The effects of third and fourth dose vaccination in immunocompromised people

Systematic review of research studies on immunogenicity, safety, and efficacy/effectiveness of third and fourth dose COVID-19 vaccines in immunocompromised individuals

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To help Canadian decision-makers as they respond to unprecedented challenges related to the COVID-19 pandemic, COVID-END in Canada is preparing rapid evidence responses like this one. The development and continued updating of this rapid synthesis has been funded by the Canadian Institutes of Health Research (CIHR) and the Public Health Agency of Canada. The opinions, results, and conclusions are those of the team that prepared the rapid synthesis, and independent of the Government of Canada, CIHR and the Public Health Agency of Canada. No endorsement by the Government of Canada, CIHR or Public Health Agency of Canada is intended or should be inferred

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General Disclaimer

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Abbreviations and Definitions

Abbreviations

- BNT162b2 (Pfizer-BioNTech)
- mRNA-1273 (Moderna)
- AZD1222 (ChAdOx1) (AstraZeneca-Oxford)
- Ad26.COV2.S (Janssen (Johnson & Johnson))
- N/A = not applicable
- N/R = not recorded
- RCT = randomized controlled trials
- Anti-S = antibody to Spike Protein
- Anti-RBD = antibody to Receptor Binding Domain of the Spike Protein
- IMM = immunocompromised
- IBD = inflammatory bowel disease
- RA = rheumatoid arthritis
- SLE = systemic lupus erythematosus
- MS = multiple sclerosis
- IMM = immunosuppressive therapy
- HM = hematological malignancy
- CLL = chronic lymphocytic leukemia
- CML = chronic myeloid leukemia
- NHL = non-Hodgkins lymphoma
- Allo-HCST = allogeneic hematopoietic stem cell transplant
- RR = relative risk
- 95% CI = 95% confidence interval

Key Definitions:

- Age in tables refers to median or mean age (whichever given in the paper)
- Days, weeks and months given in table refers to median or mean (whichever given in the paper)

EXECUTIVE SUMMARY

Objectives: Vaccination against COVID-19 may be less efficacious in immunocompromised and dialysis patients who may require booster vaccinations. We evaluated this in a systematic review of the efficacy, immunogenicity, and safety of 3rd and 4th dose vaccines in the immunocompromised and those on dialysis.

Design: This was a rapid systematic review and meta-analysis.

Methods: Two reviewers assessed studies for eligibility and performed data extraction independently. Proportions were calculated for case series and relative risk for comparative studies with 95% confidence intervals and synthesised using a random effects model.

Results: There is approximately a 20% reduction in vaccine efficacy in the immunocompromised compared to the healthy population although overall the vaccine offers 75% protection compared to the immunocompromised that are not vaccinated for the Delta variant. A third vaccine led to a 19% absolute increase in seroconversion with the least absolute increase seen in dialysis patients (9%) and the most in transplant patients (27%). A fourth vaccine resulted in 56% seroconverting who had previously been negative after three vaccinations. There are no safety concerns with COVID-19 vaccinations in the immunocompromised or in dialysis patients. A more detailed summary of the results is given in the table below.

Conclusions: Booster COVID-19 vaccination is modestly less efficacious in the immunocompromised and immunogenicity data would suggest transplant patients are particularly vulnerable. A fourth vaccination increases seroconversion.

Summary of the certainty of the evidence

Outcome	Studies included	Overall certainty of the evidence (GRADE)	Key findings
Risk of infection in the booster vaccinated immunocompromised compared to the healthy population	One case control study compared 26,683 people that tested SARS-CoV2 positive with 47,024 test negative controls.	⊕◯◯◯ Very low[1]	94% vaccine efficacy (VE) at preventing infections in the healthy for Delta. In the immunocompromised VE was 75%. For Omicron the figures were 68% for healthy and 22% for immunocompromised
Immunogenicity of a third vaccination	55 before after studies and three RCTs. Assessed improvement in seroconversion as well as proportion seroconverted in those that were negative after two doses	⊕⊕⊕◯ Moderate[2]	Overall, 5117 participants were recruited to studies with a 19% (95% CI = 14 to 24%) absolute increase in seroconversion rates. Seroconversion increase was 9% in dialysis patients and 27% in transplant patients
Immunogenicity of a fourth vaccination	Four before after studies evaluating transplant patients that had not seroconverted or had low titres after three doses of COVD-19 vaccine.	⊕◯◯◯ Very low[1]	Overall, 418 patients 56% (95% CI = 43 to 69%) seroconverted
Safety of vaccination in immunocompromised and dialysis patients	13 before after studies in over 23,000 patients	⊕⊕◯◯ Low[3]	Local pain 49% (37 to 61%), fatigue 30% (24 to 35%), myalgia 11% (5 to 19%) and fever 8% (3 to 19%)

[1]The GRADE approach gives the quality of evidence of observational studies as low and further downgraded because of imprecision.
[2]The GRADE approach gives the quality of evidence of RCTs as high but this was downgrade for imprecision. The observational studies added additional support for this quality assessment.
[3]The GRADE approach gives the quality of evidence of observational studies as low. No further reason to downgrade or upgrade the evidence.

Research Question

What is the effectiveness, immunogenicity, and safety of third and fourth dose COVID-19 vaccines in immunocompromised persons and patients on dialysis?

Rationale

COVID-END finds and uses the best available evidence available to support decision-making about COVID-19 pandemic response. To this end, this report summarizes the current evidence regarding the effects of vaccinations in immunocompromised individuals. Specifically, this rapid review synthesizes the body of evidence on the immunogenicity, safety, and efficacy/effectiveness of COVID-19 vaccines in immunocompromised persons to inform decisions regarding booster vaccinations.

PICOST Framework

	Inclusion Criteria	Exclusion Criteria
Population	Immunocompromised individuals, as defined by persons with HIV infection, primary immune or complement deficiency, malignancy, transplant, or on immunosuppressive therapy. Also, individuals on dialysis (including hemodialysis and peritoneal dialysis) are included.	
Intervention	Third and fourth dose COVID-19 vaccines which Canada has currently authorized for use: BNT162b2 (Pfizer-BioNTech); mRNA-1273 (Moderna); AZD1222 (ChAdOx1) (AstraZeneca-Oxford) and Ad26.COV2.S (Johnson & Johnson). Doses of the same eligible vaccine throughout or different vaccines types are permitted	Vaccines not approved in Canada
Comparisons	Healthy controls or disease controls (for immunosuppression e.g. inflammatory bowel disease – outcome of vaccines in	

	those with and without immunosuppressive therapy)	
Outcomes	1. Immunogenicity: • Humoral immune responses (e.g. binding antibodies, neutralizing antibodies); 2. Safety: • Overall adverse events • Individual events of interest 3. Effectiveness: • confirmed SARS-CoV-2 infection (PCR or serologic); • asymptomatic infection, symptomatic COVID-19 disease; • hospitalizations due to COVID-19; ICU admissions due to COVID-19; • deaths due to COVID-19	
Setting	Population through to tertiary care	
Study designs	Interventional trials, cohort, case-control, or before after studies. Case series with at least 100 participants for efficacy and safety and 10 participants for immunogenicity	Case reports Case series with <100 participants for efficacy and safety and <10 participants for immunogenicity

Methods

Search

A daily scan of the literature (published and preprint) is conducted by the Emerging Science Group at the Public Health Agency of Canada (PHAC). The scan has compiled COVID-19 literature since the beginning of the outbreak and is updated daily. Searches to retrieve relevant COVID-19 literature are conducted in Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv,

SSRN, Research Square and cross-referenced with the COVID-19 information centers run by Lancet, BMJ, Elsevier, Nature and Wiley using key terms: COVID-19, SARS-CoV-2, SARS-Coronavirus-2, nCov, "novel CoV", (novel AND coronavirus). Daily alerts from Epistemonikos' L·OVE and McMaster PLUS are also scanned. For this report, the search is up to date as of January 17th, 2022. The Evidence Xtraction Team for Research Analysis (EXTRA) team at PHAC performed a first level screening of titles and abstracts in DistillerSR by a single reviewer using a combination of manual review and DistillerAI's natural language processing technology. A second reviewer screened full text results of potentially relevant articles to identify articles on COVID-19 vaccines in immunocompromised persons or persons on dialysis. We reviewed any items tagged as being on autoimmune populations or other chronic conditions, as well as searching all fields for the following terms:

immunocompromised OR immunosuppressed OR immunosuppression OR immunosuppressive OR immunosuppressives OR autoimmune OR cancer OR cancers OR solid tumor OR solid tumors OR solid tumour OR solid tumours OR chemotherapy OR malignancies OR leukemia OR HIV OR rheumatic OR rheumatoid arthritis OR multiple sclerosis OR dialysis OR hemodialysis OR hemodialysis OR transplant OR transplants OR biologic OR biologics OR anti-interleukins OR anti-interleukin OR corticosteroids OR kinase inhibitors OR kinase inhibitor OR calcineurin inhibitors OR calcineurin inhibitor OR mTOR inhibitor OR mTOR inhibitors OR IMDH inhibitors OR IMDH inhibitor OR monoclonal antibodies OR immunotherapy OR immunotherapies OR immunodeficiency* OR immune deficienc* OR anti-CD38 OR anti-CD20 OR calcineurin inhibitor OR calcineurin inhibitors OR disease-modifying OR DMT OR DMTs OR cytotoxic.

Reviewing these tagged items generated 173 relevant titles (1-173). In addition, we included eight references (174-181) that were identified from a previous COVID-END review on booster vaccination. Two references (182, 183) included in the previous review were excluded and replaced with more current data from the updated search.

Study Selection Criteria

English-language, peer-reviewed sources and sources published ahead-of-print before peer review were included. The types of studies that were eligible to be considered in this rapid review included Interventional trials, cohort, case-control, or before after studies. Case series were also included provided they included at least 100 participants for efficacy and safety and at least 10 for immunogenicity

After a pilot test, two reviewers independently screened titles as potentially eligible and all studies that at least one reviewer considered eligible was formally assessed. This was again be done by two independent reviewers according to eligibility criteria and any disagreements were resolved by the senior lead.

Data Extraction

Data relevant to the research question, such as study design, setting, location, population characteristics, interventions or exposure and outcomes were extracted when reported.

