Table S1. PRISMA 2020 abstract checklist.

Section and Topic	Item #	Checklist item	Reported (Yes/No)
TITLE			
Title	1	Identify the report as a systematic review.	Lines 4-6
BACKGROUND			
Objectives	2	Provide an explicit statement of the main objective(s) or question(s) the review addresses.	Lines 4-6
METHODS			
Eligibility criteria	3	Specify the inclusion and exclusion criteria for the review.	Lines 8-10
Information sources	4	Specify the information sources (eg, databases, registers) used to identify studies and the date when each was last searched.	Lines 7-8
Risk of bias	5	Specify the methods used to assess risk of bias in the included studies.	Lines 11-13
Synthesis of results	6	Specify the methods used to present and synthesise results.	Lines 11-14
RESULTS			
Included studies	7	Give the total number of included studies and participants and summarize relevant characteristics of studies.	Lines 12-13
Synthesis of results	8	Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval. If comparing groups, indicate the direction of the effect (ie which group is favored).	Lines 13-18
DISCUSSION			
Limitations of evidence	9	Provide a brief summary of the limitations of the evidence included in the review (eg, study risk of bias, inconsistency and imprecision).	Lines 23-24
Interpretation	10	Provide a general interpretation of the results and important implications.	Lines 21-23
OTHER			
Funding	11	Specify the primary source of funding for the review.	Line 1
Registration	12	Provide the register name and registration number.	Line 7

Table S2. PRISMA 2020 checklist.

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Lines 48-49 and in Methods
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Supplemental Materials
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Introduction
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Introduction (Lines 48-51) and Methods section (Lines 75-81)
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Methods section (Lines 60-73)
Information sources	6	Specify all databases, registers, websites, organizations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Methods section (Lines 60-73)
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Supplemental Table S1
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Methods section (Lines 60-73)
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Methods section (Lines 83-92)
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (eg, for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Methods section (Lines 83-92 and Lines 60-73)
	10b	List and define all other variables for which data were sought (eg, participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Methods section (Lines 83-92 and Lines 60-73)
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Methods section (Lines 94-101)
Effect measures	12	Specify for each outcome the effect measure(s) (eg, risk ratio, mean difference) used in the synthesis or presentation of results.	Methods section (Lines 109-124)

Section and Topic	Item #	Checklist item	Location where item is reported
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (eg, tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Methods section (Lines 109-124)
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Methods section (Lines 109-124)
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Methods section (Lines 109-124)
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Methods section (Lines 109-124)
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (eg, subgroup analysis, meta-regression).	Methods section (Lines 109-124)
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Methods section (Lines 101-102)
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Methods section (Lines 101-102)
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Methods section (Lines 104-108)
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Figure S1 and Results section (Lines 129-134)
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Results section (Lines 129-134)
Study characteristics	17	Cite each included study and present its characteristics.	Table 1 and Results section (Lines 127-155)
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Table S2 and Table S3
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (eg, confidence/credible interval), ideally using structured tables or plots.	Lines 148-257
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Lines 266-270
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (eg, confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Lines 148-257
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Lines 148-160 and Figure S2

Section and Topic	Item #	Checklist item	Location where item is reported
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Lines 269-270 and Figure S5
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Lines 268-269 and Figure S4
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Lines 272-275 and Table S4
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Lines 278-411)
	23b	Discuss any limitations of the evidence included in the review.	Lines 395-404
	23c	Discuss any limitations of the review processes used.	Lines 395-404
	23d	Discuss implications of the results for practice, policy, and future research.	Lines 278-411)
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Results (Line 55)
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Results (Line 55)
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	N/A
Support	25	Describe sources of financial or nonfinancial support for the review, and the role of the funders or sponsors in the review.	Title page
Competing interests	26	Declare any competing interests of review authors.	Title page
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	N/A

Table S3. Search strategy of Medline, Embase, and CENTRAL designed by a librarian specialising in systematic searches of the literature (Risa Shorr, The Ottawa Hospital).

