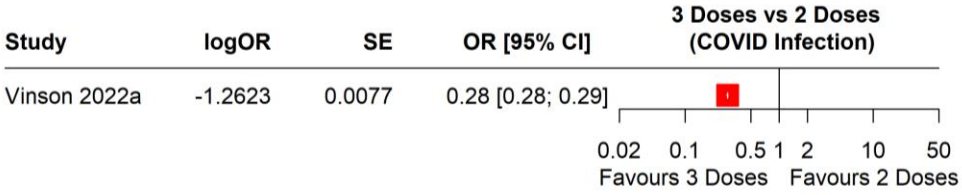
Observational evidence evaluating two doses versus no vaccination on COVID-19 infection



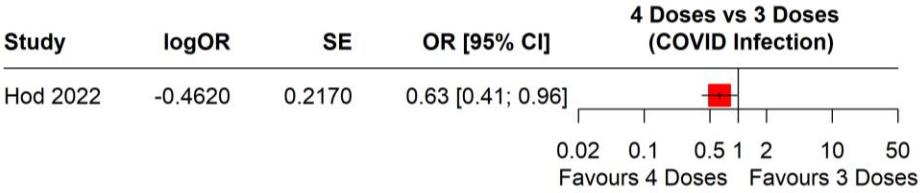
Observational evidence evaluating three doses versus no vaccination on COVID-19 infection



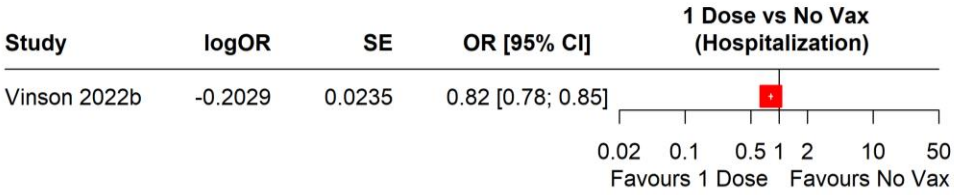
Observational evidence evaluating three versus two doses on COVID-19 infection



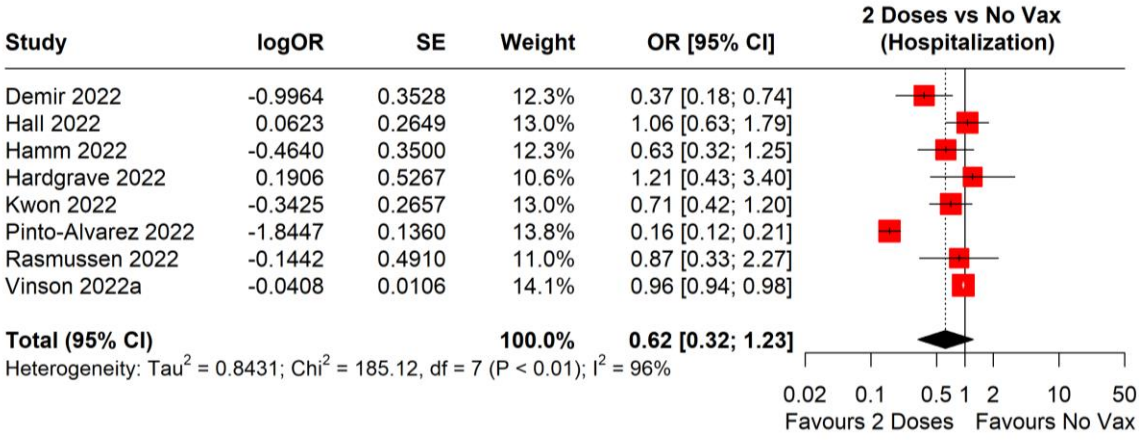
Observational evidence evaluating four versus three doses on COVID-19 infection



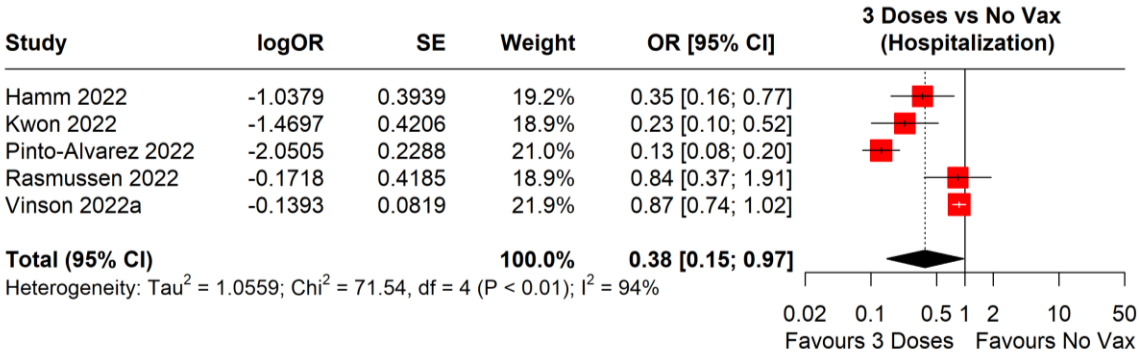
Observational evidence evaluating one dose versus no vaccination on hospitalization from COVID-19



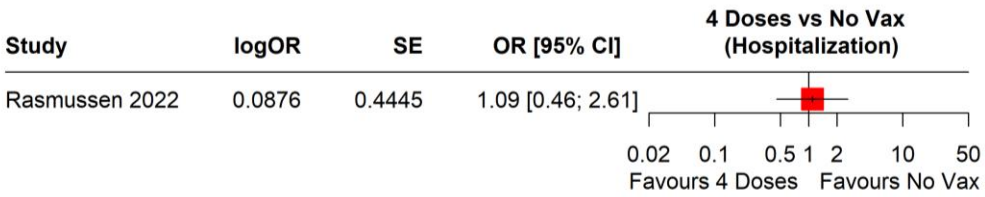
Observational evidence evaluating two doses versus no vaccination on hospitalization from COVID-19



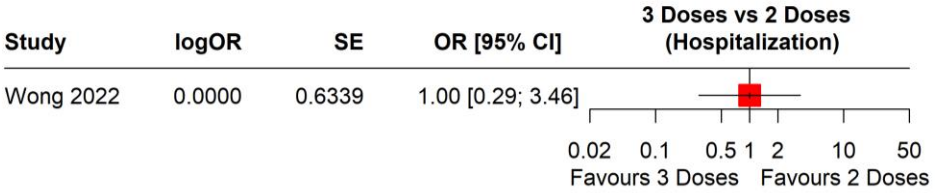
Observational evidence evaluating three doses versus no vaccination on hospitalization from COVID-19



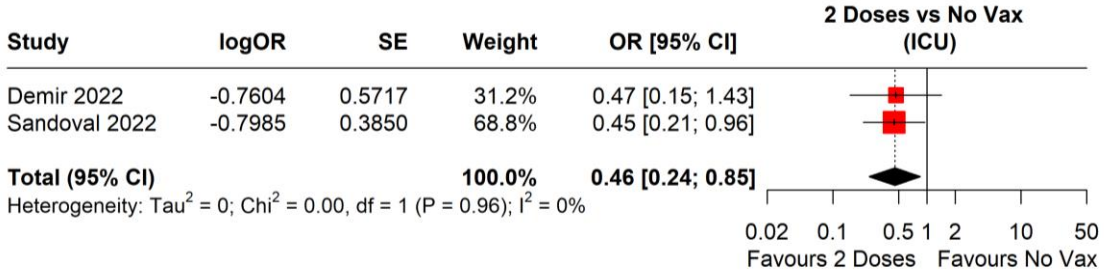
Observational evidence evaluating four doses versus no vaccination on hospitalization from COVID-19



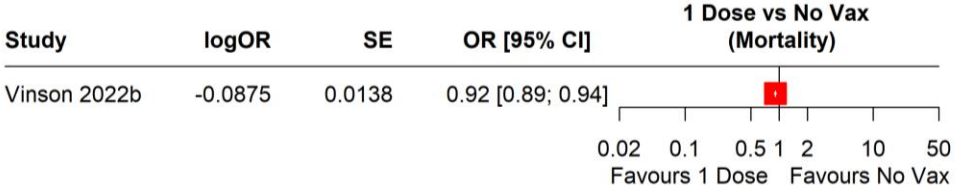
Observational evidence evaluating three versus two doses on hospitalization from COVID-19



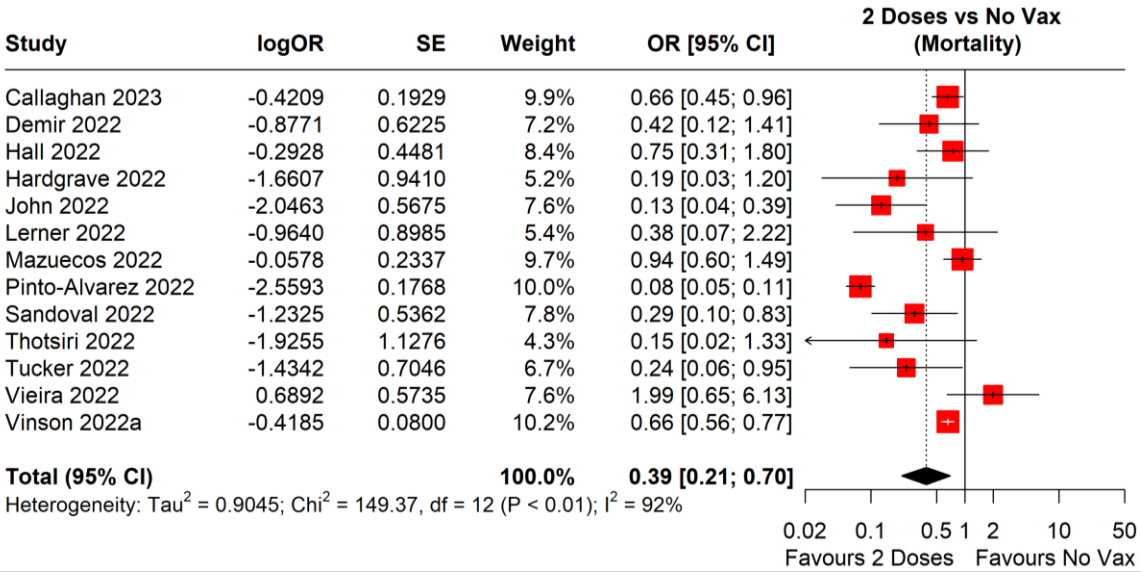
Observational evidence evaluating two doses versus no vaccination on ICU admission from COVID-19



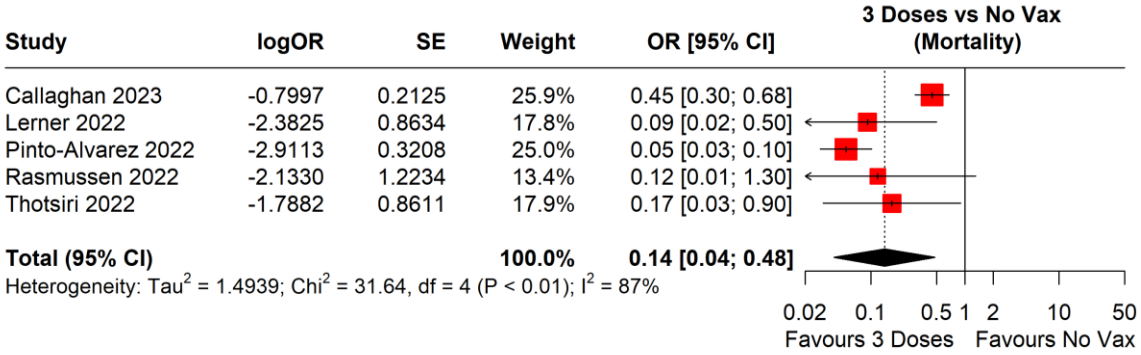
Observational evidence evaluating one dose versus no vaccination on mortality from COVID-19



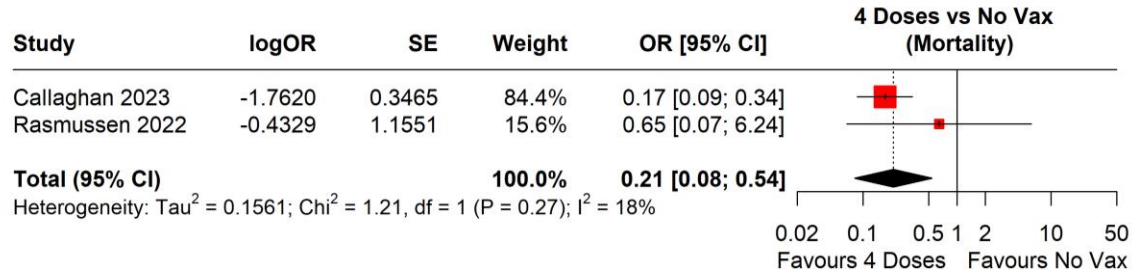
Observational evidence evaluating two doses versus no vaccination on mortality from COVID-19



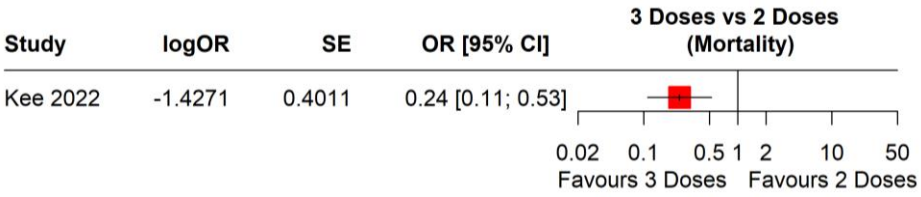
Observational evidence evaluating three doses versus no vaccination on mortality from COVID-19



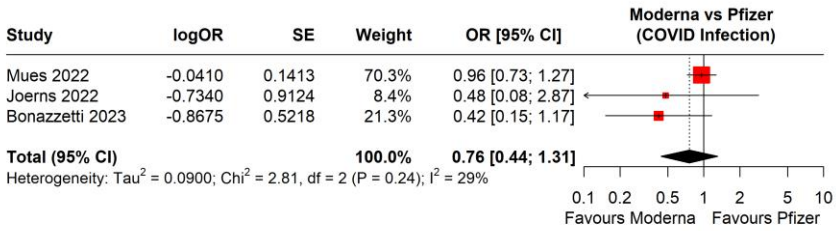
Observational evidence evaluating four doses versus no vaccination on mortality from COVID-19



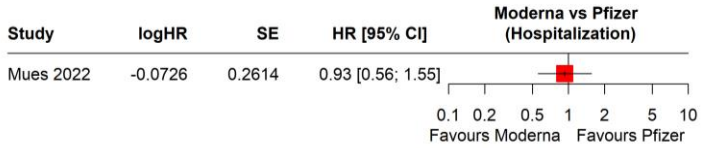
Observational evidence evaluating three versus two doses on mortality from COVID-19



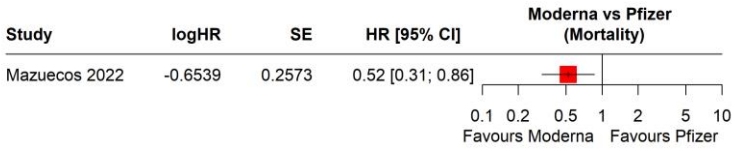
Observational evidence evaluating Moderna vs Pfizer vaccines on COVID-19 infection



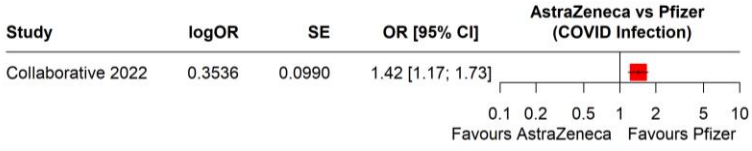
Observational evidence evaluating Moderna vs Pfizer vaccines on COVID-19 hospitalization



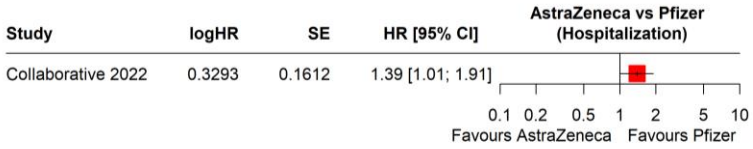
Observational evidence evaluating Moderna vs Pfizer vaccines on COVID-19 mortality