Data were extracted by one reviewer and the second reviewer verified key elements related to the outcomes of interest after pilot testing. Data that were extracted included, setting, countries, population (type of immunocompromised patients), intervention (stratified by vaccine platform (e.g. mRNA, viral vector or mixture of eligible vaccines), vaccine product, dose, interval between dose 2 and 3 of a 3-dose series (manufacture-recommended interval vs extended interval), interval between dose 4 and 4 of a 4-dose series.

Data Synthesis

We synthesized data calculating relative risk (for comparative studies) and synthesizing with a random effects model. Case series data were presented as rates and again were synthesized with a random effects model.

Appraisal of Evidence Quality

We evaluated the quality of included evidence using critical appraisal tools as indicated by the study design below. Quality assessment was completed by one reviewer and verified by a second reviewer. Conflicts were resolved through consensus.

The Grading of Recommendations, Assessment, Development and Evaluations (GRADE) (184) approach was used to assess the certainty in the findings based on eight key domains.

In the GRADE approach to quality of evidence, observational studies, as included in this review, provide low quality evidence, and this assessment can be further reduced based on other domains:

- High risk of bias
- Inconsistency in effects
- Indirectness of interventions/outcomes
- Imprecision in effect estimate
- Publication bias

and can be upgraded based on:

- Large effect
- Dose-response relationship
- Accounting for confounding.

The overall certainty in the evidence for each outcome was determined taking into account the characteristics of the available evidence (observational studies, some not peer-reviewed, unaccounted-for potential confounding factors, different tests and testing protocols, lack of valid comparison groups). A judgement of ‘overall certainty is very low’ means that the findings are very likely to change as more evidence accumulates.

Risk of Bias Assessment

The tools used for assessing risk of bias were the Cochrane Risk of Bias (ROB 2) for randomized controlled trials and the Cochrane ROBINS-I tool for observational studies.

Completed quality assessments for each included study are available on request.

Results

There were 173 titles screened (1-173). In addition, we included eight references (174-181) that were identified from a previous COVID-END review on booster vaccination. Two references (182, 183) included in the previous review were excluded and replaced with more current data from the updated search. Overall, 74 titles were eligible to be included in the review. A list of excluded and included studies are given in Tables 1 and 2 and the flow diagram and reasons for exclusion given in Figure 1.

Table 1. Ineligible studies

Reference	Author	Final excluded reason
1	Hall 2021	Duplicate of previous searches #310.
2	Schrezenmeier 2021	Duplicate of 36 (fully published)
3	Gounant 2021	Duplicate of 46 (fully published)
4	Karaba 2021	Duplicate of 87 (fully published)
5	Peluso 2021	Insufficient size
10	Flaxman 2021	Inappropriate population- not immunocompromised
13	Stumpf 2021	Duplicate of previous searches #370.
14	Lyski 2021	Insufficient size
15	Bonelli 2021	Duplicate of 111 (full published)
16	Cohen 2021	Duplicate: Pre-publication of 3#2 Cochen 2021
19	Kant 2021	Insufficient size
20	Westhoff 2021	Insufficient size
21	Caillard 2021	Duplicate replaced by full publication 104.
22	Pfizer WHO document	No relevant data -Meeting document, no raw data for immunocompromised patients
28	Saiag 2021	Inappropriate population- not immunocompromised
37	Romero-Ibarguengoitia 2021	Inappropriate population, health care workers
41	Felten 2021	Insufficient size
42	Naranbhai 2021	Insufficient size
44	Straus 2021	Inappropriate population, 151 million Vaccine Recipients Worldwide

48	Mor 2021	Inappropriate population, Israeli Ministry of Health's open COVID 19 database
49	Demonbreun 2021	Inappropriate population, healthy adults
52	Ireland 2021	Inappropriate population: 750 immunocompetent adults aged ≥50 years
57	Kant 2021	Inappropriate study design -Only pts had Anti – neutrophil cytoplasmic antibody – associated vasculitis
62	Nejad 2021	Systematic review: meta-analysis of 81 articles-Seroconversion following the first, second, and third dose vaccines in immunocompromised population
63	Armistead 2021	Inappropriate study design. Mucosal memory T cells in breastmilk
66	Wilhelm 2021	Inappropriate study design. in vitro study
69	Gruell 2021	Inappropriate population
70	Planas 2021	Inappropriate study design.
71	Liu 2021	Inappropriate study design.
72	Piñana 2021	No relevant data -No relevant outcome: hematological immunocompromised patients with prior COVID-19
73	Jordan 2022	Insufficient size
74	Garcia-Beltran 2021	Inappropriate population
76	Mielke 2022	Inappropriate population- data not reported for subgroup of immunocompromised patients
78	Haslak 2022	No relevant data- No booster (only one had three doses)
80	Faustini 2022	Duplicate, fully published in #106.
83	Yetmar 2021	No relevant data -no booster (only 4 received V4), only included who had covid after V2
84	Akyol 2021	Systematic review
86	Lamy 2021	Insufficient size
89	Ottaviani 2021	Inappropriate population- not immunocompromised patients, 10 patients
90	Zeng 2021	No relevant data -No baseline data on V2
92	Fendler 2021	Duplicate of 79
94	Zeng 2021	Duplicate of 90
95	Faustini 2022	Duplicate of 80
103	Gong 2022	Systematic review for hematologic malignancy

109	Hadjadj 2022	Insufficient size
110	Galmiche 2021	Systematic review for immunocompromised populations
113	Brunner 2022	Insufficient size
114	Zhang 2022	Non-eligible vaccine
115	Hall 2021	Duplicate of #1 and previous #310
116	Schrezenmeier 2021	Duplicate of #2 and #36, preprint of 36, fully published as #36.
117	Gounant 2021	Duplicate of #3 and #46 (preprint of 46)
118	Karaba 2021	Duplicate (preprint) of #87
119	Peluso 2021	Duplicate of #5 (case report)
120	Noble 2021	Duplicate of #6.
121	Alejo 2021	Duplicate of #7.
122	Chavarot 2021	Duplicate of #8
123	Charmetant 2021	Duplicate of #9.
124	Masset 2021	Duplicate of #11.
125	Redjoul 2021	Duplicate of #12.
126	Stumpf 2021	Duplicate of #13 and previous #370.
127	Lyski 2021	Duplicate of #14, case report
128	Bonelli 2021	Duplicate of #15 and preprint of 111.
129	Cohen 2021	Duplicate of #16 and preprint of #32
130	Connolly 2021	Duplicate of #17.
131	Bensouna 2021	Duplicate of #18.
132	Kant 2021	Duplicate of #19. case reports
133	Westhoff 2021	Duplicate of #20. 10 patients
134	Caillard 2021	Duplicate of #21, preprint of fully published in 104.
135	Peled 2021	Duplicate of #23
136	David 2021	Duplicate of #24.
137	Shroff 2021	Duplicate of #25.
138	Hause 2021	Duplicate of #26.
139	Bertrand 2021	Duplicate of #27.
140	Marlet 2021	Duplicate of #29.
141	Greenberger 2021	Duplicate of #30.
142	Robert 2021	Duplicate of #31.
143	Cohen 2021	Duplicate of #16, #32, #129, preprint of #32.
144	Konig 2021	Duplicate of #33.
145	Le Bourgeois 2021	Duplicate of #34.
146	Ben-Dov 2021	Duplicate of #35.

147	Schrezenmeier 2021	Duplicate of #2, #36 and #116, preprint of 36, fully published as #36.
148	Schmiedeberg 2021	Duplicate of #38
149	Tillmann 2021	Duplicate of #39
150	Kozak 2021	Duplicate of #40
151	Felten 2021	Duplicate of #41. Only 10 patients
152	Naranbhai 2021	Duplicate of #42 and preprint of #101
153	Massa 2021	Duplicate of #43
154	Chen 2021	Duplicate of #45
155	Gounant 2021	Duplicate of #3, # 46 and #117 (preprint of #46)
156	Sidler 2021	Duplicate of #47.
157	Kumar 2021	Duplicate of #50.
158	Rottenberg 2021	Duplicate of #51.
159	Simon 2021	Duplicate of #53.
160	Maillard 2021	Duplicate of #54.
161	Kamar 2021	Duplicate of #55.
162	Benotmane 2021	Duplicate of #56.
163	Kant 2021	Duplicate of #57.
164	Shapiro 2021	Duplicate of #58.
165	Bagacean 2021	Duplicate of #59.
166	Espi 2021	Duplicate of #60.
167	Herishanu 2021	Duplicate of #61.
168	Reimann 2021	Duplicate of #64.
169	Li 2021	Duplicate of #65.
170	Lim 2021	Duplicate of #67.
171	Konishi 2021	Duplicate of #68.
172	Henriquez 2021	Duplicate- Full publication of previous #338 (preprint)
173	Jordan 2022	Duplicate of #73, excluded 7 patients