Embase Classic+Embase <1947 to 2021 December 02>
Ovid MEDLINE(R) ALL <1946 to December 02, 2021>
EBM Reviews - Cochrane Central Register of Controlled Trials <October 2021>

1 COVID-19 Vaccines/ 14142
2 ((2019 novel coronavirus or 2019 ncov or 2019-ncov or covid 19 or covid 19 virus or covid-19 or covid-19 virus or covid19 or covid19 virus or coronavirus disease 19 or coronavirus disease 2019 or coronavirus disease 2019 virus or coronavirus disease-19 or sars cov 2 or sars coronavirus 2 or sars-cov-2 or sars2) adj3 (vaccin* or immuni*)).tw,kf. 24095
3 ((mRNA or messenger RNA) adj3 vaccin*).tw,kf. 5025
4 (BNT162b2 or BNT 162b2).tw,kf. 2409
5 pfizer vaccin*.tw,kf. 213
6 moderna vaccin*.tw,kf. 246
7 astra zeneca vaccin*.tw,kf. 9
8 (AZD1222 or azd 1222).tw,kf. 450
9 johnson vaccin*.tw,kf. 51
10 (mRNA-1273 or mRNA1273).tw,kf. 936
11 or/1-10 30561
12 ((three or third) adj3 (dos* or injection* or vaccin*)).tw,kf. 121909
13 (3rd adj3 (dos* or injection* or vaccin*)).tw,kf. 2378
14 Immunization, Secondary/ 9675
15 (booster* or secondary immuni?sation*).tw,kf. 34864
16 or/12-15 161239
17 11 and 16 1424
18 exp Organ Transplantation/ 664929
19 exp Cell Transplantation/ 301673
20 transplant*.mp. 1904697
21 Bone Marrow Transplantation/ 101940
22 (bmt or hsct or pbsct or sct).tw,kf. 109498
23 or/18-22 1928923
24 17 and 23 131
25 24 use medall 63
26 exp SARS-CoV-2 vaccine/ 15226
27 ((2019 novel coronavirus or 2019 ncov or 2019-ncov or covid 19 or covid 19 virus or covid-19 or covid-19 virus or covid19 or covid19 virus or coronavirus disease 19 or coronavirus disease 2019 or coronavirus disease 2019 virus or coronavirus disease-19 or sars cov 2 or sars coronavirus 2 or sars-cov-2 or sars2) adj3 (vaccin* or immuni*)).tw. 23875
28 mRNA vaccin*.tw. 2782
29 (BNT162b2 or BNT 162b2).tw. 2356
30 pfizer vaccin*.tw. 198
31 moderna vaccin*.tw. 234

32 astra zeneca vaccin*.tw. 9
33 (AZD1222 or azd 1222).tw. 438
34 johnson vaccin*.tw. 50
35 (mRNA-1273 or mRNA1273).tw. 898
36 or/26-35 29865
37 ((three or third) adj3 (dos* or injection* or vaccin*)).tw. 121864
38 (3rd adj3 (dos* or injection* or vaccin*)).tw. 2375
39 Immunization, Secondary/ 9675
40 (booster* or secondary immuni?sation*).tw. 34617
41 or/37-40 160969
42 36 and 41 1364
43 exp Organ Transplantation/ 664929
44 exp Cell Transplantation/ 301673
45 transplant*.mp. 1904697
46 exp bone marrow transplantation/ 116983
47 (bmt or hsct or pbsct or sct).tw. 108201
48 or/43-47 1929184
49 42 and 48 122
50 49 use emczd 55
51 COVID-19 Vaccines/ 14142
52 ((2019 novel coronavirus or 2019 ncov or 2019-ncov or covid 19 or covid 19 virus or covid-19 or covid-19 virus or covid19 or covid19 virus or coronavirus disease 19 or coronavirus disease 2019 or coronavirus disease 2019 virus or coronavirus disease-19 or sars cov 2 or sars coronavirus 2 or sars-cov-2 or sars2) adj3 (vaccin* or immuni*)).tw,kw. 26876
53 mRNA vaccin*.tw,kw. 3047
54 (BNT162b2 or BNT 162b2).tw,kw. 2385
55 pfizer vaccin*.tw,kw. 209
56 moderna vaccin*.tw,kw. 246
57 astra zeneca vaccin*.tw,kw. 9
58 (AZD1222 or azd 1222).tw,kw. 450
59 johnson vaccin*.tw,kw. 50
60 (mRNA-1273 or mRNA1273).tw,kw. 924
61 or/51-60 32028
62 ((three or third) adj3 (dos* or injection* or vaccin*)).tw,kw. 121880
63 (3rd adj3 (dos* or injection* or vaccin*)).tw,kw. 2375
64 Immunization, Secondary/ 9675
65 (booster* or secondary immuni?sation*).tw,kw. 34778
66 or/62-65 161129
67 61 and 66 1420
68 exp Organ Transplantation/ 664929
69 exp Cell Transplantation/ 301673
70 transplant*.mp. 1904697
71 (bmt or hsct or pbsct or sct).tw,kw. 108895