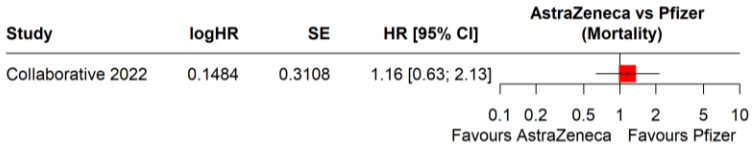
Observational evidence evaluating AstraZeneca vs Pfizer vaccines on COVID-19 infection



Observational evidence evaluating AstraZeneca vs Pfizer vaccines on COVID-19 hospitalization

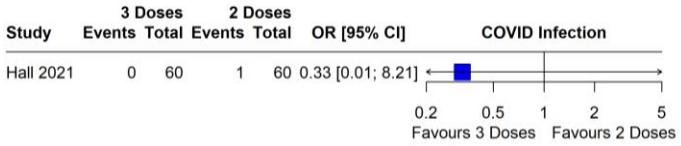


Observational evidence evaluating AstraZeneca vs Pfizer vaccines on COVID-19 mortality

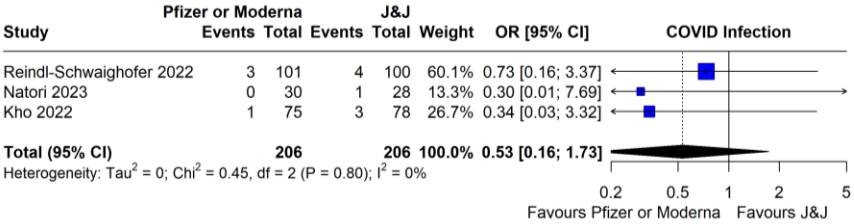


Timepoint 3 (July 1st, 2023)

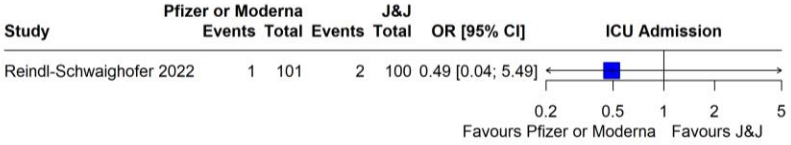
Randomized evidence evaluating three versus two doses on COVID-19 infection



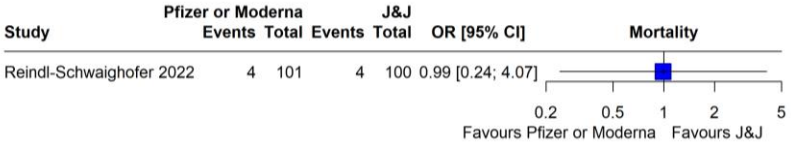
Randomized evidence evaluating mRNA versus J&J vaccines on COVID-19 infection



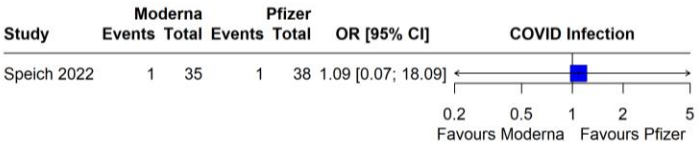
Randomized evidence evaluating mRNA versus J&J vaccines on ICU admission



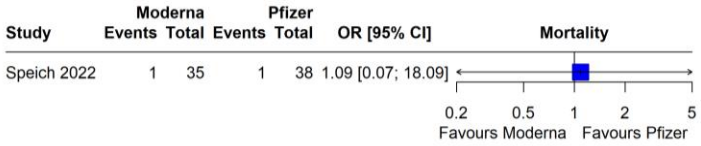
Randomized evidence evaluating mRNA versus J&J vaccines on mortality



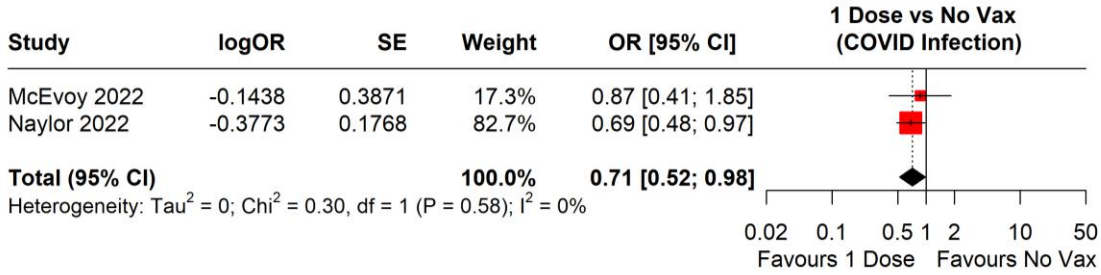
Randomized evidence evaluating Moderna versus Pfizer vaccines on COVID-19 infection



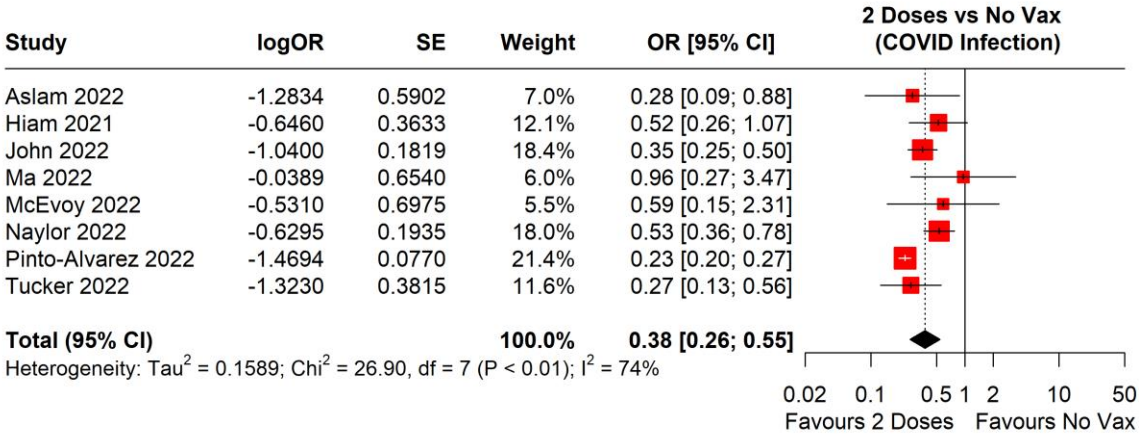
Randomized evidence evaluating Moderna versus Pfizer vaccines on mortality



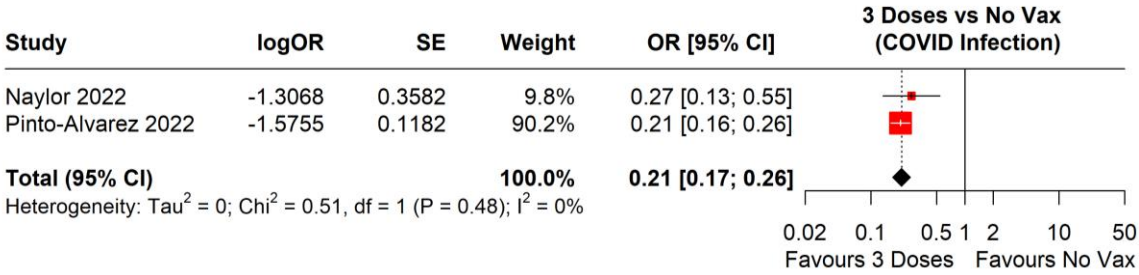
Observational evidence evaluating one dose versus no vaccination on COVID-19 infection



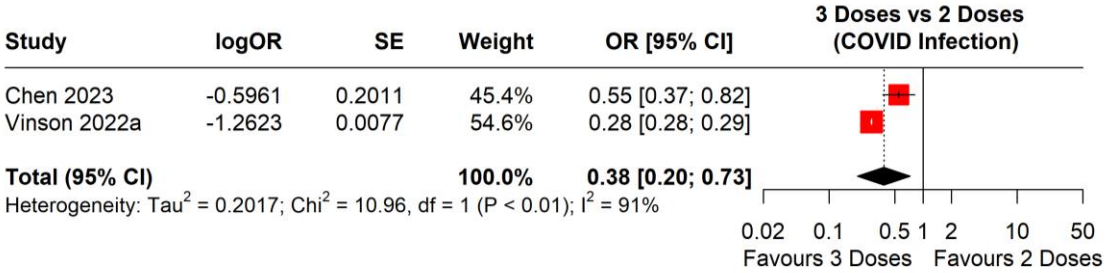
Observational evidence evaluating two doses versus no vaccination on COVID-19 infection



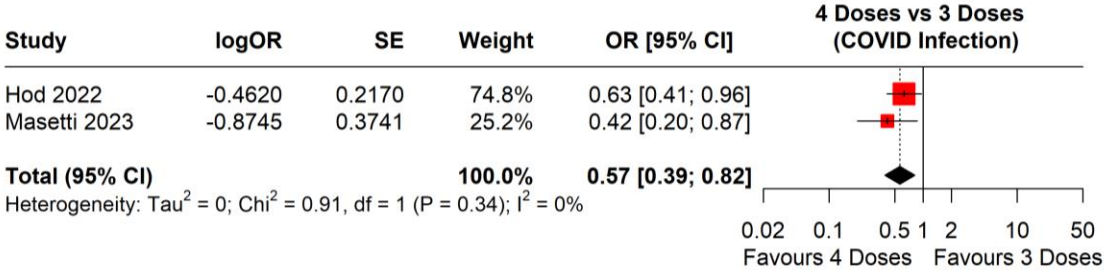
Observational evidence evaluating three doses versus no vaccination on COVID-19 infection



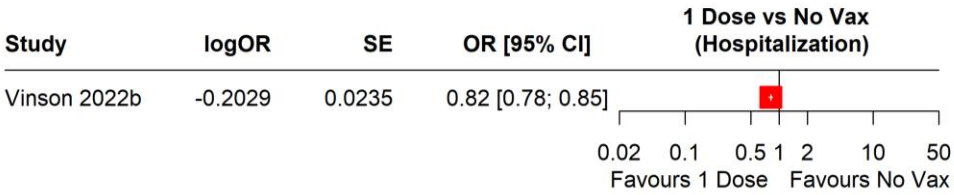
Observational evidence evaluating three versus two doses on COVID-19 infection



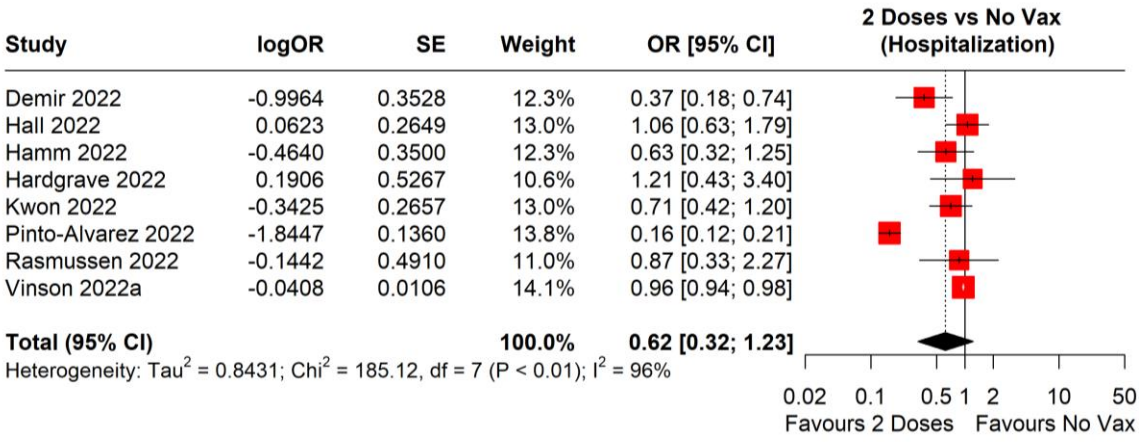
Observational evidence evaluating four versus three doses on COVID-19 infection



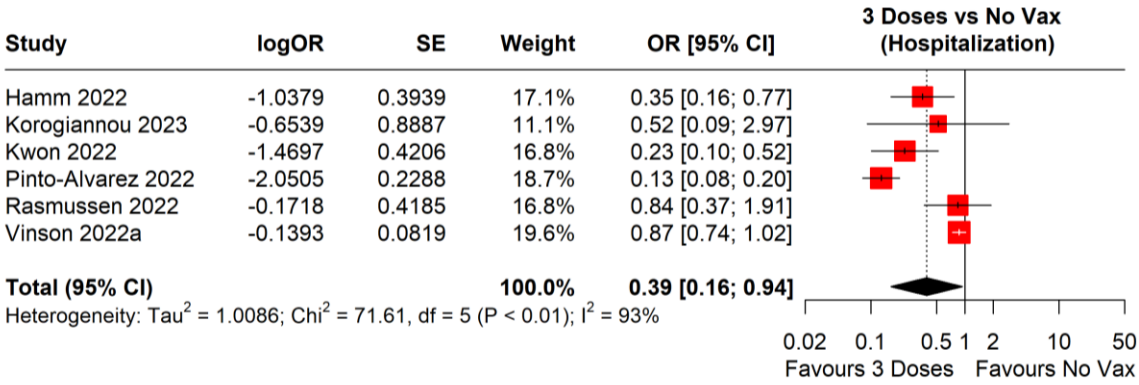
Observational evidence evaluating one dose versus no vaccination on hospitalization from COVID-19



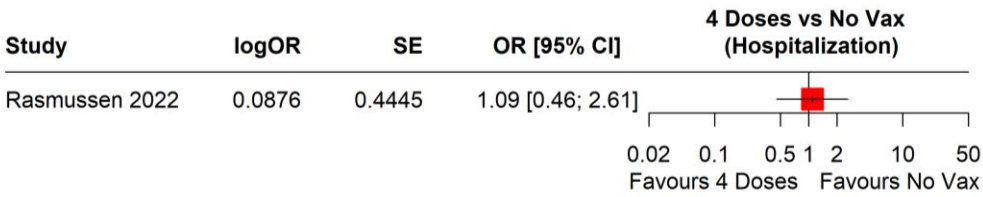
Observational evidence evaluating two doses versus no vaccination on hospitalization from COVID-19



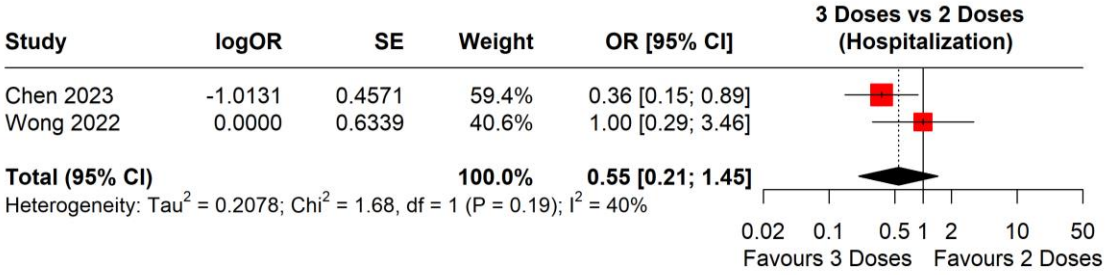
Observational evidence evaluating three doses versus no vaccination on hospitalization from COVID-19



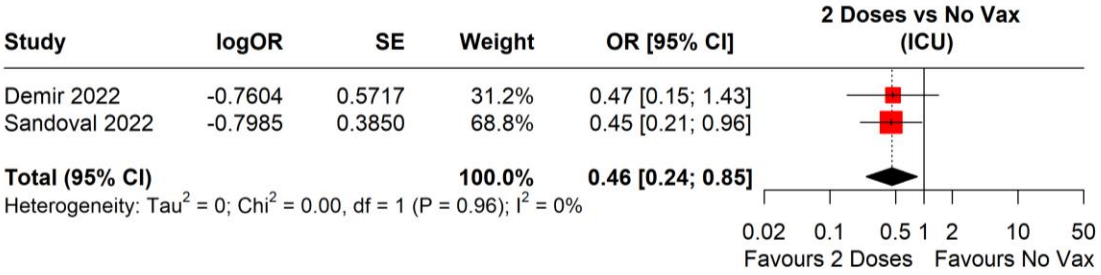
Observational evidence evaluating four doses versus no vaccination on hospitalization from COVID-19