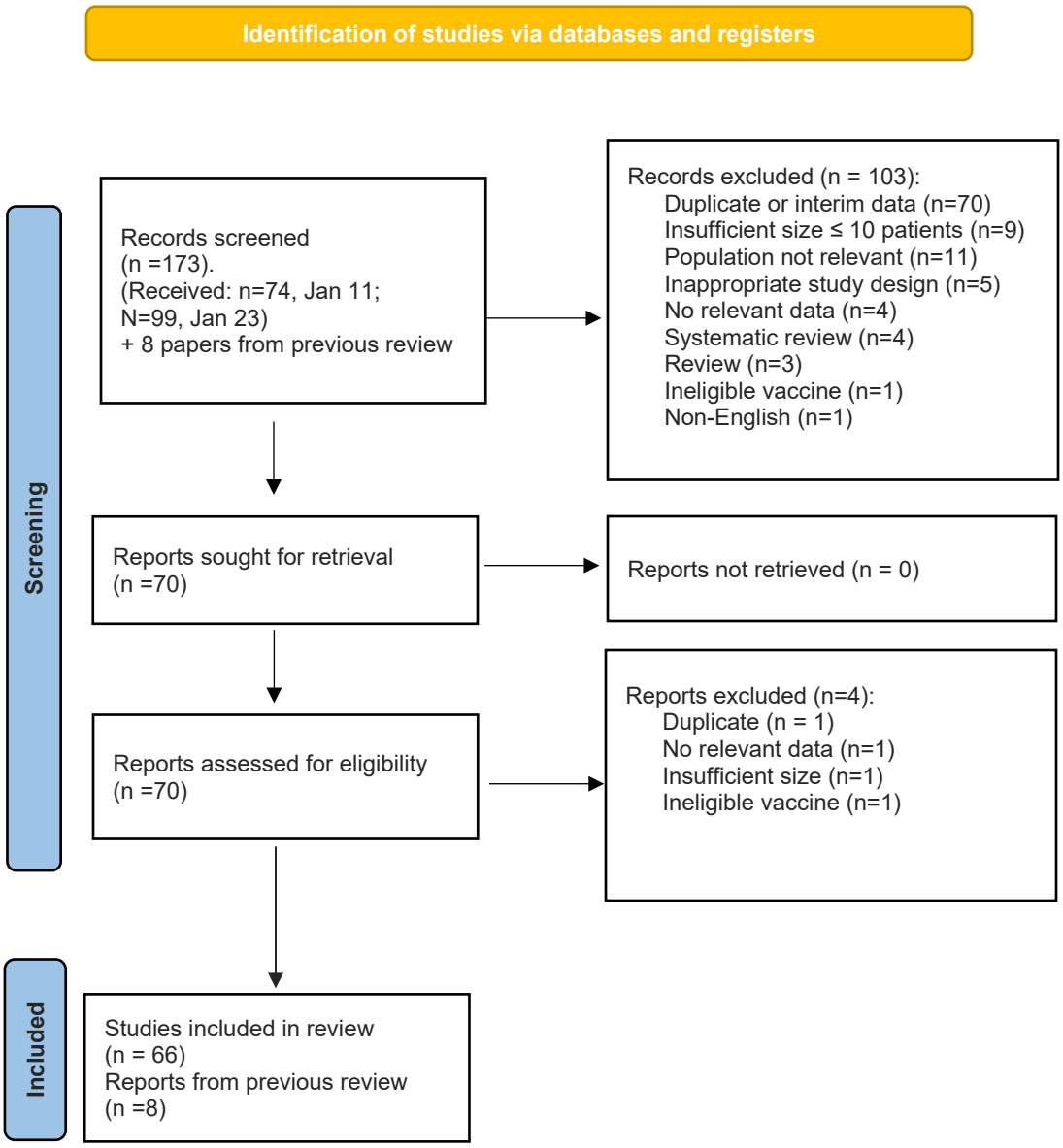
Supplementary Table 2. Eligible studies

number	Author year	Immunogenicity
6	Noble 2021	Immunogenicity
7	Alejo 2021	Immunogenicity
8	Chavarot 2021	Immunogenicity and Efficacy
9	Charmetant 2021	Immunogenicity

11	Masset 2021	Immunogenicity
12	Redjoul 2021	Immunogenicity
17	Connolly 2021	Immunogenicity
18	Bensouna 2021	Immunogenicity and efficacy and safety
23	Peled 2021	Efficacy and safety
24	David 2021	Safety
25	Shroff 2021	Immunogenicity and safety
26	Hause 2021	Safety
27	Bertrand 2021	Immunogenicity and efficacy and safety
29	Marlet 2021	Immunogenicity
30	Greenberger 2021	Immunogenicity
31	Robert 2021	Immunogenicity
32	Cohen 2021	Safety
33	Konig 2021	Immunogenicity and safety
34	Le Bourgeois 2021	Immunogenicity
35	Ben-Dov 2021	Immunogenicity
36	Schrezenmeier 2021	Immunogenicity and Efficacy
38	Schmiedeberg 2021	Immunogenicity and safety
39	Tillmann 2021	Immunogenicity
40	Kozak 2021	Immunogenicity
43	Massa 2021	Immunogenicity and safety
45	Chen 2021	Immunogenicity
46	Gounant 2021	Immunogenicity and efficacy and safety
47	Sidler 2021	Immunogenicity
50	Kumar 2021	Immunogenicity and efficacy and safety
51	Rottenberg 2021	Immunogenicity
53	Simon 2021	Immunogenicity and safety
54	Maillard 2022	Immunogenicity and Efficacy
55	Kamar 2021	Immunogenicity and safety
56	Benotmane 2021	Immunogenicity
58	Shapiro 2022	Immunogenicity
59	Bagacean 2021	Immunogenicity
60	Espi 2021	Immunogenicity and safety
61	Herishanu 2021	Immunogenicity and safety
64	Reimann 2021	Immunogenicity and safety
65	Li 2021	Safety
67	Lim 2021	Immunogenicity
68	Konishi 2022	Immunogenicity and Efficacy
75	Saharia 2022	Immunogenicity

77	Hsu 2022	Immunogenicity
79	Fendler 2021	Immunogenicity
81	Reindl-Schwaighofer 2021	Immunogenicity
82	Madelon 2021	Immunogenicity
85	Ligumsky 2021	Immunogenicity and safety
87	Karaba 2021	Immunogenicity
88	Jyssum 2021	Immunogenicity
91	Schell 2021	Immunogenicity
93	Achtnichts 2021	Immunogenicity
96	Yang 2022	Immunogenicity
97	Jurdi 2022	Immunogenicity
98	Tseng 2022	Immunogenicity
99	Fenioux 2022	Immunogenicity
100	Schrezenmeier 2022	Immunogenicity
101	Naranbhai 2021	Immunogenicity
102	Kamar 2022	Immunogenicity
104	Caillard 2022	Immunogenicity
105	Bertrand 2022	Immunogenicity
106	Faustini 2022	Immunogenicity
107	Speer 2022	Immunogenicity
108	Corradini 2022	Immunogenicity
111	Bonelli 2021	Immunogenicity
112	Tomowiak 2022	Immunogenicity

Figure 1: Flow Diagram of Study Selection



Efficacy of third dose of COVID-19 vaccination in preventing SARS-CoV2 infection in the immunocompromised

There was one case control study (98) that compared 26,683 people that tested SARS-CoV2 positive compared with 47,024 test negative controls. The study was conducted in South California, USA, from tests done on 20th of December 2021 onwards. Overall, 57% of the sample were vaccinated with either one (11,899 cases, 33,107 controls), two (23,512 cases, 73,161 controls) or three doses (14,238 cases, 66,566 controls) of mRNA-1273 vaccine. Those that received the vaccine < 14 days from the diagnosis of infection were excluded. The study was primarily in the general population but data for the 1,106 people that were immunocompromised was provided. There was no data on individual immunocompromising conditions. Data were provided for Omicron and Delta infections separately and results are given in Table 3.

Table 3. Summary of the case control study evaluating SARS-CoV2 vaccination in the general population and in the immunocompromised.

Infection type	VE dose 1	VE dose 2	VE dose 3
All Delta Infections Hospitalizations	 56% (39-68%) 76% (0-98%)	 80% (67-87%) 98.5% (92-99.7%)	 94% (92-95%) 99.6% (96-100%)
Immunocompromised Delta Infections Hospitalizations			**75% (38-90%)**
All Omicron Infections Hospitalizations	 20% (9-30%) N/A	 43% (34-51%) 75% (2-94%)	 68% (65-70%) 99.7% (82-100%)
Immunocompromised Omicron Infections Hospitalizations			**22% (0-45%)**

VE = vaccine effectiveness

N/A = not applicable

Immunogenicity of third dose of COVID-19 vaccination in the immunocompromised and dialysis patients

Studies addressing the immune response in the immunocompromised and dialysis patients are summarized in Table 4 below. There were three RCTs (1, 81, 111) that evaluated the immunogenicity of a third dose vaccine. One Canadian well conducted RCT by Hall et al. (1) involving 117 transplant patients was included with before after studies as results were similar. The RCT (1) was low risk of bias and increased the GRADE assessment of the quality of the evidence. One German RCT (81) compared a third mRNA to vector vaccine. Both vaccines had similar immunogenicity so again this study was included with before after studies. The design of these studies can be categorized as those that report on the increasing number of patients that seroconvert after a third dose of vaccine and those that select patients that were seronegative after the second vaccine and what proportion seroconvert with the third dose. These categories will be considered in turn.

Table 4. Summary of immunogenicity of third dose SARS-CoV2 vaccination studies

Author	Design	Country	Population description	Vaccine	Titre measured	Duration between 2nd and 3rd vaccine	Time after 3rd vaccine titre measured
Hall (1)	RCT	Canada	Solid organ transplant recipients that had received two mRNA-1273 vaccinations randomized to receive third dose of mRNA-1273 or placebo	mRNA-1273	anti-RBD Ig (Roche, Elecsys)	2 months	4 weeks (± 1 week)
Noble (6)	Before after	France	Kidney Transplant Recipients Receiving Belatacept or tacrolimus, SARS-CoV-2 mRNA vaccination was performed at day 21 post–infusion	BNT162b2 or mRNA-1273	Anti-S1 Ig (Wantai Biological Pharmacy Enterprise Co, Beijing, China	unclear	1 month
Alejo (7)	Before after	US	Solid Organ Transplant Recipients, four doses of mRNA, enrolled in observational study SOTRs. No history of covid (kidney liver, pancreas, heart)	BNT162b2 or mRNA-1273 or Ad26.COV2.S	Euroimmun IgG anti-S1	unclear	unclear

Chavarot (8)	Before after	France	181 KTRs treated with belatacept in center received ≥2 COVID- 19 BNT162b2 vaccines (in total, 12/181 developed symptomatic covid in median 18 (8-30) days)	BNT162b2	Anti-S IgG	40 days (IQR 36 to 69)	28 days (IQR 28 to 33)
Charmeta nt (9)	Before after	France	kidney transplant recipients received V3, 5 of 93 had covid-19 history, 66 received V3	BNT162b2	Anti-RBD IgG (Snibe Diagnostic, Shenzen, China)	Mean 50 days	Median 28 (IQR 28 to 33)
Masset (11)	Before after	France	kidney transplant recipients, no previous covid infection	BNT162b2	Elecsys Anti-S IgG (Roche Diagnostic s)	Mean 50 days	Median 30 (IQR 28 to 32)
Redjoul (12)	Before after	France	allogeneic hematopoietic stem-cell transplantation (HSCT) who were given three doses based on less than 4160 AU/mL at 28 (SD 6) days after V2	BNT162b2	Anti-RBD IgG Quant II (Abbott, Architect, Sligo Ireland)	Mean 51 days (SD = 22)	Mean 26 days (SD = 6)
Connolly (17)	Before after	US	Patients with autoimmune diseases treated with immunosuppressants	BNT162b2 or mRNA-1273 or Ad26.COV2.S	Elecsys Anti-RBD IgG (Roche Diagnostic s)	Median 77 days (IQR = 54 to 94)	Median 30 days (IQR = 27 to 36)
Bensoun a (18)	Before after	France	Patients Receiving Maintenance Hemodialysis or Peritoneal Dialysis- (38 HD and 31 PD)	BNT162b2	Elecsys Anti-S1 IgG (Roche Diagnostic s)	70 days	Median 30 days (IQR = 27 to 36)
Peled (23)	Before after	Israel	heart transplant (HT) patients. For V3 population, excluded who vaccinated before transplant, recovered from covid and high levels of neutralizing antibodies	BNT162b2	Anti-RBD IgG	Mean 167.5 days (SD = 18)	Mean 17.5 days (SD = 3.9)
Schroff (25)	Before after	US	Patients with solid tumours who were on active cytotoxic anti-	BNT162b2	NAB	42 to 111 days	5-11 days