72	"bone marrow Transplantation"/		101940
73	or/68-72	1928871	
74	67 and 73	122	
75	74 use cctr	9	
76	25 or 50 or 75	127	
77	remove duplicates from 76	84	

Table S4. Scoring distribution of quality assessment of studies according to the National Heart, Lung, and Blood Institute Quality Assessment Tool for Case Series Studies (https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools). Accessed October 14th, 2021. Y = Yes, N = No, NR = Not Reported. Full quality assessments (ie, answers to signaling questions) can be shared by contacting the corresponding author.

Study	Was the study question or objective clearly stated?	Was the study population clearly and fully described, including a case definition?	Were the cases consecutive?	Were the subjects comparable?	Was the intervention clearly described?	Were the outcome measures clearly defined, valid, reliable, and implemented consistently across all study participants?	Was the length of follow-up adequate?	Were the statistical methods well-described?	Were the results well-described?
Benotmane et al, 2021	Y	Y	Y	Y	Y	Y	Y	Y	Y
Masset et al, 2021	Y	Y	NR	Y	Y	Y	Y	Y	Y
Del Bello et al, 2021	Y	Y	NR	Y	Y	Y	Y	Y	Y
Kamar et al, 2021	Y	Y	Y	Y	Y	Y	Y	Y	Y
Westhoff et al, 2021	Y	Y	NR	Y	Y	Y	Y	Y	Y
Hall et al, 2021 and Kumar et al 2021 (intervention arms)	Y	Y	Y	Y	Y	Y	Y	Y	Y
Redjoul et al, 2021	Y	Y	NR	Y	Y	Y	Y	Y	Y
Bertrand et al, 2021	Y	Y	NR	Y	Y	Y	Y	Y	Y
Peled et al, 2021	Y	Y	NR	Y	Y	Y	Y	Y	Y

Chavarot et al, 2021	Y	Y	Y	Y	Y	Y	Y	Y	Y
Massa et al, 2021	Y	Y	Y	Y	Y	Y	Y	Y	Y

Table S5. Summary of the risk of bias assessments. N.B. The same rating was reached for all outcomes across studies. Green circles with a plus represent low risk of bias, yellow circles with a question mark represent some concerns for bias, and red circles with a minus represent high risk of bias. Full risk of bias assessments (ie, answers to signaling questions) can be shared by contacting the corresponding author.

Study	Risk of Bias Arising from the Randomization Process	Risk of Bias due to Deviations from the Intended Interventions (effect of assignment to intervention)	Risk of Bias due to Deviations from the Intended Interventions (effect of adhering to intervention)	Risk of Bias due to Missing Outcome Data	Risk of Bias in Measurement of the Outcome	Risk of Bias in Selection of the Reported Result	Overall Risk of Bias
Hall et al, 2021 and Kumar et al 2021	⊕	⊕	⊕	⊕	⊕	⊕	⊕

Table S6. GRADE assessment of outcomes. Please contact corresponding author for individual assessments.