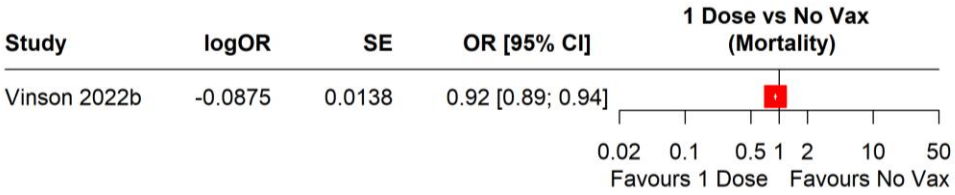
Observational evidence evaluating three versus two doses on hospitalization from COVID-19



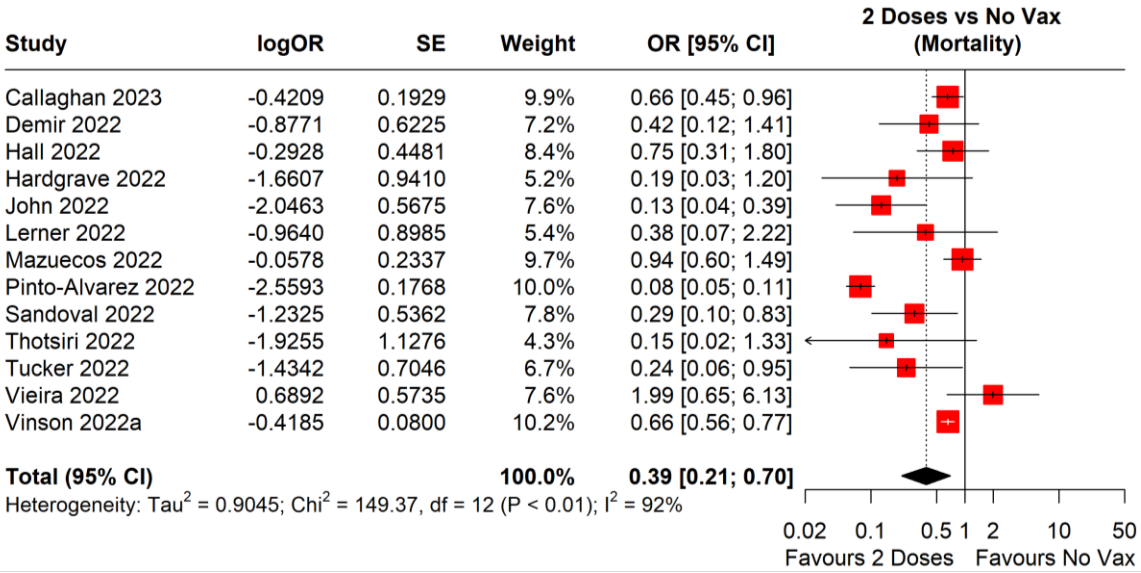
Observational evidence evaluating two doses versus no vaccination on ICU admission from COVID-19



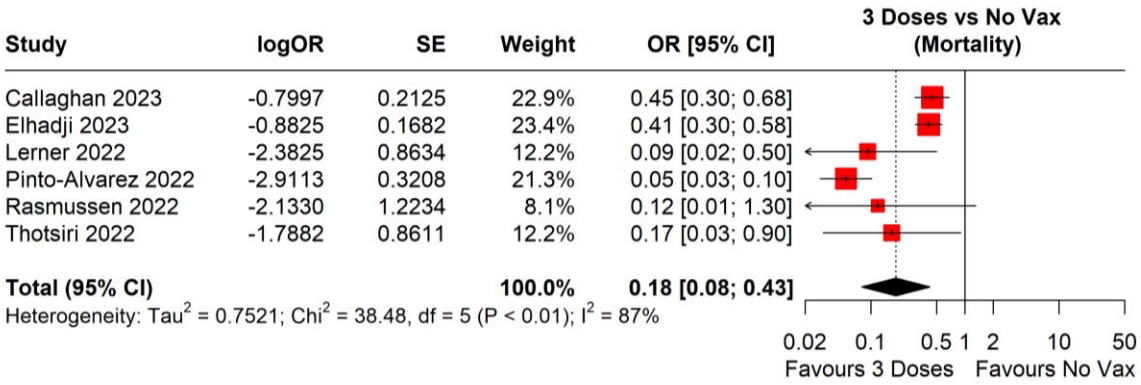
Observational evidence evaluating one dose versus no vaccination on mortality from COVID-19



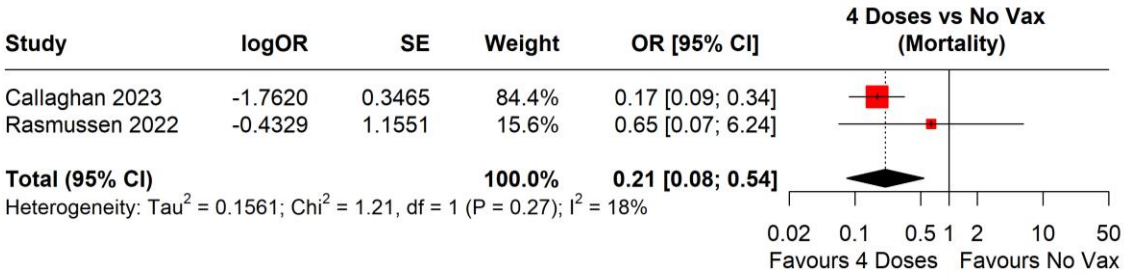
Observational evidence evaluating two doses versus no vaccination on mortality from COVID-19



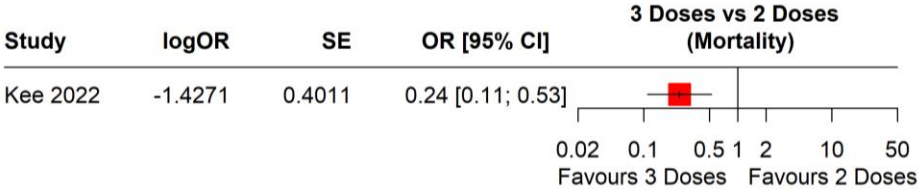
Observational evidence evaluating three doses versus no vaccination on mortality from COVID-19



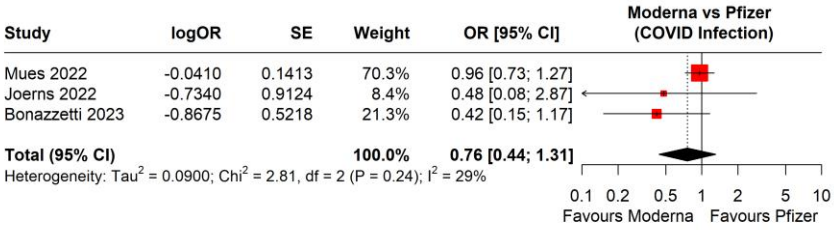
Observational evidence evaluating four doses versus no vaccination on mortality from COVID-19



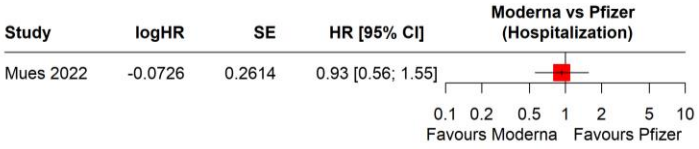
Observational evidence evaluating three versus two doses on mortality from COVID-19



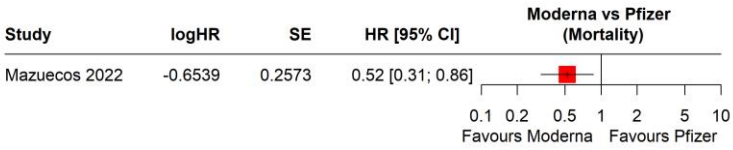
Observational evidence evaluating Moderna vs Pfizer vaccines on COVID-19 infection



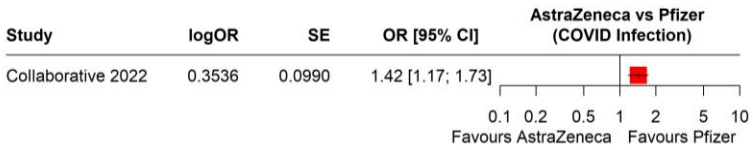
Observational evidence evaluating Moderna vs Pfizer vaccines on COVID-19 hospitalization



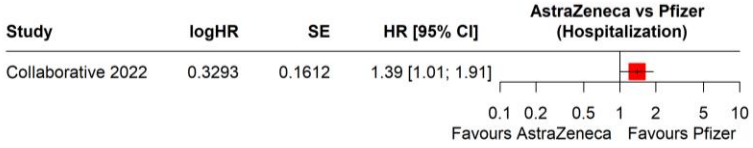
Observational evidence evaluating Moderna vs Pfizer vaccines on COVID-19 mortality



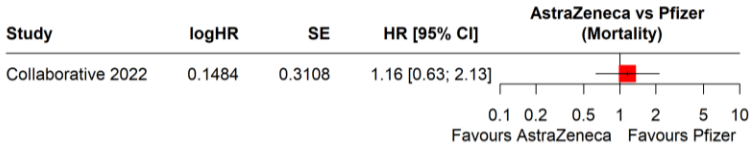
Observational evidence evaluating AstraZeneca vs Pfizer vaccines on COVID-19 infection



Observational evidence evaluating AstraZeneca vs Pfizer vaccines on COVID-19 hospitalization

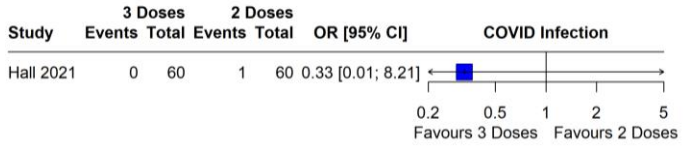


Observational evidence evaluating AstraZeneca vs Pfizer vaccines on COVID-19 mortality

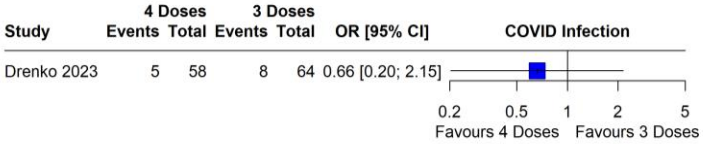


Timepoint 4 (March 1st, 2024)

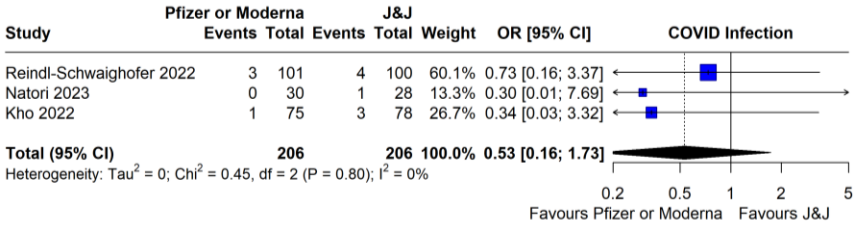
Randomized evidence evaluating three versus two doses on COVID-19 infection



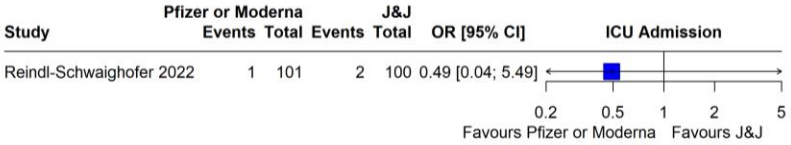
Randomized evidence evaluating four versus three doses on COVID-19 infection



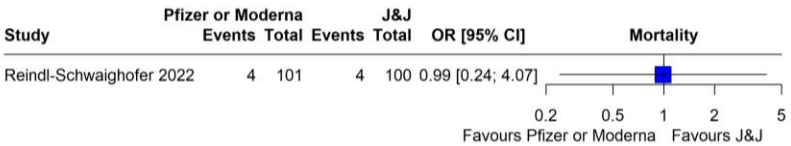
Randomized evidence evaluating mRNA versus J&J vaccines on COVID-19 infection



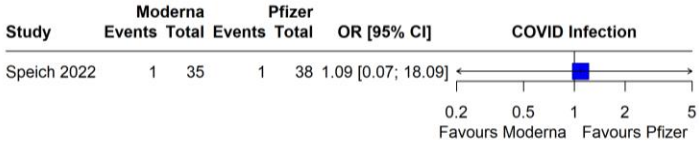
Randomized evidence evaluating mRNA versus J&J vaccines on ICU admission



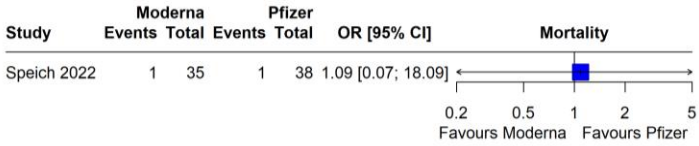
Randomized evidence evaluating mRNA versus J&J vaccines on mortality



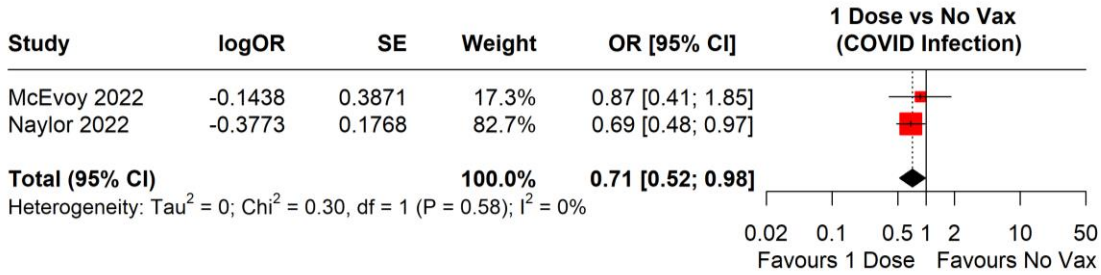
Randomized evidence evaluating Moderna versus Pfizer vaccines on COVID-19 infection



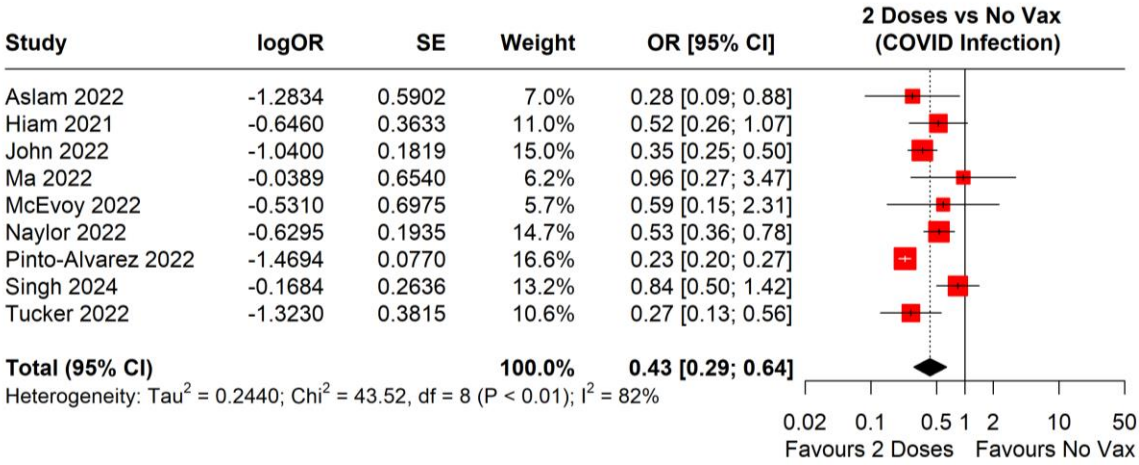
Randomized evidence evaluating Moderna versus Pfizer vaccines on mortality



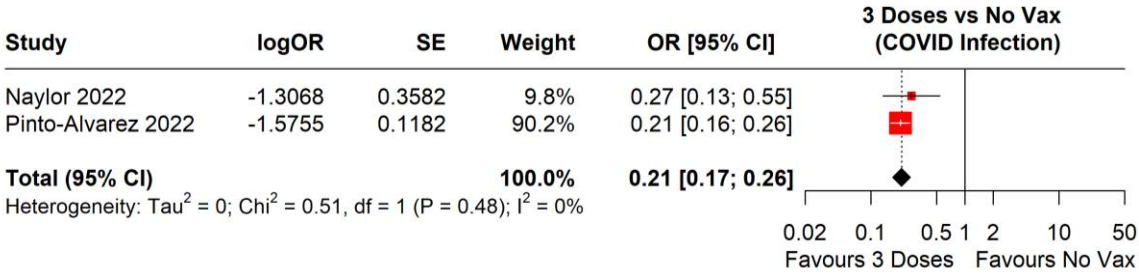
Observational evidence evaluating one dose versus no vaccination on COVID-19 infection