			cancer therapy, 8% had prior Covid-19				
Bertrand (27)	Before after	France	403 KTR followed in Rouen University Hospital, first 80 KTR pts included. None had covi d history	BNT162b 2	Anti-S IgG	Median 67.5 days (IQR = 57 to 70)	One month
Marlet (29)	Before after	France	Patients with kidney transplant and also patients with CLL	BNT162b 2 or mRNA-1273	Anti-S IgG Quant II (Abbott, Architect, Sligo Ireland)	Median 43 days (IQR 33 to 63)	Median 52 days (IQR = 34 to 76)
Greenber ger (30)	Before after	US	Patients with B cell-derived hematologic malignancies (25 CLL, 18 NHL and 1 patient with EBALD)	BNT162b 2 (65%) or mRNA-1273 (32%) or ChAdOx1 (2%)		median 77 days (range 12-141)	Median 28 days (range 12–61 days)
Robert (31)	Before after	France	90 Chronic haemodialysis (HD) patients-, 19 had covid history. Those non-responder patients after two Comirnaty Pfizer received V3 (n=18)	BNT162b 2	Anti-S IgG	unclear	One month
Konig (33)	Case series	Norway	130 Multiple sclerosis patients treated with either anti-CD20 or fingolimod with low or absent humoral immunity after two doses of vaccine	BNT162b 2 (15%) or mRNA-1273 (85%)	Anti-RBD IgG	Mean 94 days (SD = 30.8)	3-12 weeks
Schrezen meier (36)	Case series	Germany	25 kidney transplant recipients (KTR) without humoral response after two doses of BNT162b2 (without anti–spike S1 IgG response)	BNT162b 2 or ChAdOx1	Anti-S1 IgG (Euroimmun)	Mean 90 days (SD = 7) for ChAdOx1 and mean 127 (SD = 1) for BNT162b2	19-27 days
Schmiede berger (38)	Case series	Switzerl and	rheumatoid arthritis with absent or minimal serological response to two previous doses within 12 weeks,	BNT162b 2	Elecsys Anti-S1 IgG (Roche Diagnostic s)	unclear	2 weeks

			participated in the RECOVER trial , all treated with immunosuppressives				
Tillman (39)	Case control	Germany	hemodialysis patients > 18 yrs, only patients with vaccination failure were offered V3- none had previous infection	BNT162b2 (97%) or ChAdOx1 (3%)	anti-RBD IgG (Snibe Diagnostic, Shenzen, China)	unclear	27-36 days
Kozak (40)	Before after	US	Myeloproliferative disorders	BNT162b2 or mRNA-1273	anti-S Ig	Median 6.8 months	unclear
Sidler (47)	Case control	Switzerland	RituxiVac study population receiving anti-CD20	BNT162b2 or mRNA-1273	Anti-S1 IgG	unclear	Median 5 months after second vaccine (IQR 4.1 to 6)
Rottenberg (51)	Before after	Israel	Patients with solid tumors treated with chemotherapy, biologics, checkpoint inhibitors, or combinations, had two BNT162b2 vaccines	BNT162b2	Anti-S IgG (Liaison,Diasorin)	Median 214 days (range = 172 to 229)	Median 13 days (IQR 1-29)
Simon (53)	Before after	Germany	Patients with immune mediated inflammatory diseases treated with immunosuppressants (rituximab and non-rituximab analysed separately)	BNT162b2 (88%) or ChAdOx1 (12%)	Anti-S1 IgG	83 days (55 to 112)	20 days (15.5 to 28)
Malliard (54)	Before after	France	allogeneic hematopoietic cell transplant recipients-687 consecutive HSCT recipients-All included patients completed the 2-dose mRNA vaccine , of 687 patients, 181 received three doses (116/181 No or minimal response after V2)	BNT162b2 (96%) or mRNA-1273 (4%)	Anti-S1 and anti-RBD IgG all main companies (mainly Abbott and Roche)	Median 54 days (IQR = 34-74)	Median 30 days (IQR = 27 to 35)
Shapiro (58)	Before after	US	pts with cancer (mixed 57% hematologic	BNT162b2 (70%) or mRNA-	Anti-S IgG	Median 177 days	unclear

			malignancy and s31% olid cancer): with one of the following: receiving active treatment, recipient of SCT or CAR-T in last 2 yrs, having a negative spike IgG despite standard vaccination. Of 189, 88 had 4 weeks follow up, of 88, 32 had seronegative before third dose, therefore two cohorts: 88 for all had V3, of them, 32 had negative IgG before V3. (7 of them had prior covid19 infection)	1273 (25%) or ChAdOx1 (5%)			
Bagacean (59)	Before after	France	with chronic lymphocytic leukemia (CLL) with confirmed previous COVID-19	BNT162b2 (84%) or mRNA-1273 (16%)	Anti-S IgG Quant II (Abbott, Architect, Sligo Ireland)	6-8 weeks	unclear
Espi (60)	Before after	France	Maintenance hemodialysis patients from two centres that had received two BNT162b2 vaccinations and had not had COVID-19 within the last 3 months	BNT162b2	anti-RBD IgG (Snibe Diagnostic, Shenzen, China)	Within 3 months	10-14 days
Herishanu (61)	Before after	Israel	172 chronic lymphocytic leukemia (CLL) small lymphocytic lymphoma (SLL) who Failed Standard Two-dose Vaccination	BNT162b2	Anti-RBD IgG Quant II (Abbott, Architect, Lake Forest, IL, US)	unclear	3 weeks
Reimann (64)	Before after	Austria	32 haemato-oncological non-responders to double-dose BNT162b2	Ad26.COV2.S	Anti-RBD IgG Quant II (Abbott, Architect, Lake Forest, IL, US)	Median 124 days (IQR = 124 to 167)	28 days

Saharia (75)	Case control	US	Solid Organ Transplant Recipient receiving care at University of Maryland who received two vaccines. Median of 6.2 years after transplant. 24 kidney, 12 liver, 6 lung, 5 heart, 6 other transplant.	BNT162b2 (60%) or mRNA-1273 (34%) or Ad26.COV2.S (6%)	cPass Neutralization Antibody Detection Kit (GenScript, Cat. No. L00847) - neutralization activity (cut off >30%) RBD IgG	3-4 weeks	unclear
Hsu (77)	Before after	US	dialysis patients attending Dialysis Inc	BNT162b2 (39%) or mRNA-1273 (61%)	anti-spike IgG	3-4 weeks	>14 days
Fendler (79)	Case control	UK	patients with solid and hematological malignancy	BNT162b2 (67%) or ChAdOx1 (33%)	NAB to Delta variant	176 days median (range 65-274)	median 23 days (range 11-47 days)
Reindl-Schwaighofer (81)	RCT	Austria	kidney transplant patients who did not respond to V2 randomized to mRNA or vector vaccination (mean time from transplant 4.6 years)	Randomized 1:1 to mRNA or vector vaccine	Elecsys Anti RBD (Roche Diagnostics)	80 days	29 days (IQR 28-32)
Madelon (82)	Before after	Switzerland	MS patients treated with anti-CD20	BNT162b2 (20%) or mRNA-1273 (80%)	anti-RBD	Median 26.7 weeks	One month
Ligumsky (85)	Case control	Israel	Active cancer patients	BNT162b2	anti-S Ab II Quant (Abbott)	Median 217 days	33 days (IQR 21-44)
Karaba (87)	Case control	US	solid organ transplant patients who had received two vaccines - median transplant 4.5 years (probably also selected on titre response to second vaccine)	mRNA-1273 (70%) or Ad26.COV2.S (30%)	Euroimmun IgG anti-S1	Median 102 days (70-124)	unclear
Jyssum (88)	Case control	Norway	rituximab treated RA patients	BNT162b2 (80%) or mRNA-	anti-RBD	unclear	unclear

				1273 (20%)			
Schell (91)	Before after	US	IBD patients on immunosuppression	BNT162b2 (59%) or mRNA-1273 (41%)	anti-RBD	unclear	Median 37 days (IQR 32-47)
Achtnichts (93)	Before after	Switzerland	MS patients treated with anti-CD20	BNT162b2 (81%) or mRNA-1273 (19%)	anti-RBD Abbott IgG Quant Assay	median 14.9 weeks (range 6.6. to 30.1)	unclear
Yang (96)	Before after	US	Various categories of immunosuppressed patients	BNT162b2 or mRNA-1273 or Ad26.COV2.S	anti-S1 IgG	unclear	unclear
Jurdi (97)	Before after	US	Kidney transplant patients	BNT162b2 (94%) or mRNA-1273 (6%)	Anti-RBD	187 days (IQR 181-193)	Median 29 days median 29
Fenioux (99)	Before after	France	solid malignancy treated with anti-cancer agents	BNT162b2	anti-S1 (Architect, Abbott) - week response < 1000 AU/ml	1 month	28 days
Kamar (102)	Before after	France	solid organ transplant patients	BNT162b2 (98%) or mRNA-1273 (1%) or ChAdOx1 (1%)	anti-S Ig (Beijing Wantai Biological Pharmacy Ent Co)	unclear	1 month
Speer (107)	Before after	Germany	ANCA associated vasculitis on IMM subgrouped by whether on rituximab	BNT162b2	anti-S1 IgG	median 103 days (IQR 72-126)	Median 21 days (IQR 21 to 21)
Corradini (108)	Before after	Italy	Various categories of immunosuppressed patients	BNT162b2 or mRNA-1273	anti-RBD IgG	5 months	unclear
Bonelli (111)	RCT	Austria	Patients taking rituximab for autoimmune disease all having 2 mRNA vaccines.	BNT162b2 (50%) or ChAdOx1 (50%) (random)	Anti-S-IgG	unclear	Week 4
Tomowiak (112)	Before after	France	Patients with waldenstrom macroglobulienmia not responding to second vaccine	BNT162b2	Anti-S-IgG	unclear	unclear