Number of Studies (Study Design)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	Reasons to increase level of evidence	Quality	N	Prevalence/ Effect	Importance
Prevalence of humoral response after 3 doses										
7 Observational	No serious risk of bias	Not serious	Serious	Not serious	Unable to assess funnel plot asymmetry	None	Moderate	801	66.1% (62.8%-69.4%)	Critical
Prevalence of humoral response after 3 doses according to transplant type										
7 Observational	No serious risk of bias	Not serious	Serious	Serious	Unable to assess funnel plot asymmetry	None	Low	141 Kidney 96 Heart	Kidney 61.7% (53.7%-69.7%) vs Heart 66.7% (57.2%-76.1%) (P=0.56)	Critical
Prevalence of humoral response after 3 doses according to mRNA vaccine										
7 Observational	No serious risk of bias	Not serious	Serious	Serious	Unable to assess funnel plot asymmetry	None	Low	741 BNT162b2 60 mRNA-1273	BNT162b2 66.9% (63.5%-70.3%) vs mRNA-1273 55.0% (42.4%-67.6%) (P=0.07)	Critical
Prevalence of humoral response after humoral nonresponse to 2 doses										
9 Observational	No serious risk of bias	Not serious	Serious	Not serious	Not serious	None	Moderate	789	45.9% (42.3%-49.4%)	Critical
Prevalence of humoral response after humoral nonresponse to 2 doses according to transplant type										

9 Observational	No serious risk of bias	Not serious	Serious	Serious	Unable to assess funnel plot asymmetry	None	Low	253 Kidney 70 Heart 42 aHSCT	Kidney 43.2% (33.6%-52.9%) vs Heart 54.3% (42.6%-66.0%) vs aHSCT 47.6% (32.5%-62.7%) (P=0.48)	Critical
Risk ratio of humoral response in patients receiving mRNA-1273 vs placebo										
1 RCT	No serious risk of bias	Not serious	Not Serious	Serious	Unable to assess funnel plot asymmetry	Large Effect	High	60E 57C	RR 3.1 (1.7-5.8)	Critical
Prevalence of humoral response after humoral nonresponse to 2 doses according to mRNA vaccine										
9 Observational	No serious risk of bias	Not serious	Serious	Serious	Unable to assess funnel plot asymmetry	None	Low	567 BNT162b2 222 mRNA-1273	BNT162b2 44.3% (39.7%-49.0%) vs mRNA-1273 49.6% (43.0%-56.1%) (P=0.616)	Critical
Prevalence of humoral response after humoral nonresponse to 2 doses according to study threshold										
9 Observational	No serious risk of bias	Not serious	Serious	Serious	Unable to assess funnel plot asymmetry	None	Low	567 BNT162b2 222 mRNA-1273	BNT162b2 44.3% (39.7%-49.0%) vs mRNA-1273 49.6% (43.0%-56.1%) (P=0.616)	Critical
Prevalence of cellular response to 3 doses										

4 Observational	No serious risk of bias	Not serious	Serious	Serious	Unable to assess funnel plot asymmetry	None	Low	139	75.3% (66.6%-83.9%)	Critical
Prevalence of cellular response to 2 doses										
2 Observational	No serious risk of bias	Not serious	Serious	Serious	Unable to assess funnel plot asymmetry	None	Low	99	49.3% (39.5%-59.1%)	Critical
Prevalence of cellular response after cellular nonresponse to 2 doses										
3 Observational	No serious risk of bias	Not serious (explained)	Serious	Very Serious	Unable to assess funnel plot asymmetry	None	Very Low	50	57.8% (30.0%-85.6%)	Critical
Prevalence of neutralizing antibody response above threshold										
2 Observational	No serious risk of bias	Not serious	Serious	Not serious	Unable to assess funnel plot asymmetry	None	Low	156	60.9% (53.2%-68.6%)	Critical

*E=Experimental group. C=Control group.