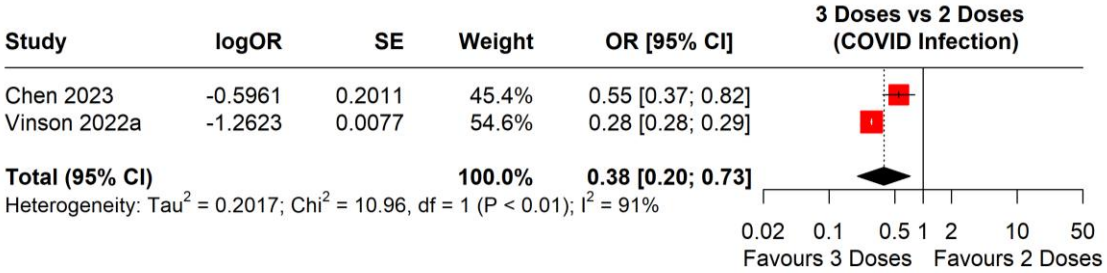
Observational evidence evaluating two doses versus no vaccination on COVID-19 infection



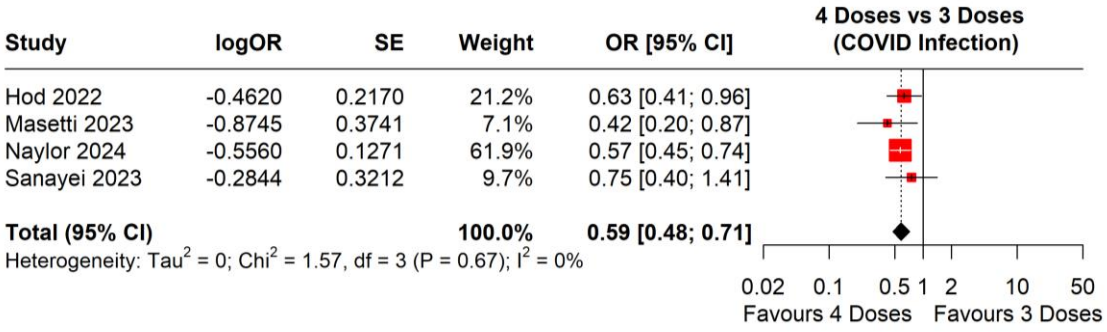
Observational evidence evaluating three doses versus no vaccination on COVID-19 infection



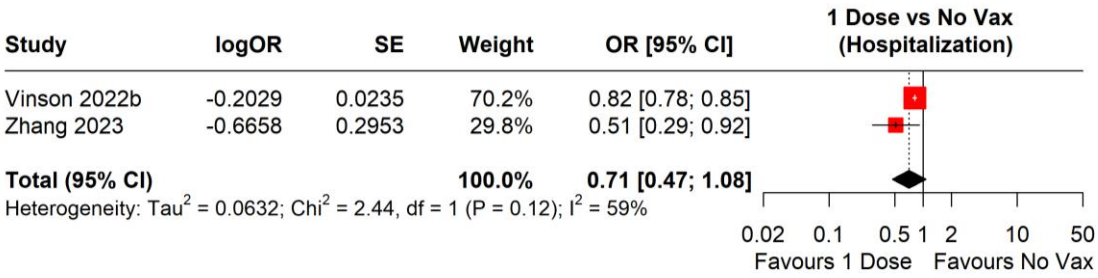
Observational evidence evaluating three versus two doses on COVID-19 infection



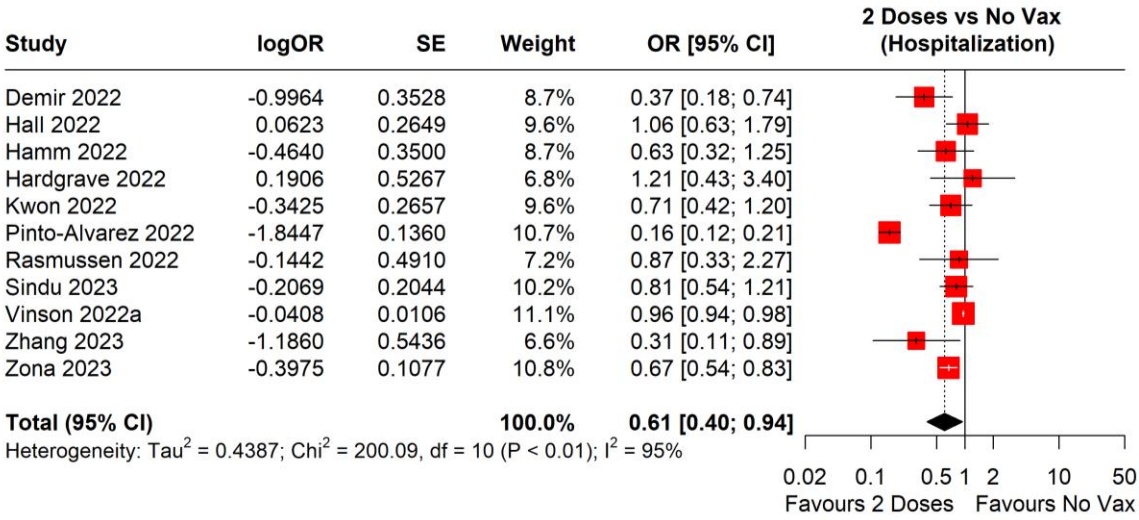
Observational evidence evaluating four versus three doses on COVID-19 infection



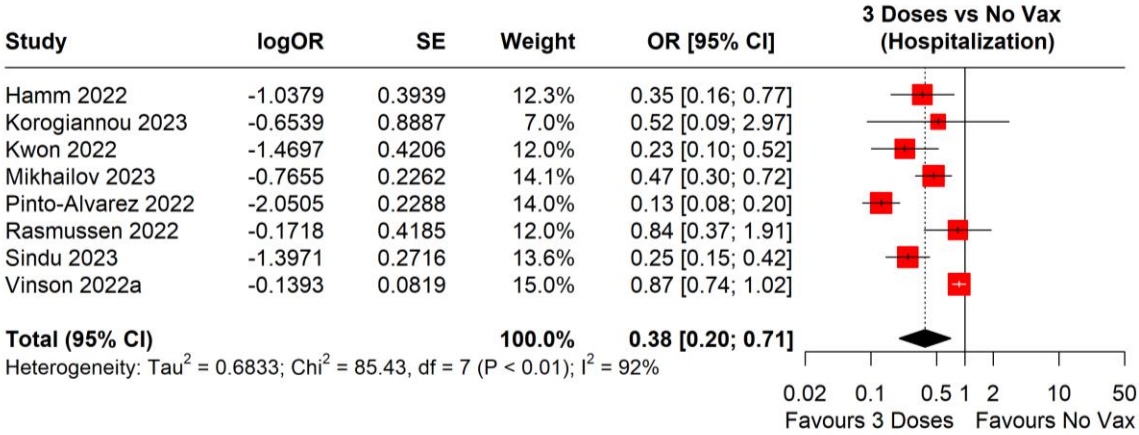
Observational evidence evaluating one dose versus no vaccination on hospitalization from COVID-19



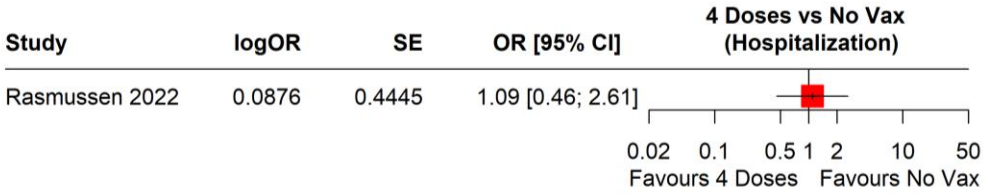
Observational evidence evaluating two doses versus no vaccination on hospitalization from COVID-19



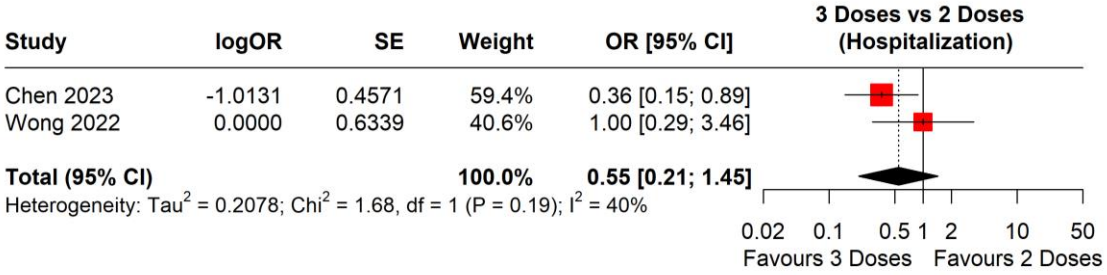
Observational evidence evaluating three doses versus no vaccination on hospitalization from COVID-19



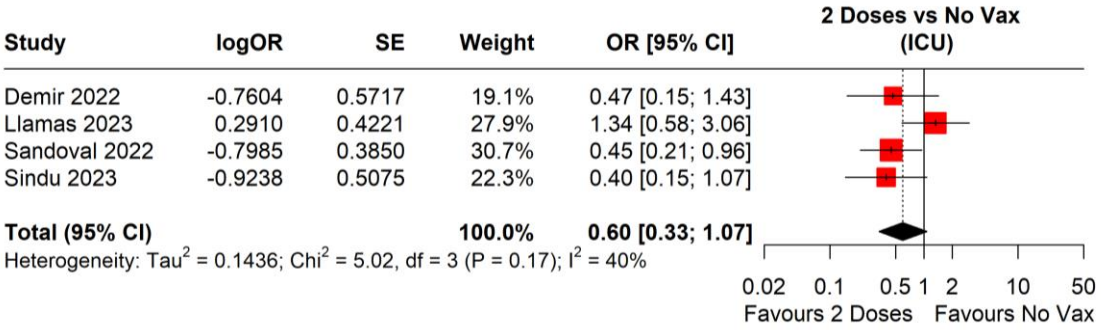
Observational evidence evaluating four doses versus no vaccination on hospitalization from COVID-19



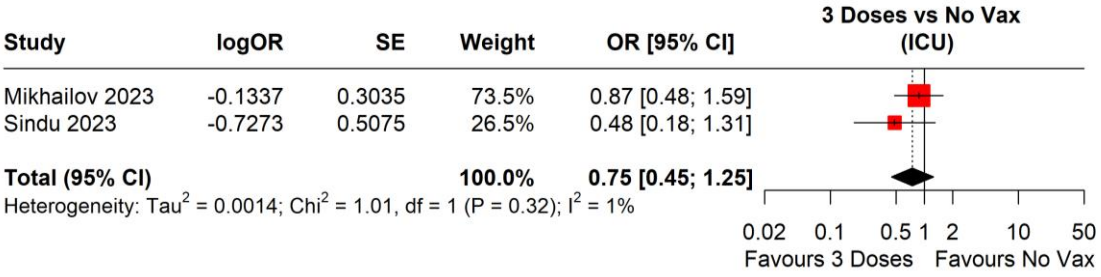
Observational evidence evaluating three versus two doses on hospitalization from COVID-19



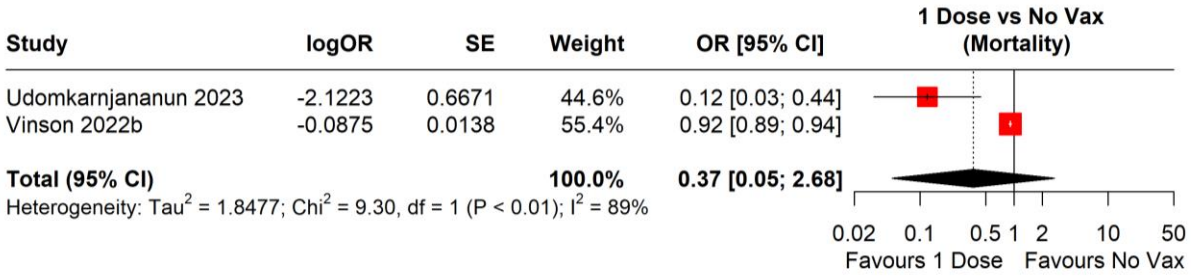
Observational evidence evaluating two doses versus no vaccination on ICU admission from COVID-19



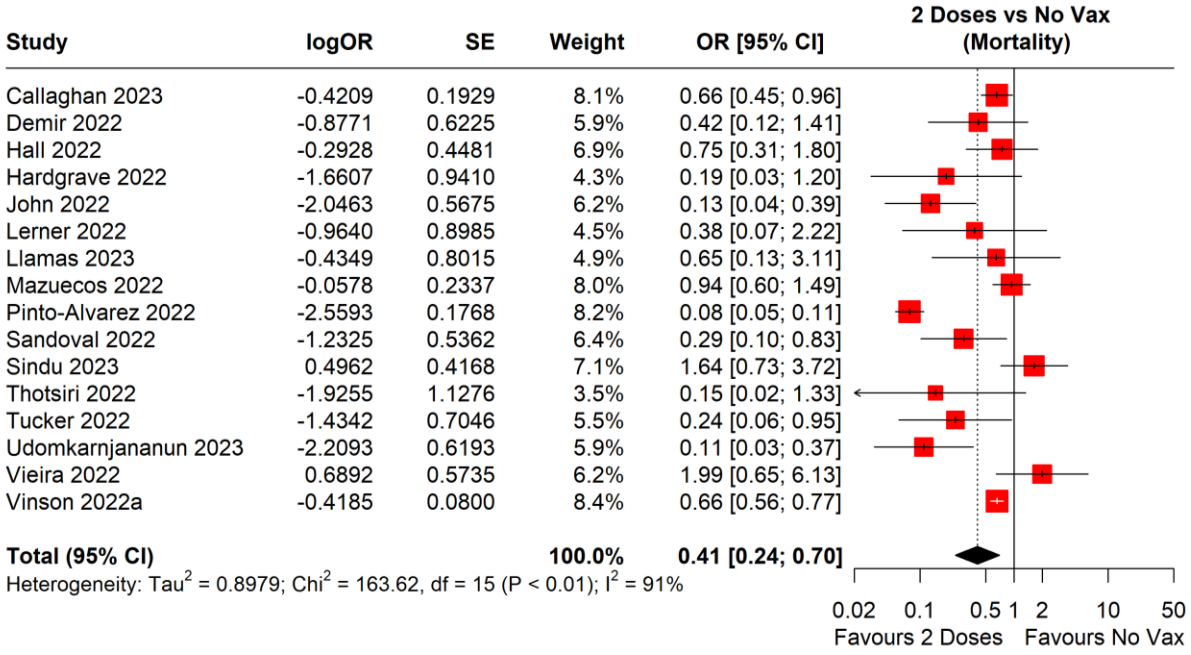
Observational evidence evaluating three doses versus no vaccination on ICU admission from COVID-19



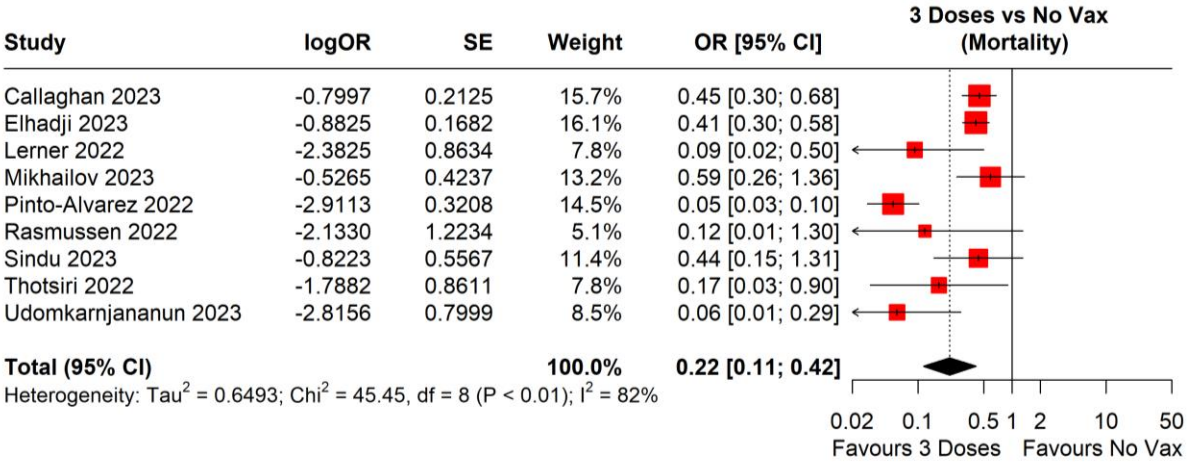
Observational evidence evaluating one dose versus no vaccination on mortality from COVID-19