Ducloux (174)	Before after	France	Hemodialysis patients that had not had previous COVID-19 infection (by history and serology) and had two BNT162b2 vaccinations	BNT162b2	anti-S1 IgG (Abbott)	N/R	1 month
Longlune (175)	Before after	France	Dialysis patients (88, hemodialysis, 24 peritoneal dialysis) that had two BNT162b2 vaccinations	BNT162b2	anti-S total Ig (Beijing Wantai Biological Pharmacy Ent)	1 month	1 month
Massa (176)	Before after	France	Consecutive kidney transplant patients from a single centre that had received two BNT162b2 vaccinations	BNT162b2	anti-RBD IgG (Abbott)	28 days	28 days
Frantzen (177)	Before after	France	Maintenance hemodialysis patients from two centres that had received two BNT162b2 vaccinations	BNT162b2 (58%), mRNA-1273 (31%) and Ad26.COV2.S (10%)	anti-S Ig (Roche, Elecsys)	At least one month	1 month
Re (178)	Before after	France	Patients with hematological malignancies (CLL, NHL and MM) that had received two BNT162b2 vaccinations	BNT162b2	anti-RBD total Ig (Roche, Elecsys)	N/R	3-4 weeks
Benotmane (179)	Before after	France	Kidney transplant patients from a single centre that had no history of prior COVID-19 and an anti-S IgG of less than 50 after receiving two BNT162b2 vaccinations	BNT162b2	anti-S IgG (Abbott, ARCHITECT IgG Quant test)	51 days	28 days
Del Bello (180)	Before after	France	Consecutive solid organ transplants (majority liver and kidney) that had received two BNT162b2 vaccinations	BNT162b2	anti-S IgG (Beijing Wantai Biological Pharmacy Ent) (58%), other anti-S IgG assay (42%)	59 days	28 days
Stumpf (181)	Before after	Germany	Kidney transplant recipients that received	BNT162b2	Anti-RBD IgG	68 days	4 weeks

			two BNT162b2 vaccinations		(Euroimmun)		

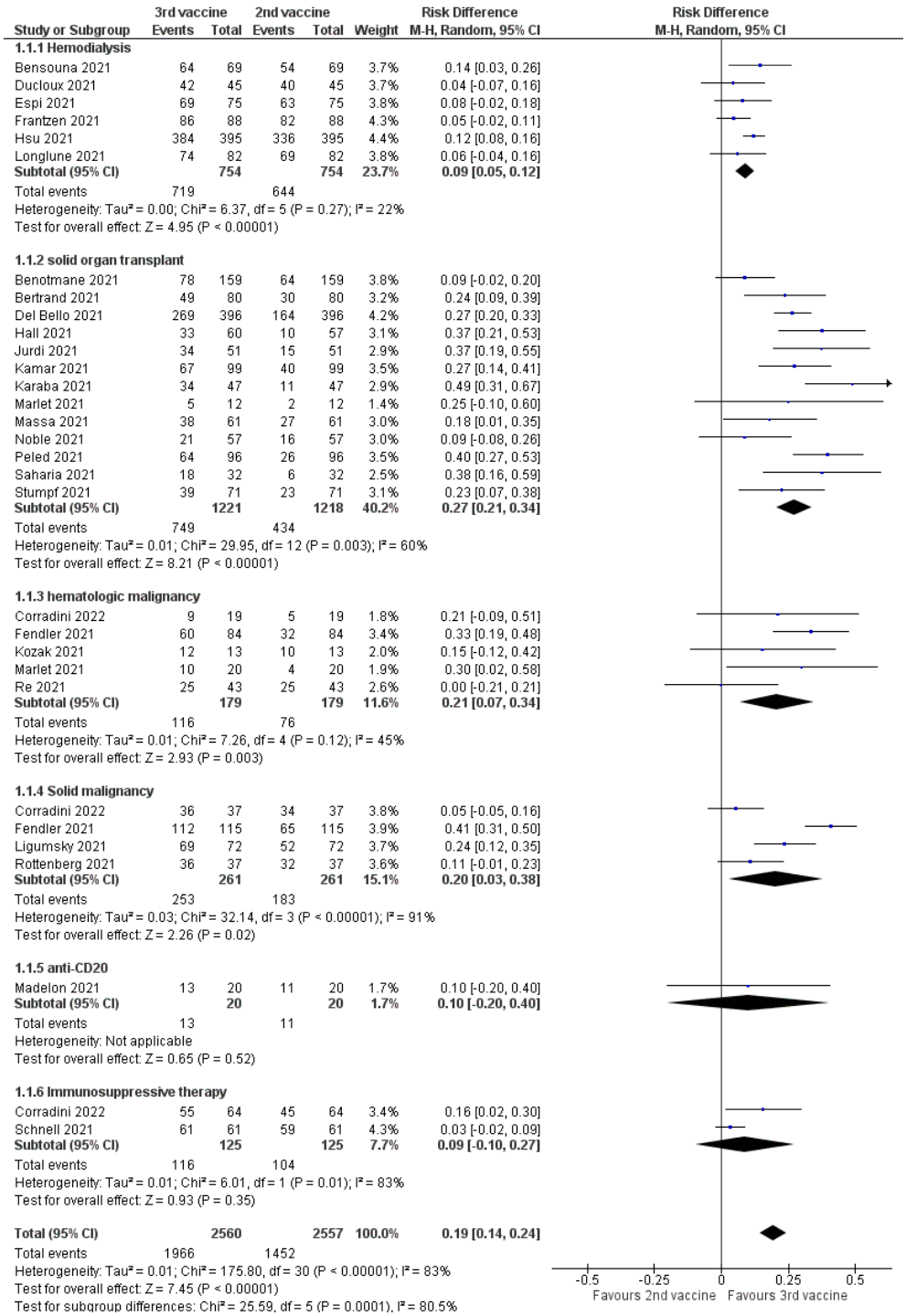
Increase in the proportion seroconverting after third dose of COVID-19 vaccination in the immunocompromised and dialysis patients

There were 27 studies (1, 6, 18, 23, 27, 29, 40, 51, 60, 75, 77, 79, 82, 85, 87, 91, 97, 102, 108, 174, 175, 176, 177, 178, 179, 180, 181) that reported on this outcome. Overall, 5117 participants were recruited to studies with a 19% (95% CI = 14 to 24%) absolute increase in seroconversion rates (Figure 2). The absolute increase in seroconversion varied according to the type of immunocompromised group (Table 5). There were 6 studies in 1508 dialysis patients with a 9% (95% CI = 5 to 12%) increase in seroconversion compared to 13 studies in 2439 solid organ transplant patients with a 27% (95% CI = 21 to 34%) increase in seroconversion (Table 5).

Table 5. Increase in seroconversion from the second to third dose of vaccine in the immunocompromised and dialysis patients

Disease group	No. Studies	Participants	I^2	Absolute increase in seroconversion
Hemodialysis	6	1508	22%	9% (5 to 12%)
Anti-CD20	1	40	N/A	10% (-20 to 40%)
Other immunosuppression	2	250	83%	9% (-10 to 27%)
Solid malignancy	4	522	91%	20% (3 to 38%)
Hematological malignancy	5	358	45%	21% (7 to 34%)
Solid organ transplant	13	2439	60%	27% (21 to 34%)

Figure 2. Increased proportion of seroconversion after a third COVID-19 vaccine in the immunocompromised and dialysis populations.



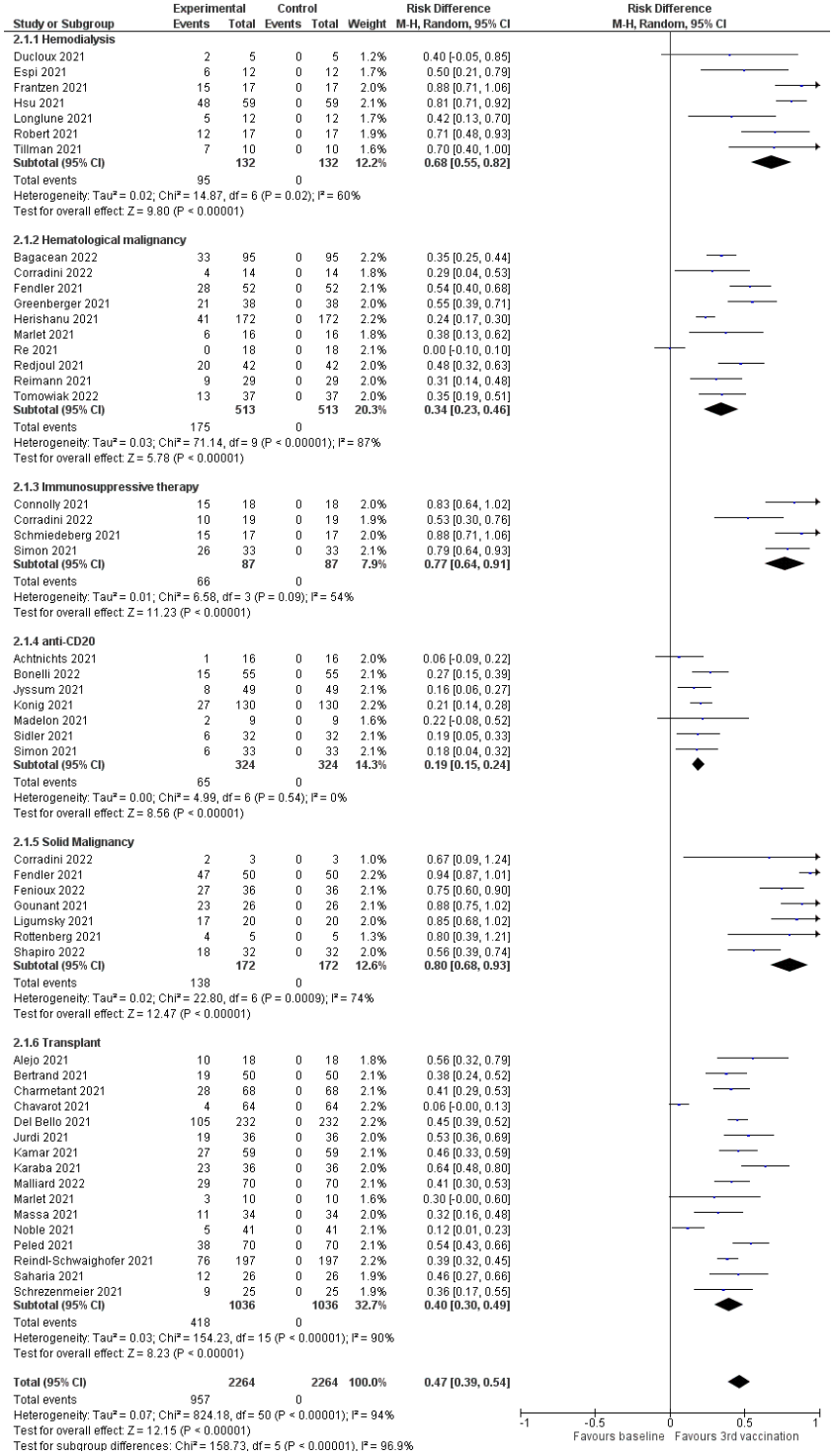
Proportion of immunocompromised and dialysis patients negative after second dose seroconverting after third dose of COVID-19 vaccination