Figure S1. PRISMA flow diagram for study selection process. Other sources of records included manual searches through reference lists of included articles or captured review articles.

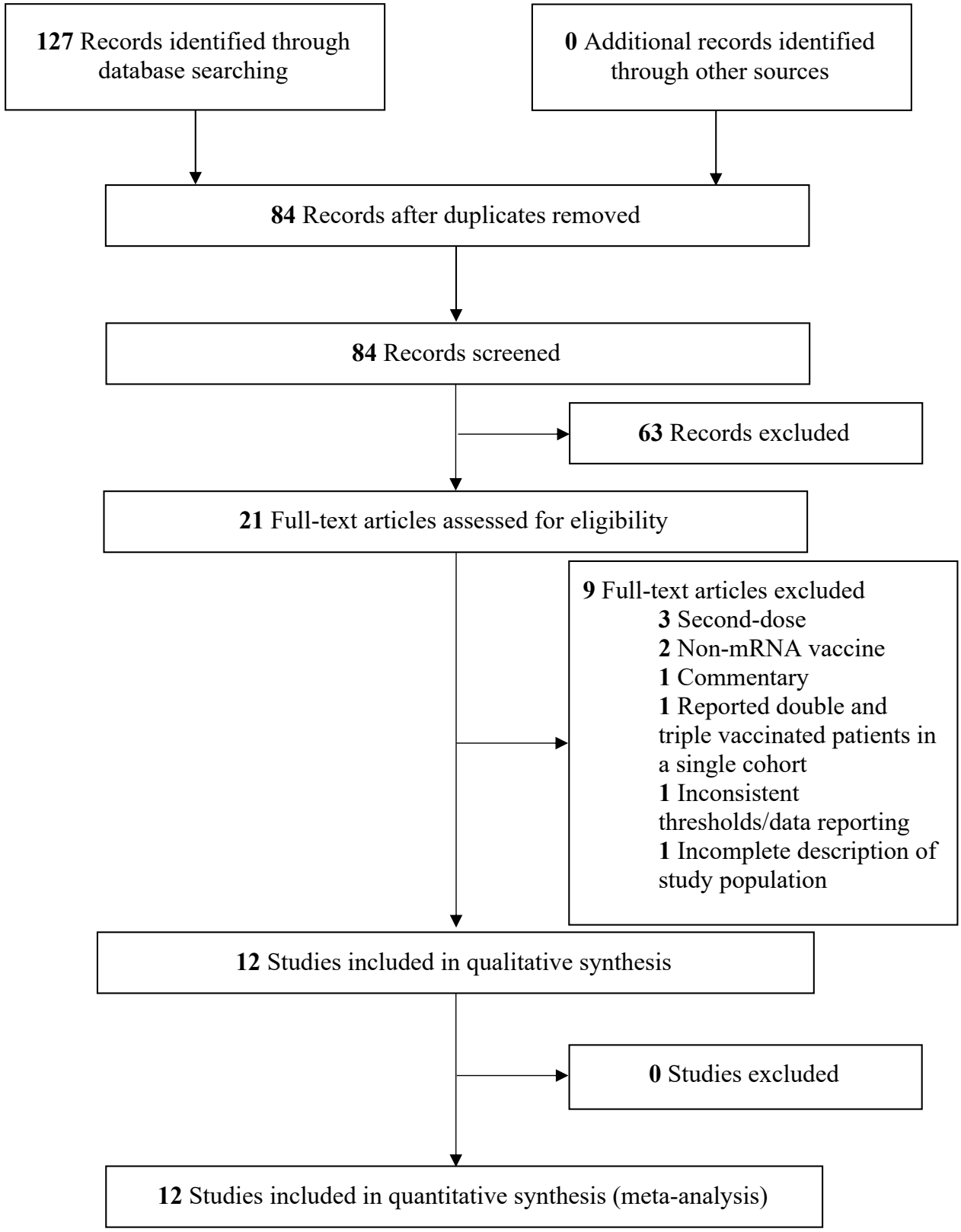


Figure S2. Prevalence of humoral response after 3 doses of any mRNA SARS-CoV-2 vaccine in transplant recipients, with outlier study included.