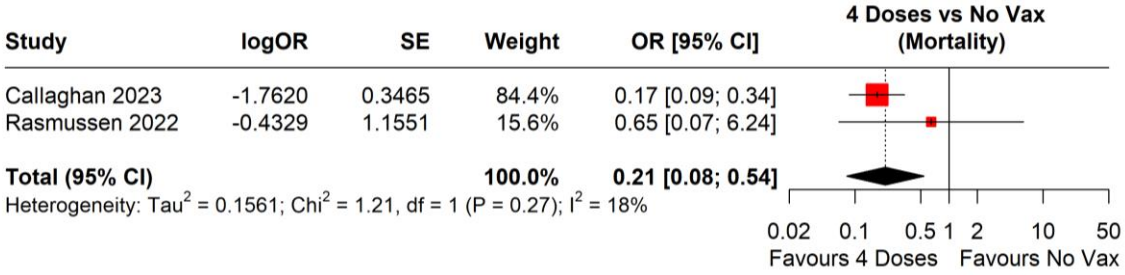
Observational evidence evaluating two doses versus no vaccination on mortality from COVID-19



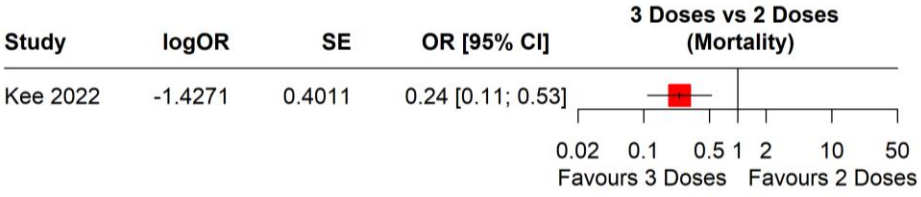
Observational evidence evaluating three doses versus no vaccination on mortality from COVID-19



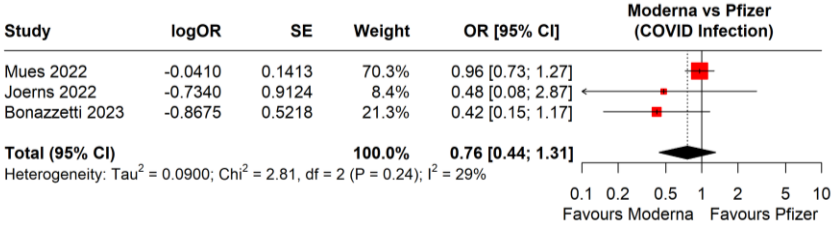
Observational evidence evaluating four doses versus no vaccination on mortality from COVID-19



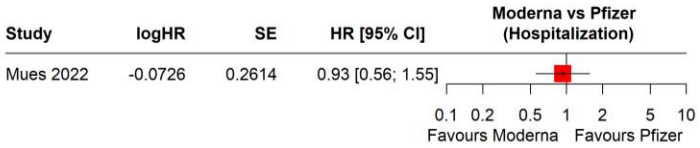
Observational evidence evaluating three versus two doses on mortality from COVID-19



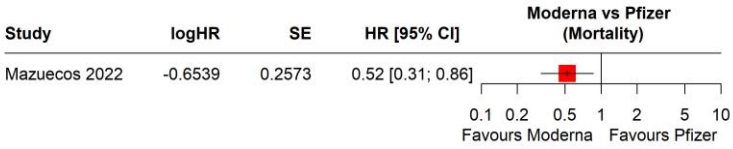
Observational evidence evaluating Moderna vs Pfizer vaccines on COVID-19 infection



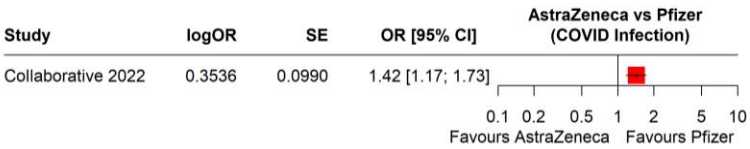
Observational evidence evaluating Moderna vs Pfizer vaccines on COVID-19 hospitalization



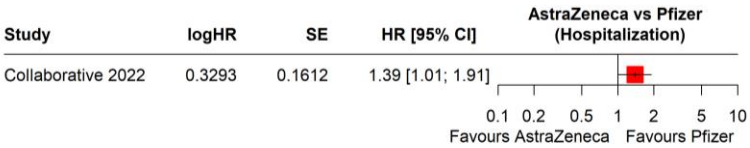
Observational evidence evaluating Moderna vs Pfizer vaccines on COVID-19 mortality



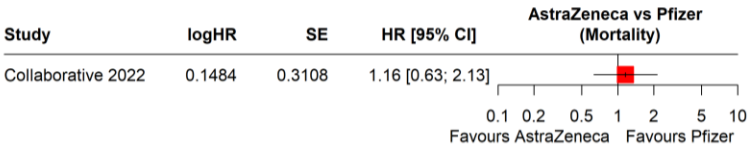
Observational evidence evaluating AstraZeneca vs Pfizer vaccines on COVID-19 infection



Observational evidence evaluating AstraZeneca vs Pfizer vaccines on COVID-19 hospitalization



Observational evidence evaluating AstraZeneca vs Pfizer vaccines on COVID-19 mortality



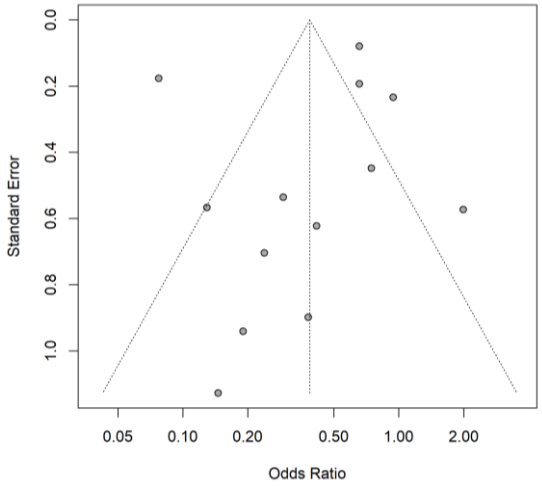
Appendix 6. Pairwise funnel plots.

Timepoint 1 (October 1st, 2022)

There were an insufficient number of studies to construct funnel plots for all pairwise analyses (i.e., less than 10 studies).

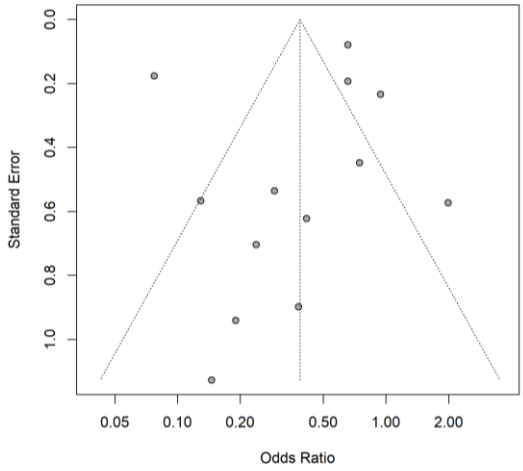
Timepoint 2 (March 1st, 2023)

Funnel plot for evidence evaluating two doses vs no vaccination on mortality from COVID-19



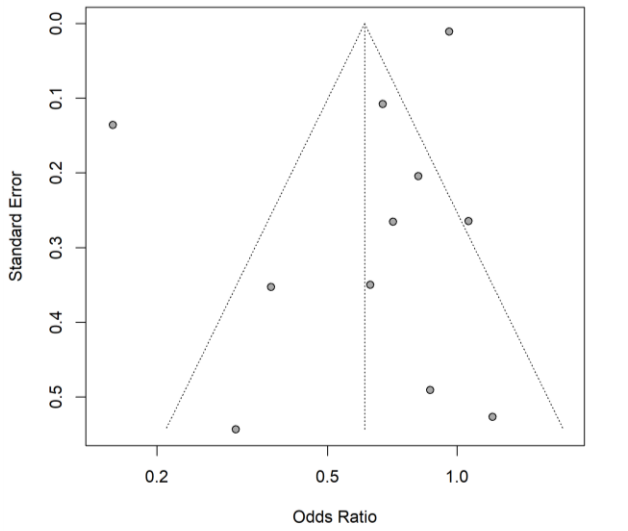
Timepoint 3 (July 1st, 2023)

Funnel plot for evidence evaluating two doses vs no vaccination on mortality from COVID-19

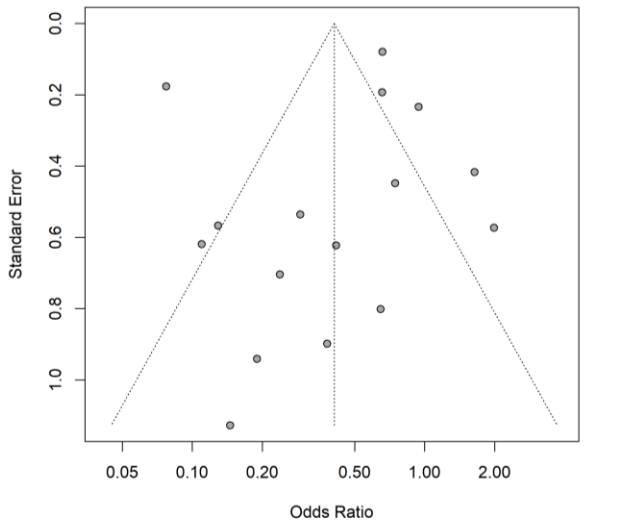


Timepoint 4 (March 1st, 2024)

Funnel plot for evidence evaluating two doses vs no vaccination on hospitalization from COVID-19



Funnel plot for evidence evaluating two doses vs no vaccination on mortality from COVID-19



Appendix 7. Subgroup analyses.

Timepoint 1 (October 1st, 2022)

Two doses vs no vaccination			
Organ Group	**COVID-19 Infection OR (95%CI)**	**Hospitalization from COVID-19 OR (95%CI)**	**Mortality from COVID-19 OR (95%CI)**
Mixed	0.39 (0.24 to 0.65)	N/A	0.65 (0.56 to 0.76)
Kidney	0.54 (0.29 to 1.01)	N/A	0.95 (0.49 to 1.84)
Liver	0.35 (0.25 to 0.50)	N/A	0.13 (0.04 to 0.39)
Lung	N/A	N/A	N/A
Heart	N/A	N/A	N/A
Interaction p-value	0.5274	N/A	0.0095
Credibility	N/A	N/A	Very Low

Note: CI = Confidence interval; OR = Odds ratio.

Timepoint 2 (March 1st, 2023)

Two doses vs no vaccination			
Organ Group	**COVID-19 Infection OR (95%CI)**	**Hospitalization from COVID-19 OR (95%CI)**	**Mortality from COVID-19 OR (95%CI)**
Mixed	0.31 (0.18 to 0.54)	N/A	0.33 (0.15 to 0.75)
Kidney	0.54 (0.29 to 1.01)	N/A	0.79 (0.37 to 1.69)
Liver	0.48 (0.19 to 1.18)	N/A	0.13 (0.04 to 0.39)
Lung	N/A	N/A	N/A
Heart	N/A	N/A	N/A
Interaction p-value	0.4172	N/A	0.0280
Credibility	N/A	N/A	Very Low

Note: CI = Confidence interval; OR = Odds ratio.

Timepoint 3 (July 1st, 2023)

Three doses vs no vaccination			
Organ Group	**COVID-19 Infection OR (95%CI)**	**Hospitalization from COVID-19 OR (95%CI)**	**Mortality from COVID-19 OR (95%CI)**
Mixed	N/A	N/A	0.13 (0.03 to 0.57)
Kidney	N/A	N/A	0.39 (0.25 to 0.60)
Liver	N/A	N/A	N/A
Lung	N/A	N/A	N/A
Heart	N/A	N/A	N/A
Interaction p-value	N/A	N/A	0.1672
Credibility	N/A	N/A	N/A
Two doses vs no vaccination			
Organ Group	**COVID-19 Infection OR (95%CI)**	**Hospitalization from COVID-19 OR (95%CI)**	**Mortality from COVID-19 OR (95%CI)**
Mixed	0.31 (0.18 to 0.54)	N/A	0.33 (0.15 to 0.75)
Kidney	0.54 (0.29 to 1.01)	N/A	0.79 (0.37 to 1.69)
Liver	0.48 (0.19 to 1.18)	N/A	0.13 (0.04 to 0.39)
Lung	N/A	N/A	N/A
Heart	N/A	N/A	N/A
Interaction p-value	0.4172	N/A	0.0280
Credibility	N/A	N/A	Very Low

Note: CI = Confidence interval; OR = Odds ratio.

Timepoint 4 (March 1st, 2024)

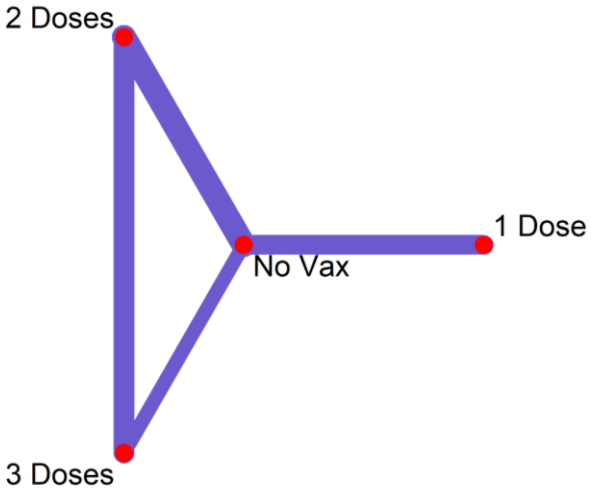
Three doses vs no vaccination			
Organ Group	**COVID-19 Infection OR (95%CI)**	**Hospitalization from COVID-19 OR (95%CI)**	**Mortality from COVID-19 OR (95%CI)**
Mixed	N/A	0.38 (0.15 to 0.97)	0.13 (0.03 to 0.57)
Kidney	N/A	0.47 (0.30 to 0.72)	0.30 (0.14 to 0.64)
Liver	N/A	N/A	N/A
Lung	N/A	0.25 (0.15 to 0.42)	0.44 (0.15 to 1.31)
Heart	N/A	N/A	N/A
Interaction p-value	N/A	0.1872	0.4376
Credibility	N/A	N/A	N/A
Two doses vs no vaccination			
Organ Group	**COVID-19 Infection OR (95%CI)**	**Hospitalization from COVID-19 OR (95%CI)**	**Mortality from COVID-19 OR (95%CI)**
Mixed	0.31 (0.18 to 0.54)	0.67 (0.32 to 1.40)	0.33 (0.15 to 0.75)
Kidney	0.70 (0.47 to 1.05)	0.55 (0.31 to 0.96)	0.49 (0.18 to 1.31)
Liver	0.48 (0.19 to 1.18)	0.31 (0.11 to 0.89)	0.26 (0.05 to 1.25)
Lung	N/A	0.81 (0.54 to 1.21)	1.64 (0.73 to 3.72)
Heart	N/A	N/A	N/A
Interaction p-value	0.0610	0.3225	0.0280
Credibility	Very Low	N/A	Very Low

Note: CI = Confidence interval; OR = Odds ratio.

Appendix 8. Network plots, league tables, and node-splitting plots.