There were 46 studies (6, 7, 8, 9, 12, 17, 18, 23, 27, 29, 30, 31, 33, 36, 38, 40, 47, 51, 53, 54, 60, 61, 64, 75, 77, 79, 81, 82, 85, 87, 88, 91, 93, 97, 99, 102, 108, 111, 112, 174, 175, 176, 177, 178, 180, 181) that reported on this outcome. Overall, 4528 participants were recruited to studies with a 47% (95% CI = 39 to 54%) that were previously negative after two vaccines seroconverting with the third vaccine (Figure 3). The proportion seroconverting varied according to the type of immunocompromised group (Table 6). There were 7 studies in 648 patients taking ant-CD20 drugs with 19% (95% CI = 15 to 24%) seroconverting compared to 16 studies in 2072 solid organ transplant patients with 40% (95% CI = 30 to 49%) seroconverting and 7 studies in 344 solid malignancy patients with 80% (68 to 93%) seroconverting (Table 6).

Table 6. Seroconversion after the third dose in those that were negative after the second dose of vaccine in the immunocompromised and dialysis patients

Disease group	No. Studies	Participants	I^2	Absolute increase in seroconversion
Hemodialysis	7	264	60%	68% (55 to 82%)
Anti-CD20	7	648	0%	19% (15 to 24%)
Other immunosuppression	4	174	54%	77% (64 to 91%)
Solid malignancy	7	344	74%	80% (68 to 93%)
Hematological malignancy	10	1026	87%	34% (23 to 46%)
Solid organ transplant	16	2072	90%	40% (30 to 49%)

Figure 3. Proportion seroconverting after a third COVID-19 vaccine in the immunocompromised and dialysis populations that were negative after the second dose.



Immunogenicity of fourth dose of COVID-19 vaccination in the immunocompromised and dialysis patients

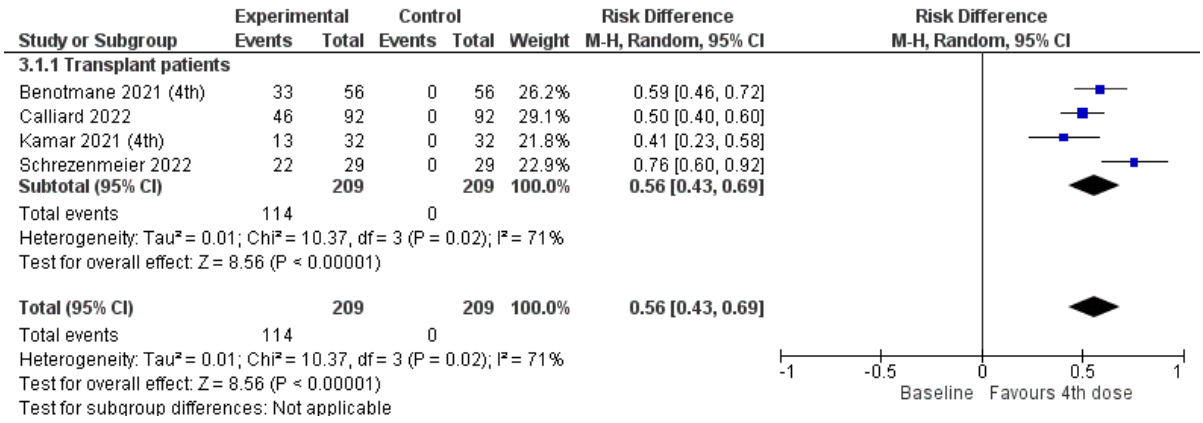
There were four case series (55, 56, 100, 104) that evaluated seroconversion with a fourth vaccine in patients that had failed to seroconvert or had low titres after three COVID-19 vaccinations. All studies (55, 56, 100, 104) evaluated solid organ transplant patients, three from France (55, 56, 104) and one from Germany (100). There was one study (7) that evaluated increase in seroconversion after the fourth vaccine which reported an increase in 12/18 to 15/18 seroconverting in solid organ transplant patients. The summary of these studies is given in Table 7.

Table 7. Summary of immunogenicity of fourth dose SARS-CoV2 vaccination studies

Author	Design	Country	Population description	Vaccine	Titre measured	Duration between 3rd and 4th vaccine	Time after 4th vaccine titre measured
Alejo (7)	Before after	US	Solid Organ Transplant Recipients, four doses of mRNA, enrolled in observational study SOTRs. No history of covid (kidney liver, pancreas, heart)	BNT162b2 or mRNA-1273 or Ad26.COV2.S	Euroimmun IgG anti-S1	unclear	28 days
Kamar (55)	Case series	France	Solid organ transplant patients	BNT162b2	Anti-S Ig (Wantai)	65 days (SD = 9)	1 month
Benotmane (56)	Case series	France	Kidney transplant patients	mRNA-1273	Anti-RBD IgG (Abbott, ARCHITECT IgG Quant test)	68 days (IQR = 63 to 82)	1 month
Schrezenmeier (100)	Case series	Germany	kidney transplant patients with no response after 3 vaccines	BNT162b2	Euroimmun Anti-S1 IgG	Mean 59.1 days (SD = 12.6)	Mean 32 days
Calliard (104)	Case series	France	kidney transplant patients with anti-S1 < 143 BAU/ml after V3	BNT162b2 (37%) or mRNA-1273 (63%)	Anti-S IgG	Median 68 days (61 to 74.7)	Median 29 days (IQR = 26 to 34)

Four studies (55, 56, 100, 104) evaluated 418 transplant patients that had not seroconverted or had low titres after three doses of COVD-19 vaccine. Overall, 56% (95% CI = 43 to 69%) seroconverted (Figure 4).

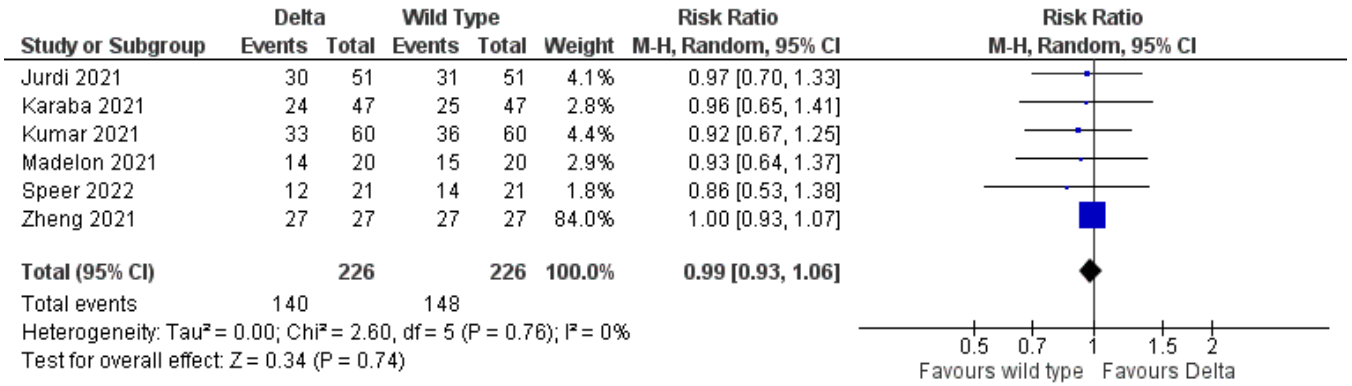
Figure 4. Proportion seroconverting after a fourth COVID-19 vaccine in solid organ transplant populations that were negative after the third dose.

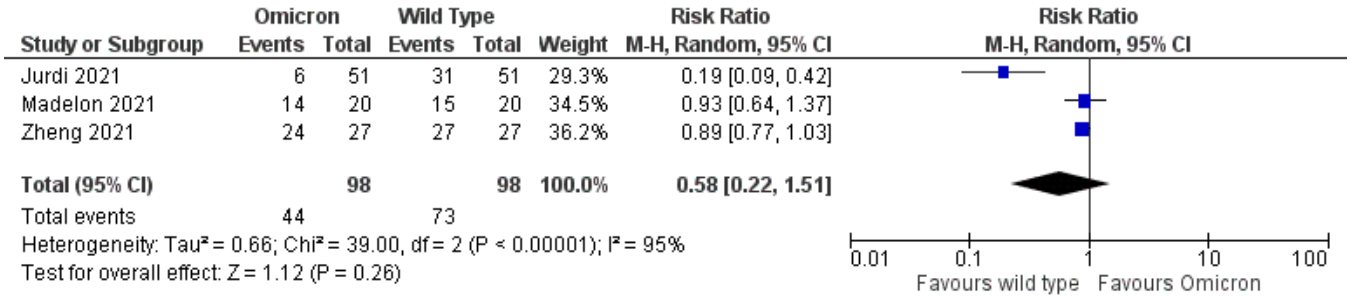


Comparison of immunogenicity to Omicron, versus Delta, versus wild type

There were 6 studies (4, 50, 82, 90, 97, 107) that compared seroconversion against Delta versus wild type strains in 452 patients. Three studies (4, 50, 97) involved transplant patients, two studies (82, 107) evaluated patients on immunosuppressive therapy and one study (90) evaluated solid cancer patients. There was no difference in seroconversion between the strains with all studies showing similar results and no heterogeneity between studies (RR seroconversion = 0.99; 95% CI = 0.93 to 1.03) (Figure 5).