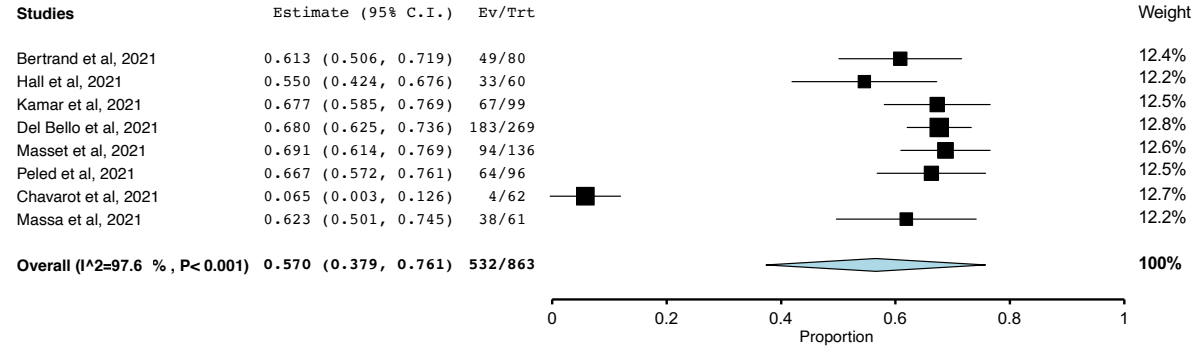
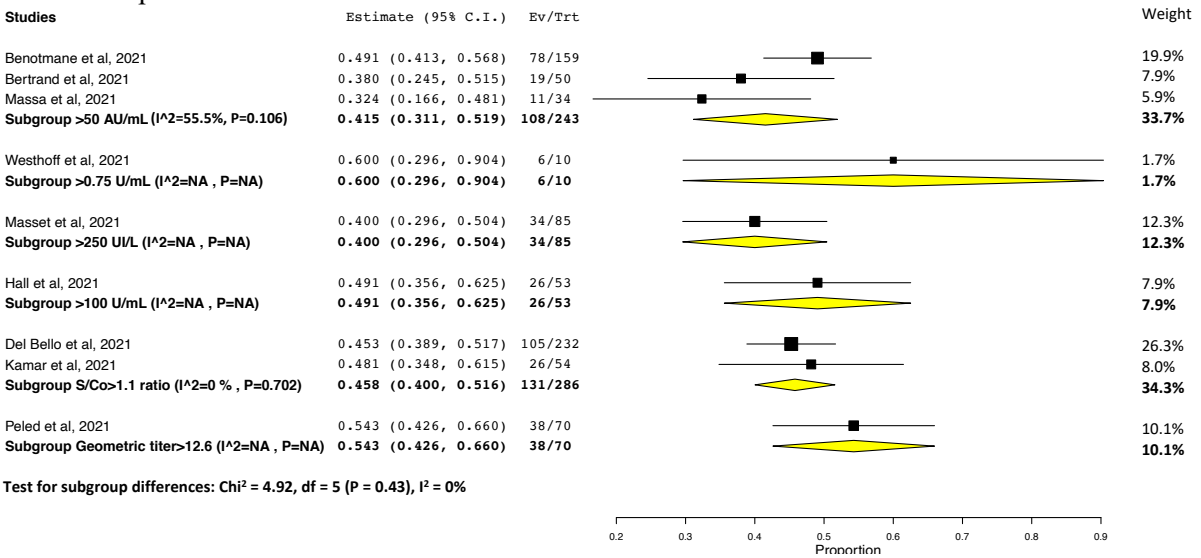


Figure S3. Prevalence of humoral response after 3 doses of any mRNA SARS-CoV-2 vaccine in transplant recipients (A, top panel), according to threshold for humoral response, and response after 3 doses of any mRNA SARS-CoV-2 vaccine in in transplant recipients that did not display a humoral response to 2 doses of an mRNA SARS-CoV-2 vaccine (B, bottom panel), according to threshold for humoral response.