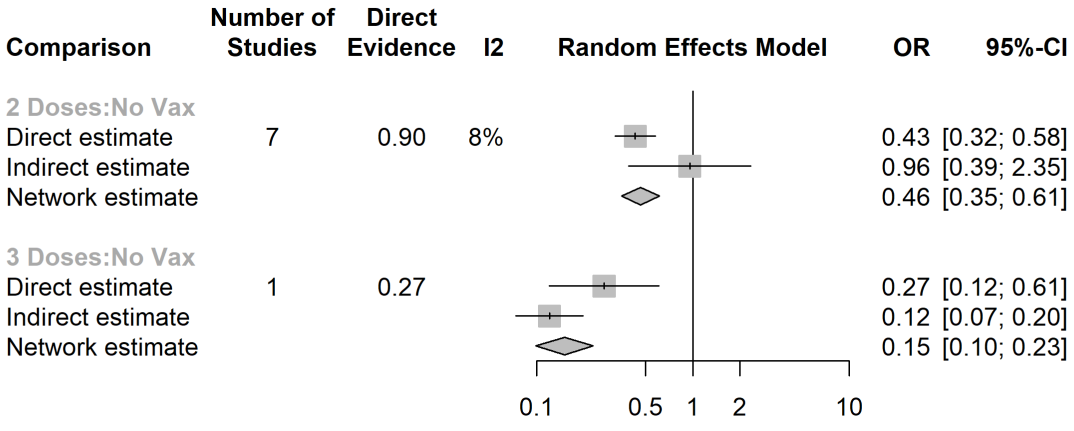
Timepoint 1 (October 1st, 2022)

Network evaluating the number of vaccines on COVID-19 infection

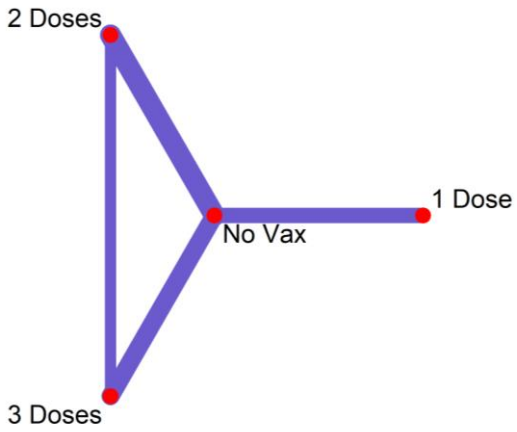


Four doses				
-	**Three doses**			
-	0.33 (0.23 to 0.47)	**Two doses**		
-	0.21 (0.11 to 0.38)	0.63 (0.37 to 1.08)	**One dose**	
-	0.15 (0.10 to 0.23)	0.46 (0.35 to 0.61)	0.73 (0.47 to 1.15)	**No vaccination**

Note: Values are reported in odds ratios.

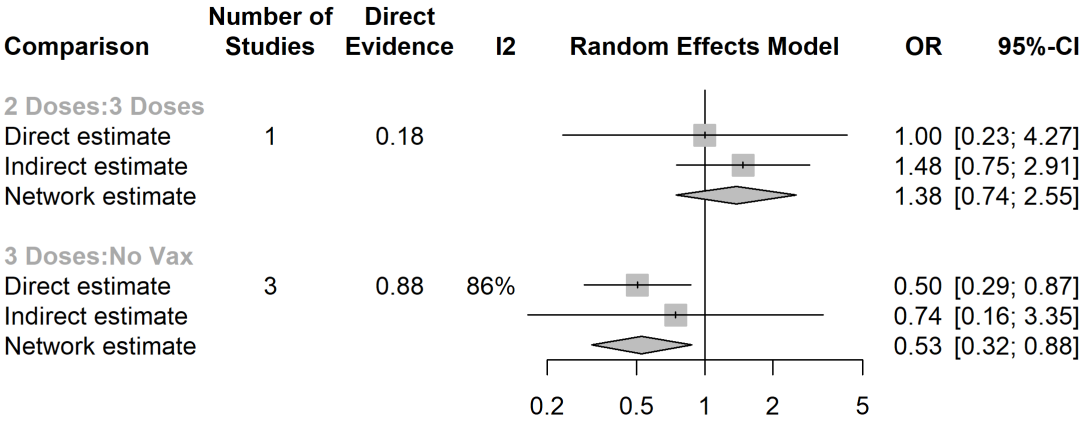


Network evaluating the number of vaccines on hospitalization from COVID-19

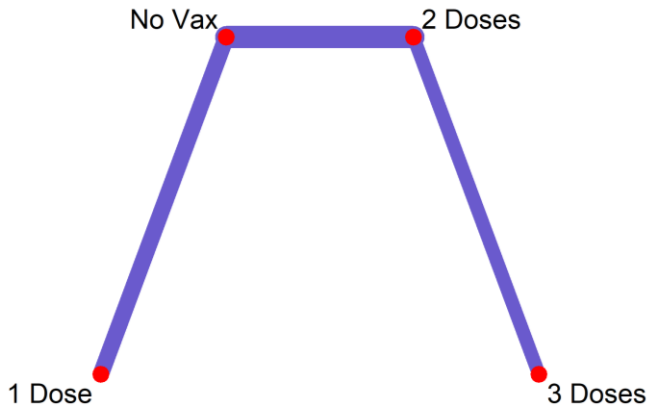


Four doses				
-	Three doses			
-	0.73 (0.39 to 1.34)	Two doses		
-	0.64 (0.26 to 1.60)	0.89 (0.38 to 2.07)	One dose	
-	0.53 (0.32 to 0.88)	0.72 (0.49 to 1.07)	0.82 (0.38 to 1.73)	No vaccination

Note: Values are reported in odds ratios.



Network evaluating the number of vaccines on mortality from COVID-19

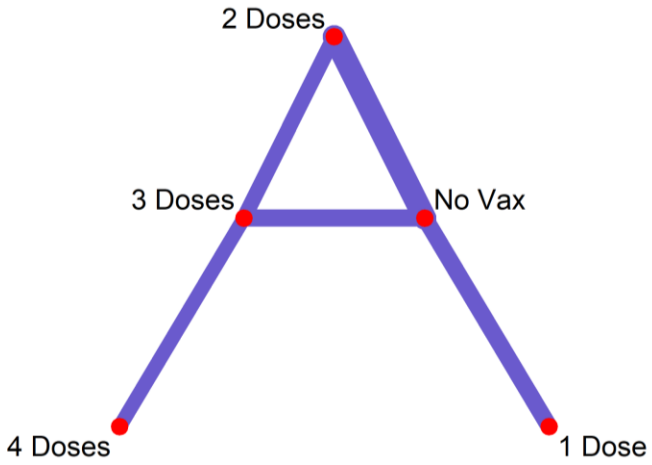


Four doses				
-	**Three doses**			
-	0.28 (0.08 to 0.76)	**Two doses**		
-	0.16 (0.04 to 0.71)	0.66 (0.26 to 1.72)	**One dose**	
-	0.15 (0.04 to 0.50)	0.61 (0.39 to 0.95)	0.92 (0.40 to 2.12)	**No vaccination**

Note: Values are reported in odds ratios.

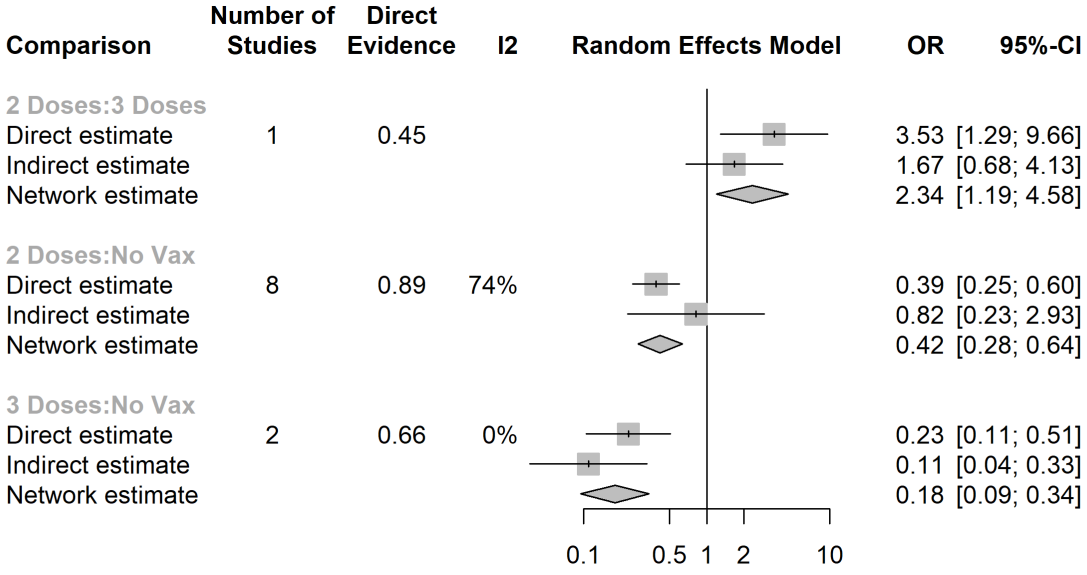
Timepoint 2 (March 1st, 2023)

Network evaluating the number of vaccines on COVID-19 infection

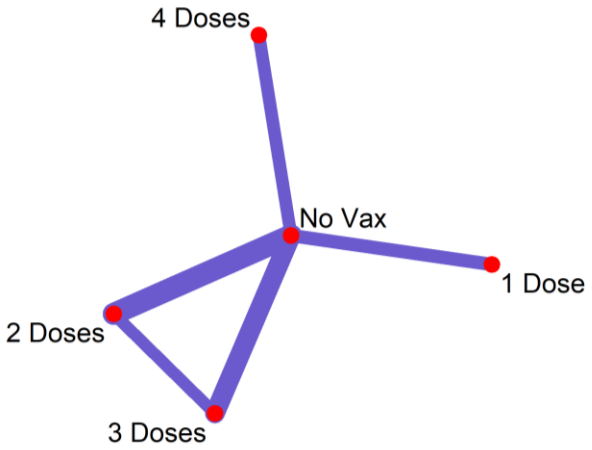


Four doses				
0.63 (0.21 to 1.88)	Three doses			
0.27 (0.07 to 0.97)	0.43 (0.22 to 0.84)	Two doses		
0.15 (0.03 to 0.67)	0.24 (0.08 to 0.67)	0.55 (0.22 to 1.38)	One dose	
0.11 (0.03 to 0.40)	0.18 (0.09 to 0.34)	0.42 (0.28 to 0.64)	0.76 (0.34 to 1.70)	No vaccination

Note: Values are reported in odds ratios.

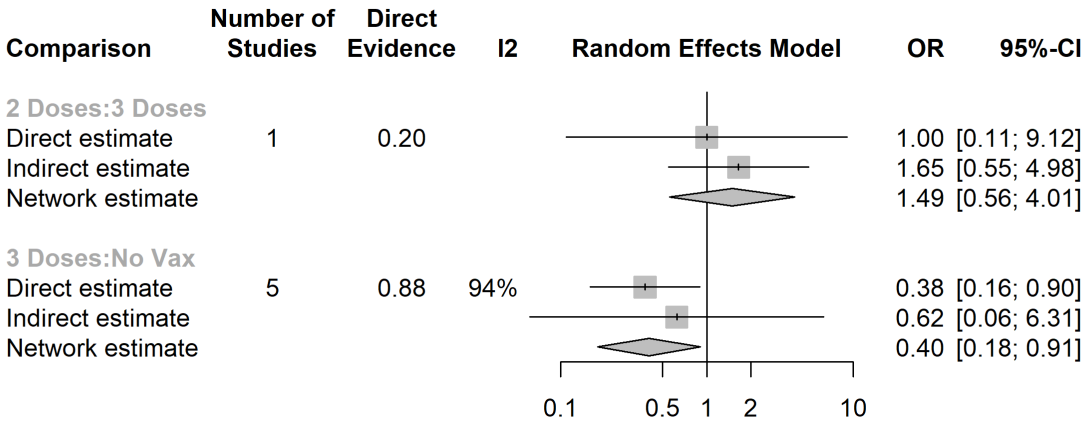


Network evaluating the number of vaccines on hospitalization from COVID-19

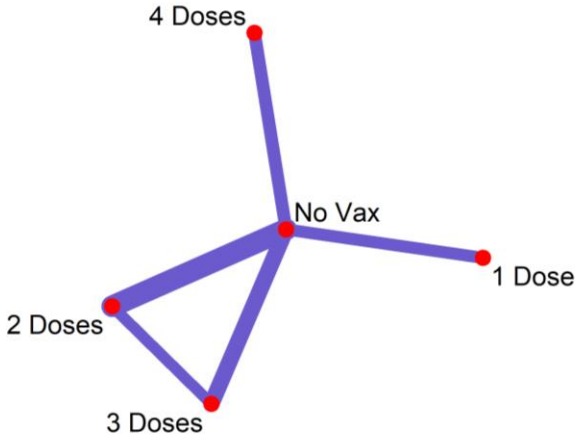


Four doses				
2.71 (0.31 to 24.00)	**Three doses**			
1.82 (0.22 to 15.27)	0.67 (0.25 to 1.80)	**Two doses**		
1.34 (0.09 to 20.46)	0.49 (0.07 to 3.65)	0.74 (0.11 to 5.14)	**One dose**	
1.09 (0.14 to 8.27)	0.40 (0.18 to 0.91)	0.60 (0.31 to 1.16)	0.82 (0.13 to 5.08)	**No vaccination**

Note: Values are reported in odds ratios.

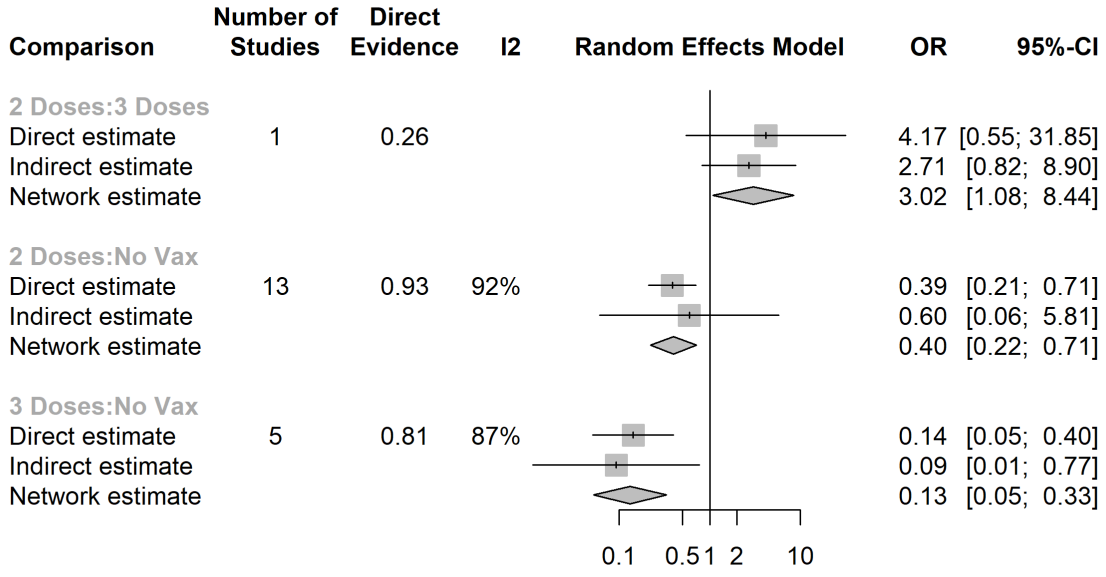


Network evaluating the number of vaccines on mortality from COVID-19



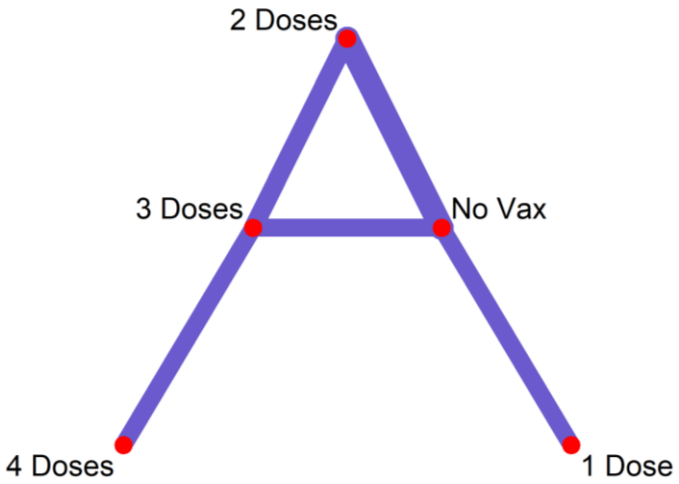
Four doses				
1.98 (0.30 to 13.15)	**Three doses**			
0.66 (0.11 to 3.78)	0.33 (0.12 to 0.92)	**Two doses**		
0.28 (0.02 to 3.47)	0.14 (0.02 to 1.16)	0.43 (0.06 to 3.09)	**One dose**	
0.26 (0.05 to 1.36)	0.13 (0.05 to 0.33)	0.40 (0.22 to 0.71)	0.92 (0.14 to 5.98)	**No vaccination**

Note: Values are reported in odds ratios.