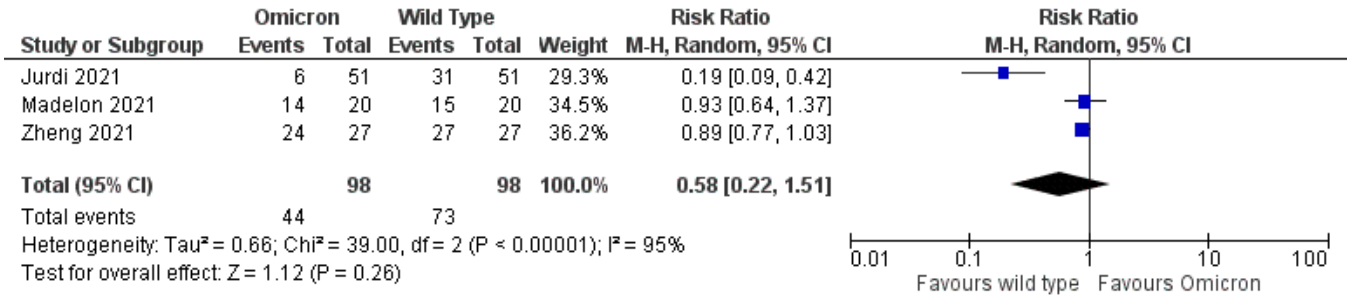
Figure 5. Proportion seroconverting after third or fourth COVID-19 vaccine comparing Delta variants versus wild type strains.





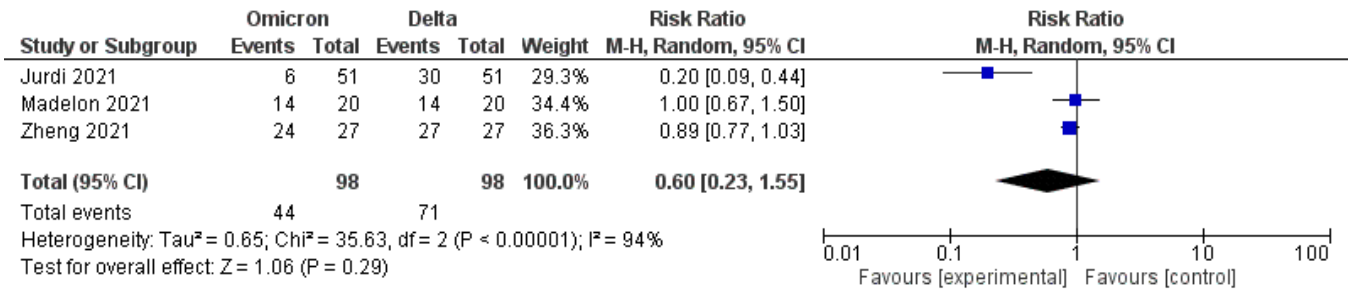
There were three studies (82, 90, 97) that compared seroconversion against Omicron versus wild type strains in 196 patients. One study (82) evaluated patients on immunosuppressive therapy, one study (90) evaluated solid cancer patients and the final study evaluated transplant patients (97). Two studies (82, 90) found no difference in seroconversion whilst one study (97) reported that seroconversion was less against Omicron strains. Overall, there was no statistically significant impact of seroconversion in different strains (RR seroconversion with Omicron = 0.58; 95% CI = 0.22 to 1.51) (Figure 6).

Figure 6. Proportion seroconverting after third or fourth COVID-19 vaccine comparing Omicron variants versus wild type strains.



Similarly, there were three studies (82, 90, 97) that compared seroconversion against Omicron versus Delta type strains in 196 patients. One study (82) evaluated patients on immunosuppressive therapy, one study (90) evaluated solid cancer patients and the final study evaluated transplant patients (97). Two studies (82, 90) found no difference in seroconversion whilst one study (97) reported that seroconversion was less against Omicron strains. Overall, there was no statistically significant impact of seroconversion in different strains (RR seroconversion with Omicron = 0.60; 95% CI = 0.23 to 1.55) (Figure 7).

Figure 7. Proportion seroconverting after third or fourth COVID-19 vaccine comparing Omicron variants versus Delta type strains.



Safety of COVID-19 vaccination in immunocompromised and dialysis patients

Studies evaluating safety predominantly described individual adverse events in case series data. There was no report of serious adverse events or worsening of disease. The summary of results is given in Table 8. There were 12 studies (18, 26, 33, 38, 43, 50, 53, 60, 61, 64, 85, 169) evaluating 23,228 participants that described local pain at site of vaccination. This was reported by 48% (95% CI = 36 to 60%) of participants with severe heterogeneity between results (I^2 = 97%; χ^2 = 348 (degrees of freedom = 11) p < 0.0001) (Figure 8). There were 12 studies (18, 24, 26, 33, 43, 50, 53, 60, 61, 64, 85, 169) evaluating 26,406 participants that described malaise or fatigue following vaccination. This was reported by 30% (95% CI = 24 to 35%) of participants with severe heterogeneity between results (I^2 = 96%; χ^2 = 278 (degrees of freedom = 11) p < 0.0001) (Figure 9). There were 12 studies (18, 24, 26, 33, 43, 50, 53, 60, 61, 64, 85, 169) evaluating 26,406 participants that described fever following vaccination. This was reported by 11% (95% CI = 5 to 19%) of participants with severe heterogeneity between results (I^2 = 99%; χ^2 = 1046 (degrees of freedom = 11) p < 0.0001) (Figure 10). There were 10 studies (18, 24, 26, 33, 43, 50, 53, 61, 85, 169) evaluating 26,315 participants that described myalgia following vaccination. This was reported by 16% (95% CI = 6 to 31%) of participants with severe heterogeneity between results (I^2 = 100%; χ^2 = 2091 (degrees of freedom = 9) p < 0.0001) (Figure 11). There were 11 studies (18, 24, 26, 33, 43, 50, 53, 61, 64, 85, 169) evaluating 26,238 participants that described headache following vaccination. This was reported by 16% (95% CI = 5 to 30%) of participants with severe heterogeneity between results (I^2 = 100%; χ^2 = 2063 (degrees of freedom = 10) p < 0.0001) (Figure 12).

Figure 8. Local pain in immunocompromised and dialysis patients receiving 3rd COVID-19 vaccination

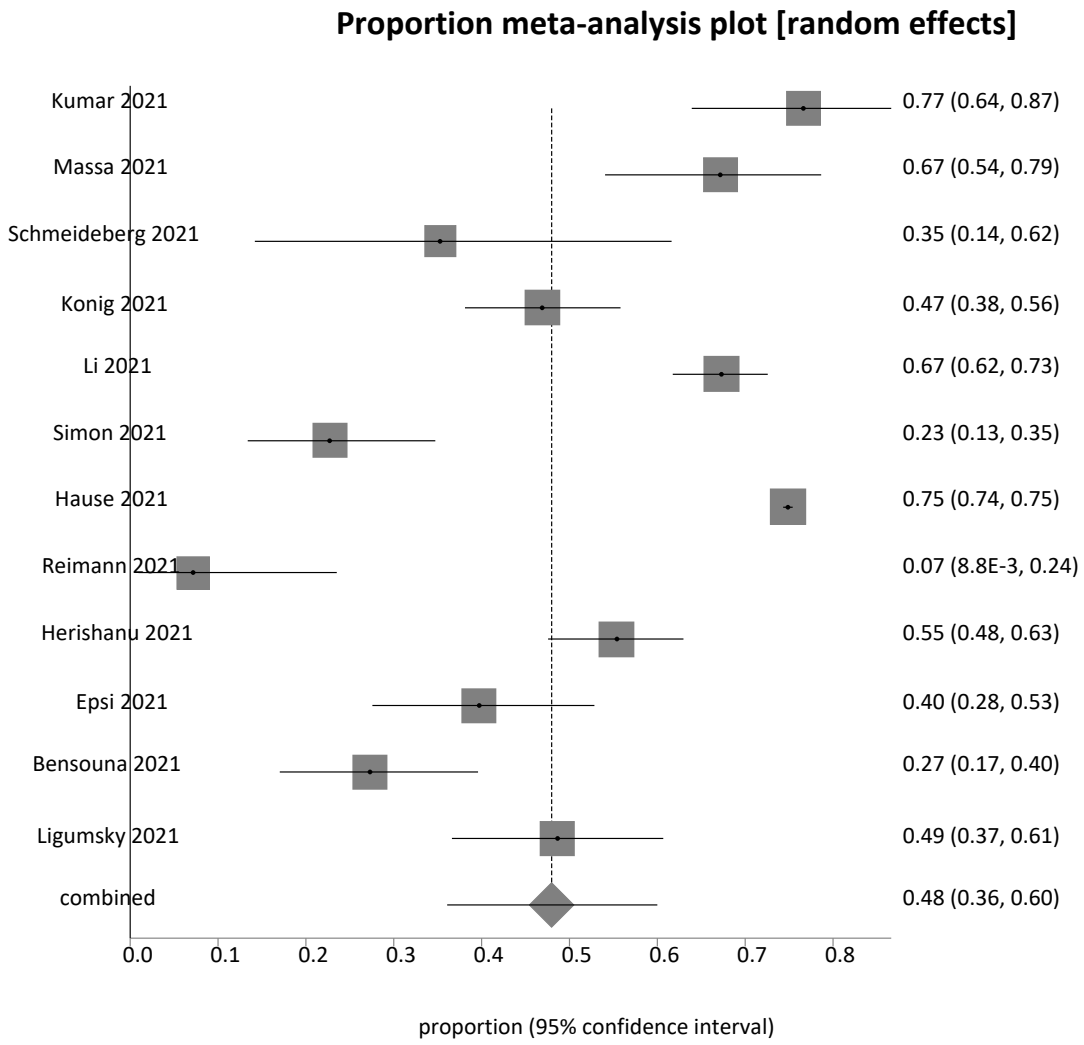


Figure 9. Fatigue or malaise in immunocompromised and dialysis patients receiving 3rd COVID-19 vaccination