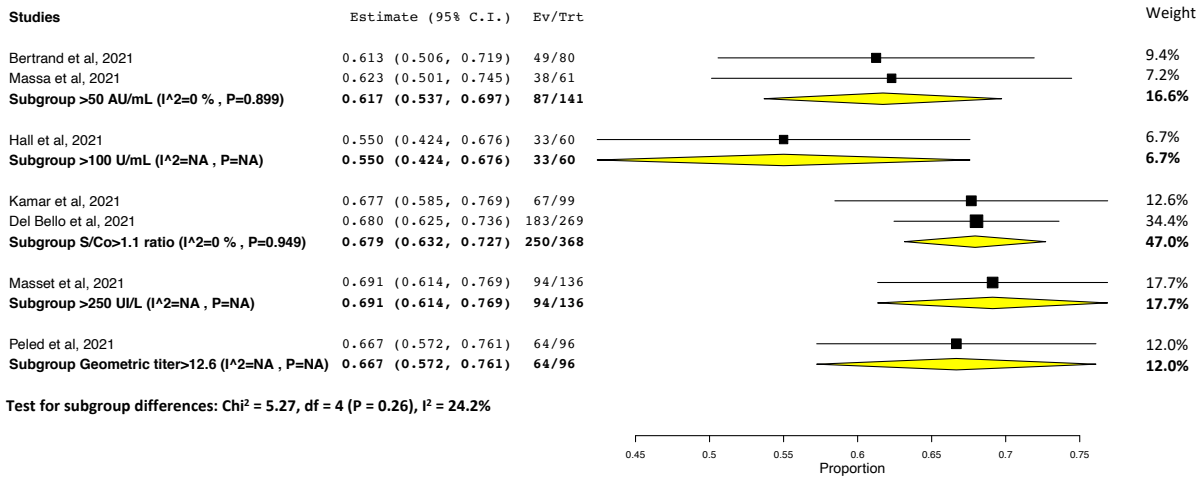


Figure S4. Prevalence of humoral response after three doses according to humoral correlates of protection for the wild type, alpha variant, and delta variant.

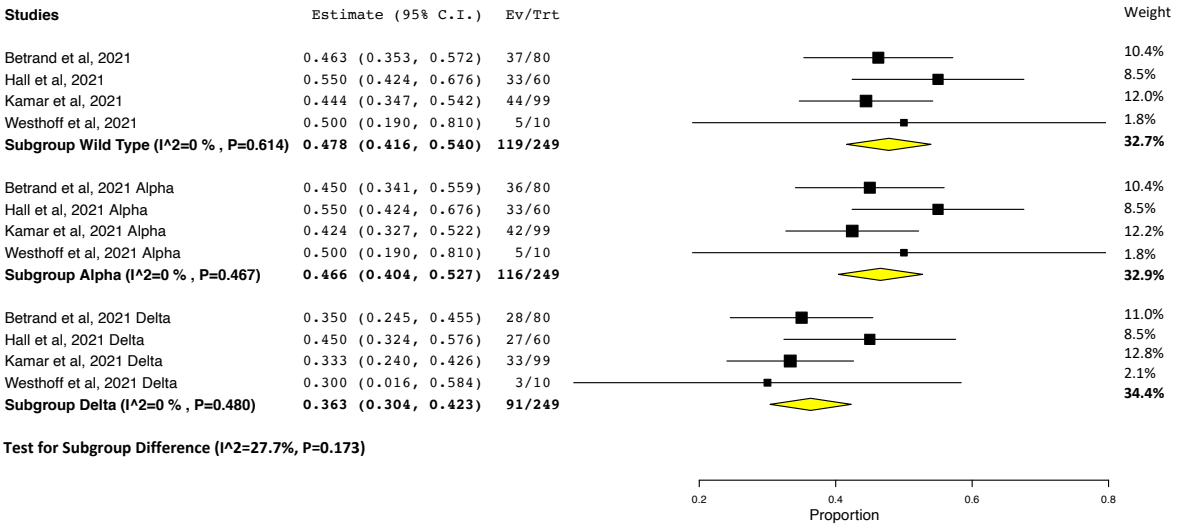


Figure S4. Funnel plot of the prevalence of humoral response after three doses of any mRNA SARS-CoV-2 vaccine in transplant recipients who did not display a humoral response to two doses.