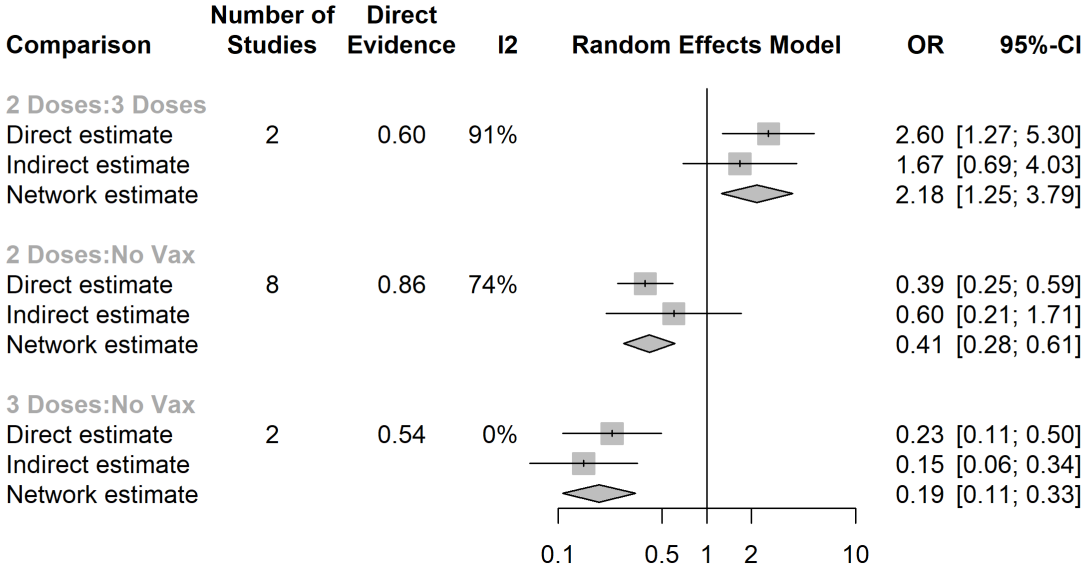
Timepoint 3 (July 1st, 2023)

Network evaluating the number of vaccines on COVID-19 infection

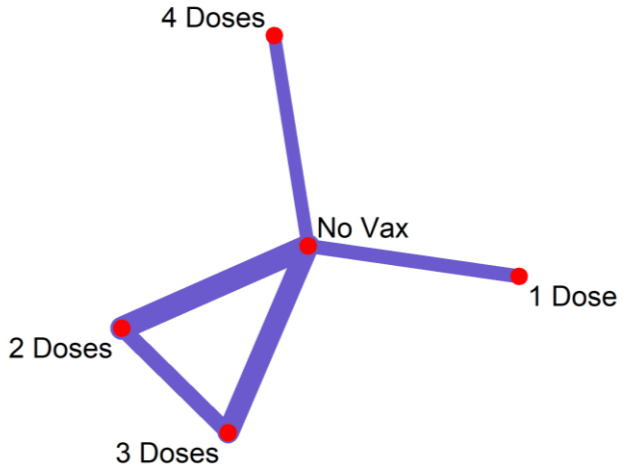


Four doses				
0.53 (0.24 to 1.17)	**Three doses**			
0.24 (0.09 to 0.64)	0.46 (0.26 to 0.80)	**Two doses**		
0.13 (0.04 to 0.46)	0.25 (0.09 to 0.66)	0.54 (0.22 to 1.32)	**One dose**	
0.10 (0.04 to 0.26)	0.19 (0.11 to 0.33)	0.41 (0.28 to 0.61)	0.75 (0.34 to 1.67)	**No vaccination**

Note: Values are reported in odds ratios.

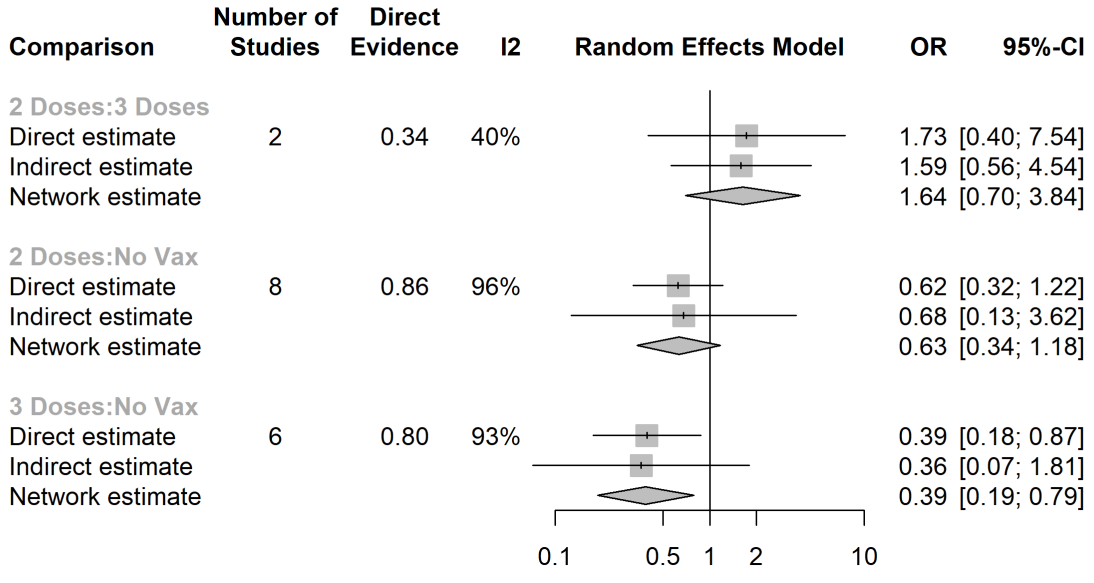


Network evaluating the number of vaccines on hospitalization from COVID-19

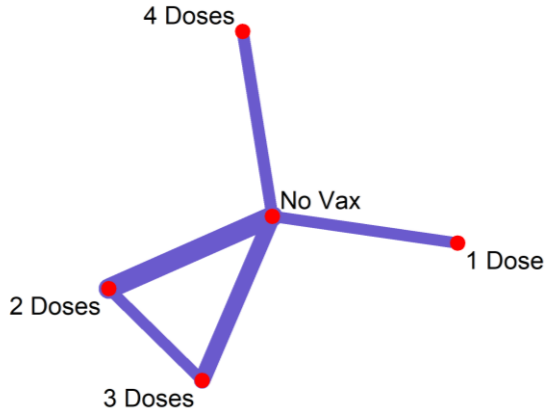


Four doses				
2.83 (0.34 to 23.42)	**Three doses**			
1.73 (0.22 to 13.85)	0.61 (0.26 to 1.43)	**Two doses**		
1.34 (0.09 to 19.30)	0.47 (0.07 to 3.23)	0.77 (0.12 to 5.12)	**One dose**	
1.09 (0.15 to 7.95)	0.39 (0.19 to 0.79)	0.63 (0.34 to 1.18)	0.82 (0.14 to 4.86)	**No vaccination**

Note: Values are reported in odds ratios.

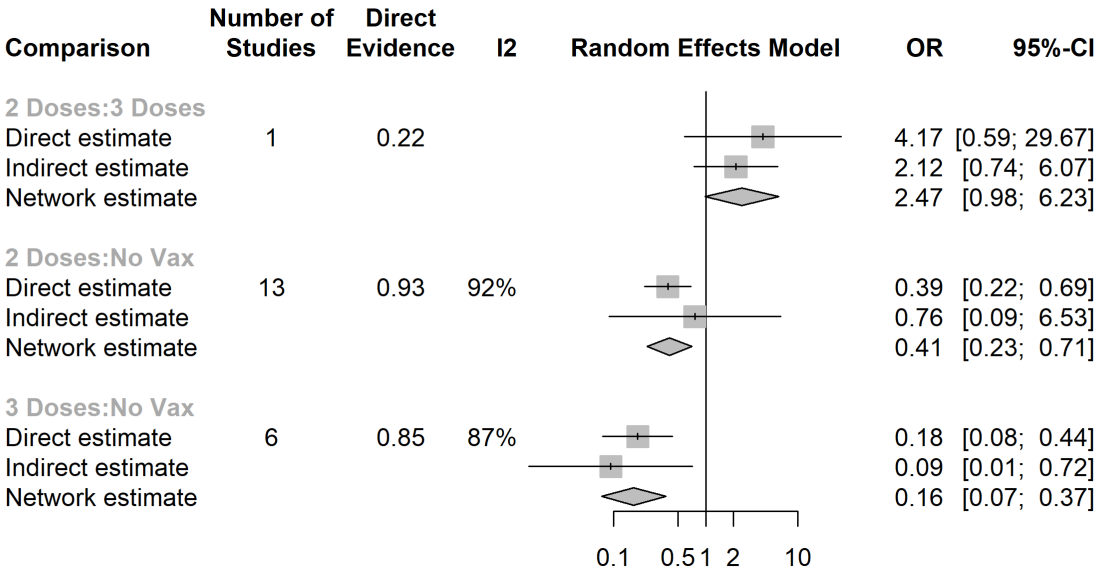


Network evaluating the number of vaccines on mortality from COVID-19



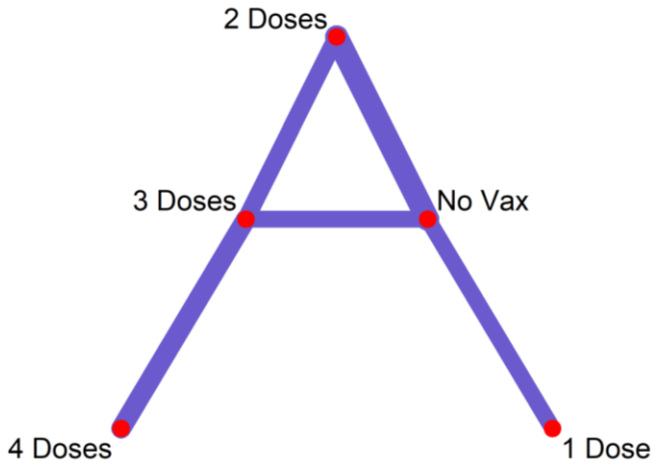
Four doses				
1.57 (0.26 to 9.40)	**Three doses**			
0.64 (0.12 to 3.47)	0.41 (0.16 to 1.02)	**Two doses**		
0.28 (0.03 to 3.13)	0.18 (0.03 to 1.29)	0.44 (0.07 to 2.92)	**One dose**	
0.26 (0.05 to 1.28)	0.16 (0.07 to 0.37)	0.41 (0.23 to 0.71)	0.92 (0.15 to 5.54)	**No vaccination**

Note: Values are reported in odds ratios.



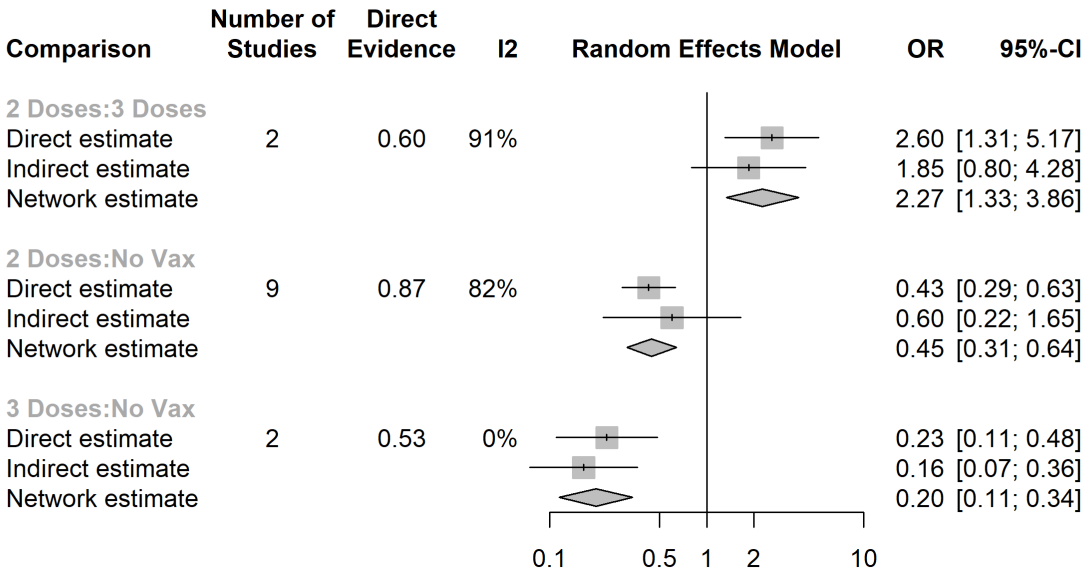
Timepoint 4 (March 1st, 2024)

Network evaluating the number of vaccines on COVID-19 infection

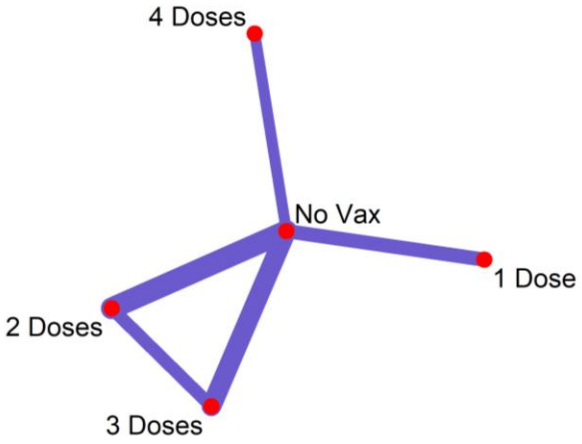


Four doses				
0.59 (0.34 to 1.00)	**Three doses**			
0.26 (0.12 to 0.55)	0.44 (0.26 to 0.75)	**Two doses**		
0.15 (0.05 to 0.45)	0.26 (0.10 to 0.67)	0.59 (0.25 to 1.38)	**One dose**	
0.12 (0.05 to 0.25)	0.20 (0.11 to 0.34)	0.45 (0.31 to 0.64)	0.75 (0.35 to 1.62)	**No vaccination**

Note: Values are reported in odds ratios.

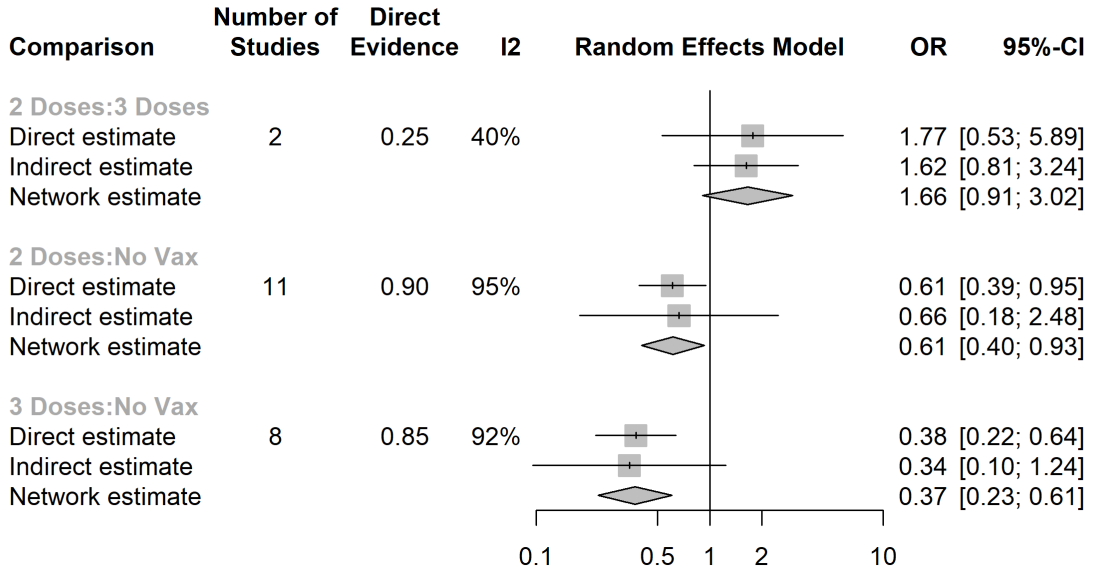


Network evaluating the number of vaccines on hospitalization from COVID-19

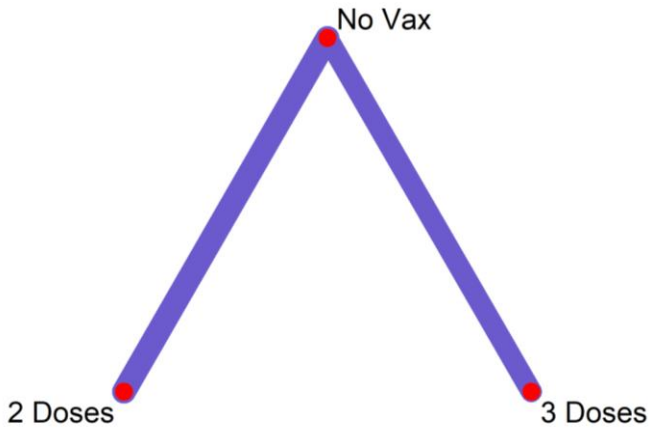


Four doses				
2.94 (0.56 to 15.51)	**Three doses**			
1.78 (0.34 to 9.17)	0.60 (0.33 to 1.10)	**Two doses**		
1.65 (0.26 to 10.67)	0.56 (0.19 to 1.68)	0.93 (0.32 to 2.70)	**One dose**	
1.09 (0.22 to 5.34)	0.37 (0.23 to 0.61)	0.61 (0.40 to 0.93)	0.66 (0.25 to 1.76)	**No vaccination**

Note: Values are reported in odds ratios.