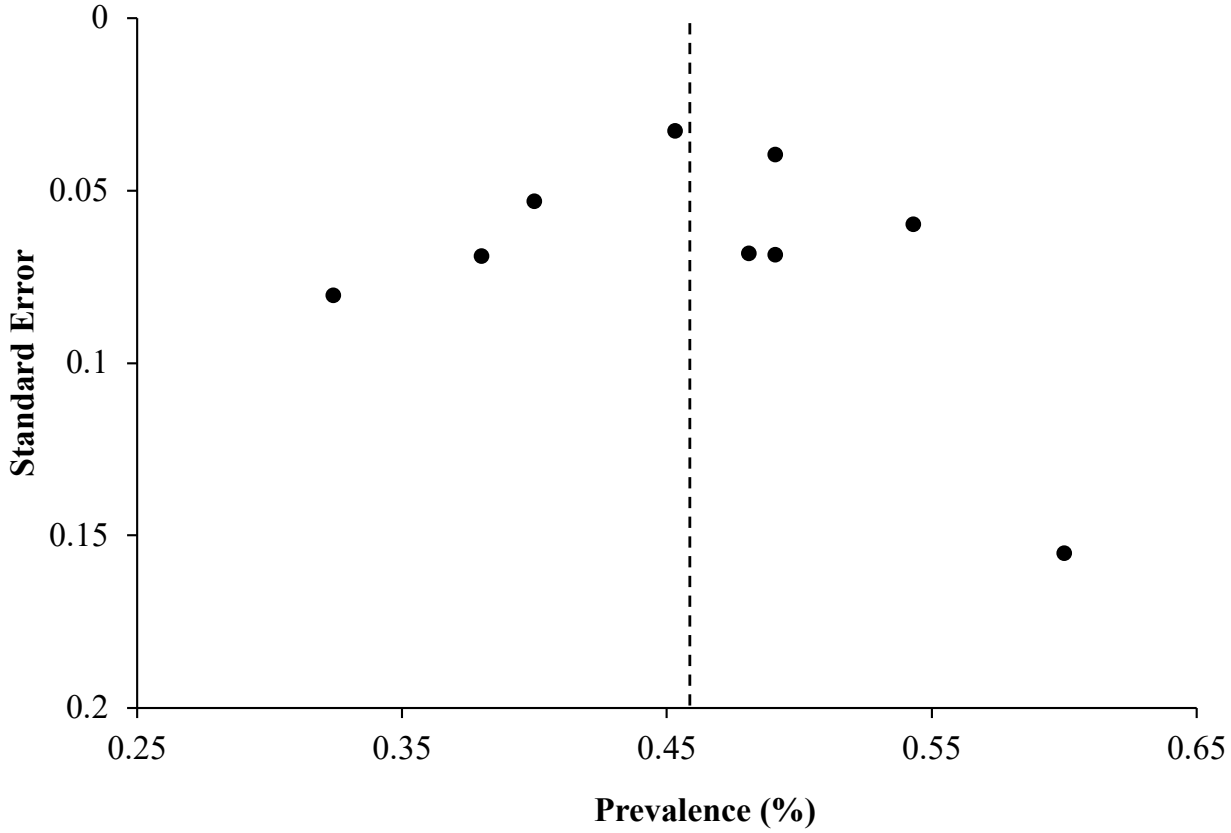


Figure S5. Forest plot demonstrating the prevalence of humoral response after 3 doses of any mRNA SARS-CoV-2 vaccine in transplant recipients, with the poor-quality study included.