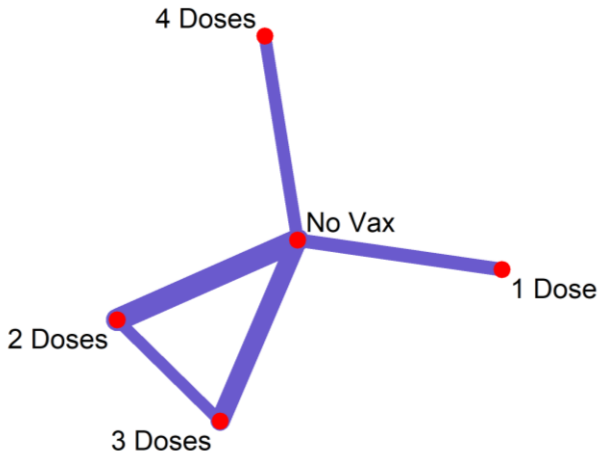
Network evaluating the number of vaccines on ICU admission from COVID-19



Four doses				
-	**Three doses**			
-	1.19 (0.49 to 2.88)	**Two doses**		
-	-	-	**One dose**	
-	0.71 (0.35 to 1.43)	0.60 (0.35 to 1.04)	-	**No vaccination**

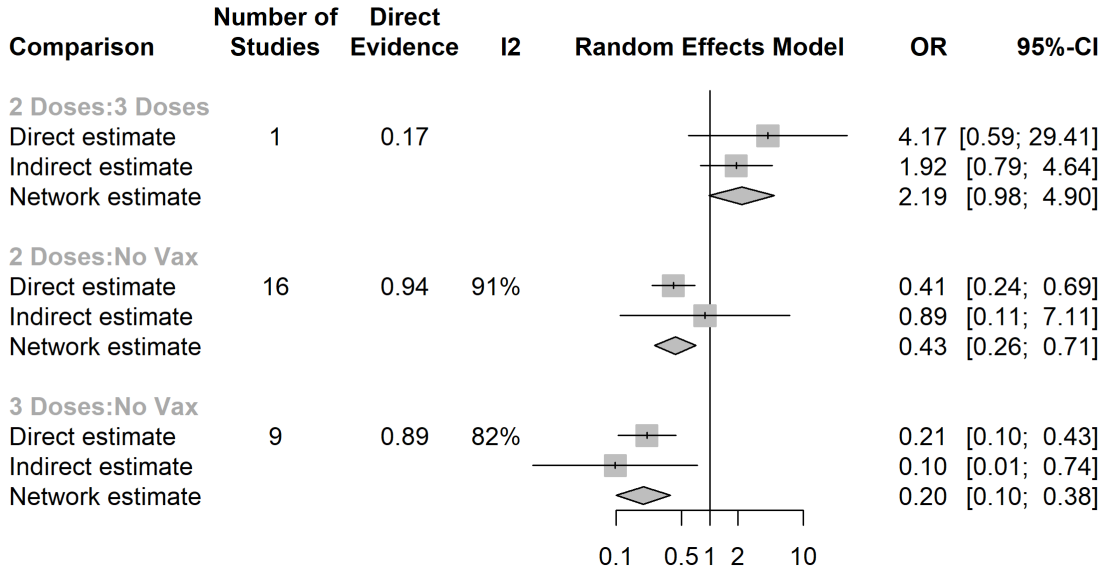
Note: Values are reported in odds ratios.

Network evaluating the number of vaccines on mortality from COVID-19



Four doses				
1.32 (0.23 to 7.42)	**Three doses**			
0.60 (0.11 to 3.21)	0.46 (0.20 to 1.02)	**Two doses**		
0.63 (0.08 to 5.21)	0.48 (0.10 to 2.24)	1.04 (0.24 to 4.60)	**One dose**	
0.26 (0.05 to 1.27)	0.20 (0.10 to 0.38)	0.43 (0.26 to 0.71)	0.41 (0.10 to 1.65)	**No vaccination**

Note: Values are reported in odds ratios.



Appendix 9. Intransitivity assessments.

Timepoint 1 (October 1st, 2022)

Pairwise Comparison	N Studies	N Patients	Median of Cohort Mean Ages (Years)	Median of Cohort Proportion Female (%)	Median of Cohort Mean Time from Transplant (Years)	Recruitment Period
3 Doses vs 2 Doses	3	13667	52.0	45%	8.5	Dec 2020 - May 2022
3 Doses vs No Vax	5	26284	52.8	40%	6.2	Dec 2020 - May 2022
2 Doses vs No Vax	13	35109	55.1	38%	7.2	Jan 2020 - May 2022
1 Dose vs No Vax	3	30195	59.0	37%	8.1	Mar 2020 - Nov 2021

Note: NR = Not reported.

Timepoint 2 (March 1st, 2023)

Pairwise Comparison	N Studies	N Patients	Median of Cohort Mean Ages (Years)	Median of Cohort Proportion Female (%)	Median of Cohort Mean Time from Transplant (Years)	Recruitment Period
4 Doses vs 3 Doses	1	447	61.5	70%	4.6	Dec 2021 - Mar 2022
4 Doses vs No Vax	2	13254	52.9	42%	NR	Dec 2020 - Jul 2022
3 Doses vs 2 Doses	3	13667	52.0	45%	8.5	Dec 2020 - May 2022
3 Doses vs No Vax	9	46647	51.8	42%	6.2	Dec 2020 - Jul 2022
2 Doses vs No Vax	21	58590	53.9	41%	6.2	Jan 2020 - Jul 2022
1 Dose vs No Vax	3	30195	59.0	37%	8.1	Mar 2020 - Nov 2021

Note: NR = Not reported.

Timepoint 3 (July 1st, 2023)

Pairwise Comparison	N Studies	N Patients	Median of Cohort Mean Ages (Years)	Median of Cohort Proportion Female (%)	Median of Cohort Mean Time from Transplant (Years)	Recruitment Period
4 Doses vs 3 Doses	2	715	61.5	48%	8.5	Dec 2021 - Nov 2022
4 Doses vs No Vax	2	13254	52.9	42%	NR	Dec 2020 - Jul 2022
3 Doses vs 2 Doses	3	13667	52.0	45%	8.5	Dec 2020 - Aug 2022
3 Doses vs No Vax	11	57735	51.8	41%	6.2	Jan 2015 - Sep 2022
2 Doses vs No Vax	21	58590	53.9	41%	6.2	Jan 2020 - Jul 2022
1 Dose vs No Vax	3	30195	59.0	37%	8.1	Mar 2020 - Nov 2021

Note: NR = Not reported.

Timepoint 4 (March 1st, 2024)

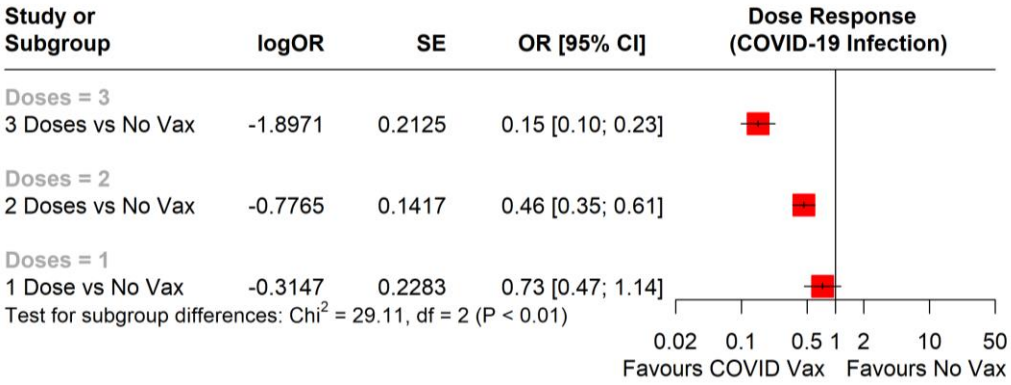
Pairwise Comparison	N Studies	N Patients	Median of Cohort Mean Ages (Years)	Median of Cohort Proportion Female (%)	Median of Cohort Mean Time from Transplant (Years)	Recruitment Period
4 Doses vs 3 Doses	4	7278	61.5	38%	7.4	Dec 2021 - Nov 2022
4 Doses vs No Vax	2	13254	52.9	42%	NR	Dec 2020 - Jul 2022
3 Doses vs 2 Doses	4	14289	52.8	49%	10.0	Dec 2020 - Aug 2022
3 Doses vs No Vax	14	58921	52.3	43%	6.2	Jan 2015 - Oct 2022
2 Doses vs No Vax	27	61660	54.5	42%	5.5	Jan 2020 - May 2023
1 Dose vs No Vax	5	31538	54.5	37%	6.4	Mar 2020 - May 2023

Note: NR = Not reported.

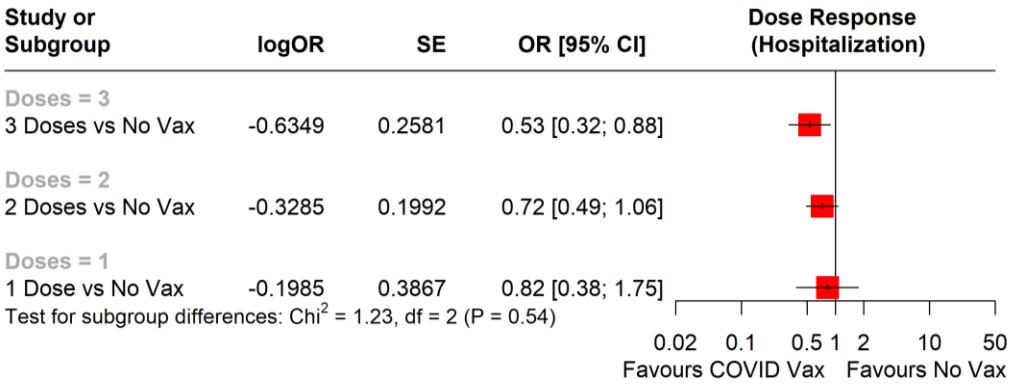
Appendix 10. Dose-response gradient assessments.

Timepoint 1 (October 1st, 2022)

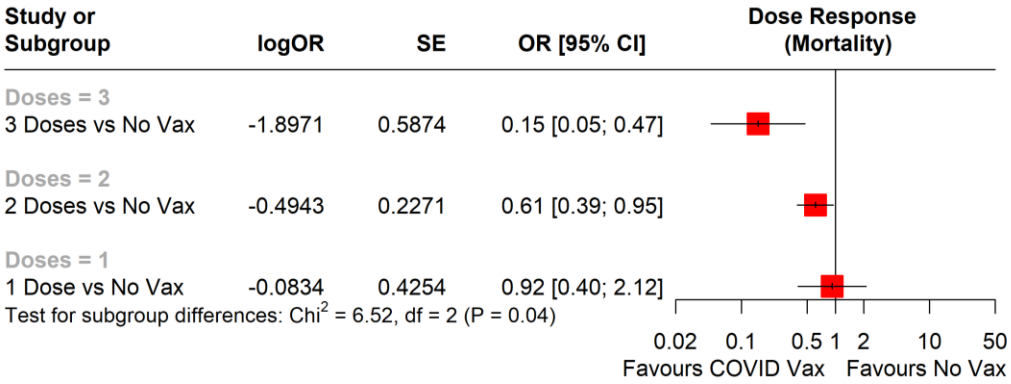
Potential dose-response gradient for number of vaccines and risk of COVID-19 infection ($p < 0.0001$)



Potential dose-response gradient for number of vaccines and risk of hospitalization from COVID-19 ($p = 0.5418$)

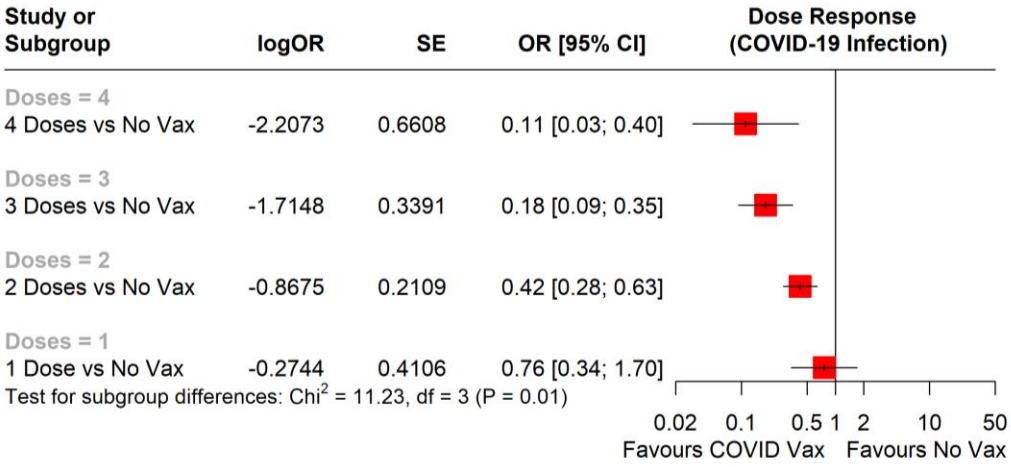


Potential dose-response gradient for number of vaccines and risk of mortality from COVID-19 (p = 0.0384)



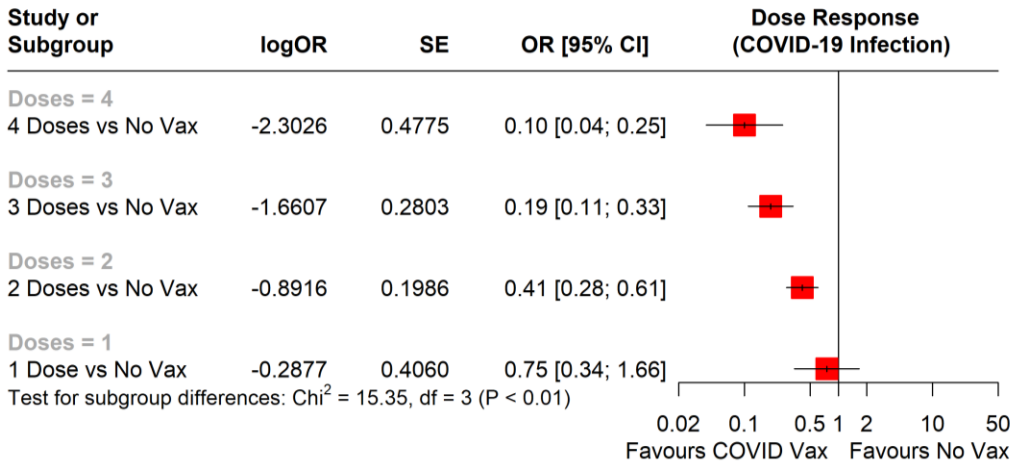
Timepoint 2 (March 1st, 2023)

Potential dose-response gradient for number of vaccines and risk of COVID-19 infection (p = 0.0106)



Timepoint 3 (July 1st, 2023)

Potential dose-response gradient for number of vaccines and risk of COVID-19 infection (p = 0.0015)



Timepoint 4 (March 1st, 2024)

Potential dose-response gradient for number of vaccines and risk of COVID-19 infection (p = 0.0010)