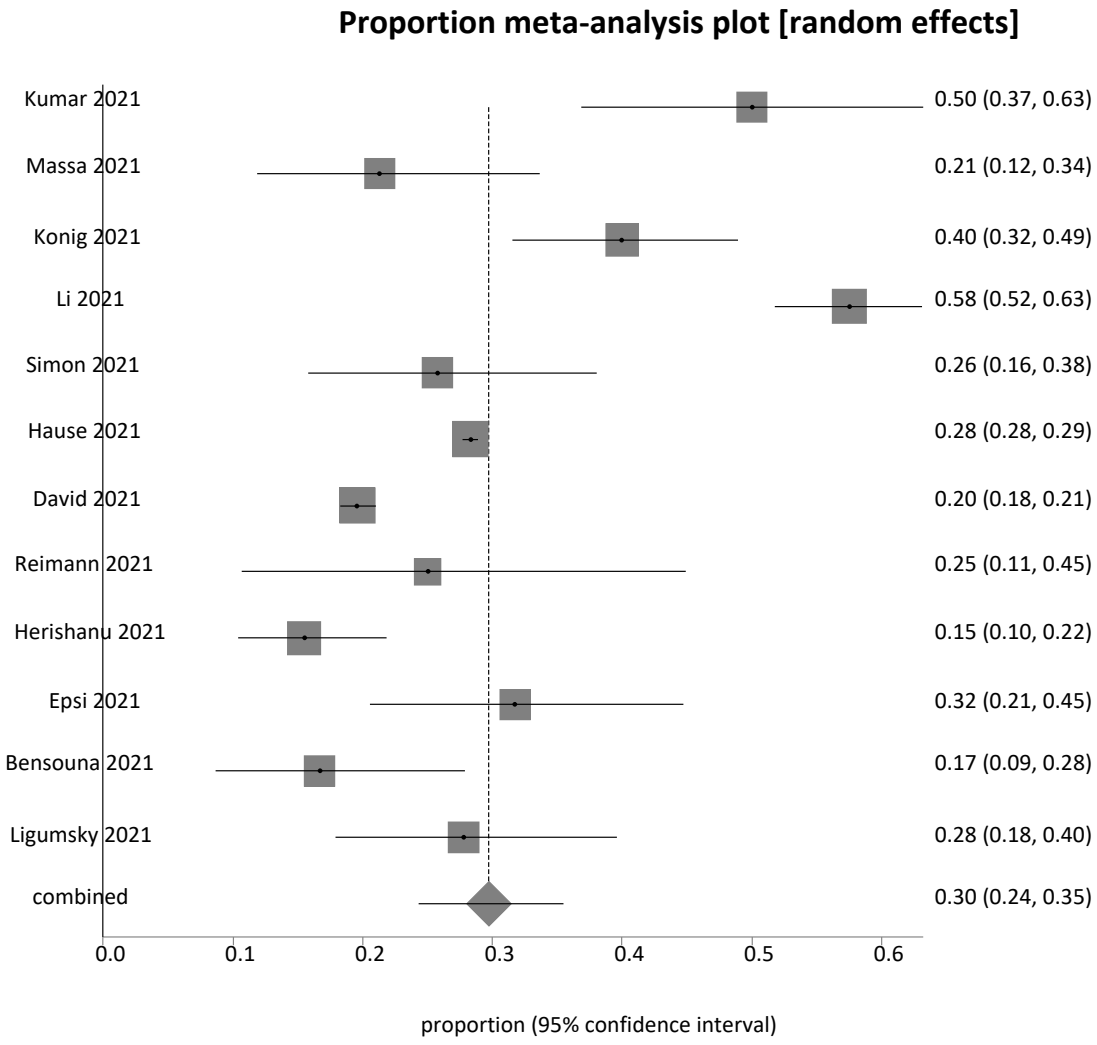


Figure 10. Fever in immunocompromised and dialysis patients receiving 3rd COVID-19 vaccination

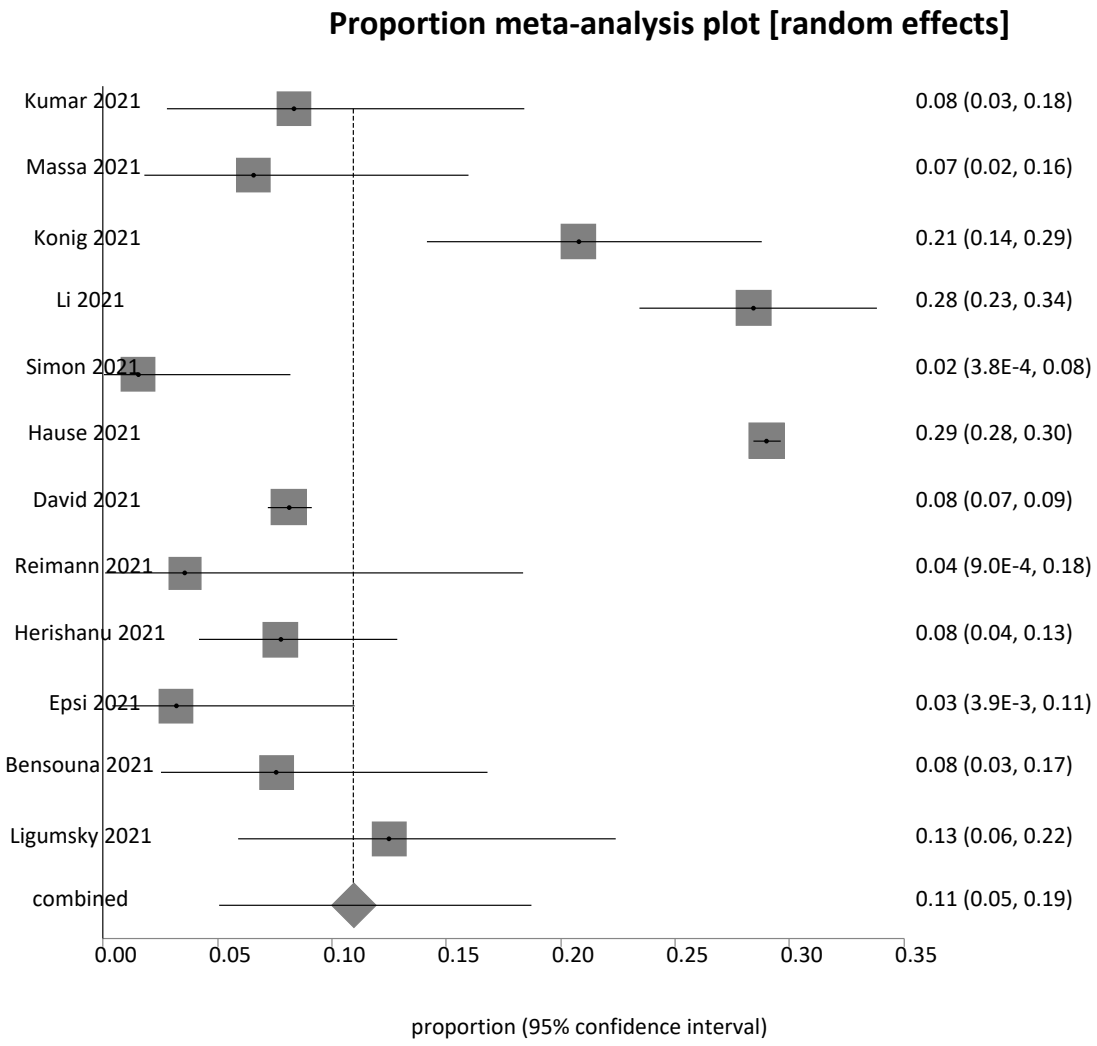


Figure 11. Myalgia in immunocompromised and dialysis patients receiving 3rd COVID-19 vaccination

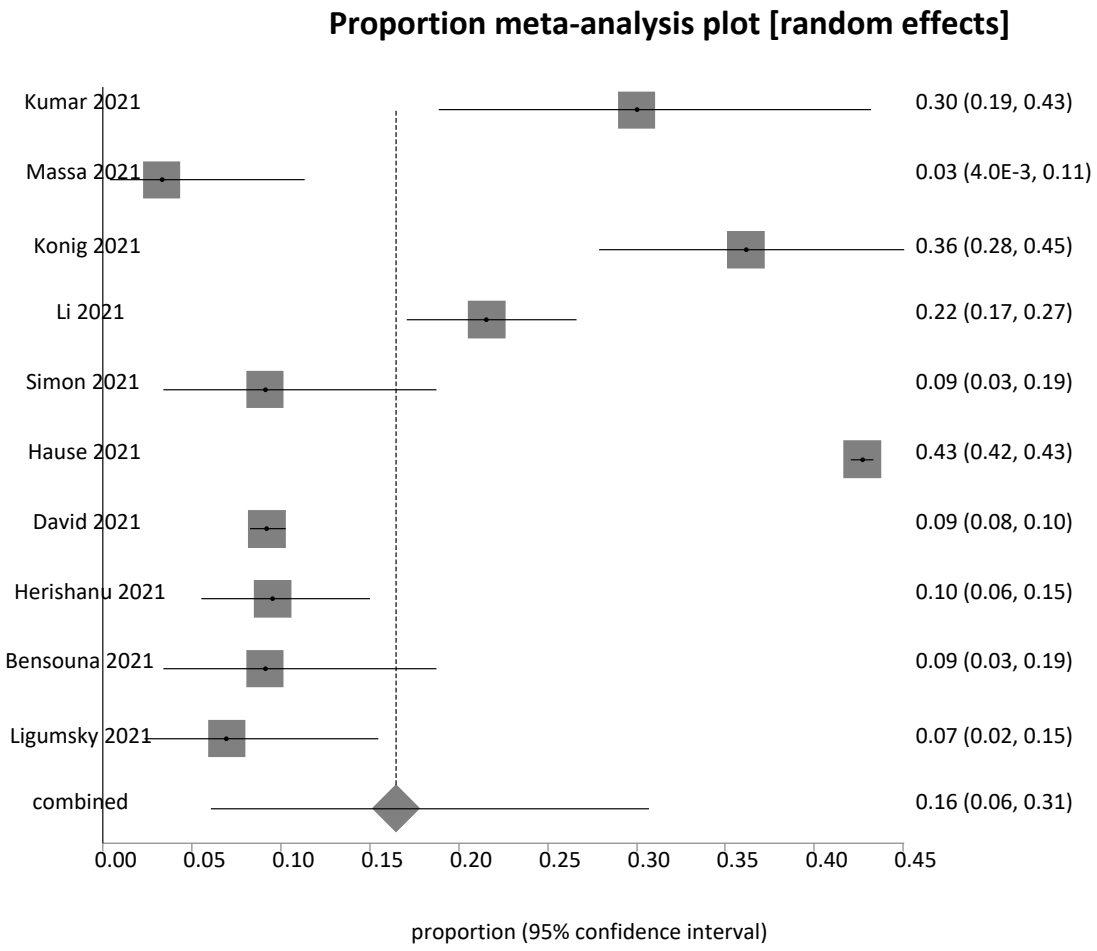
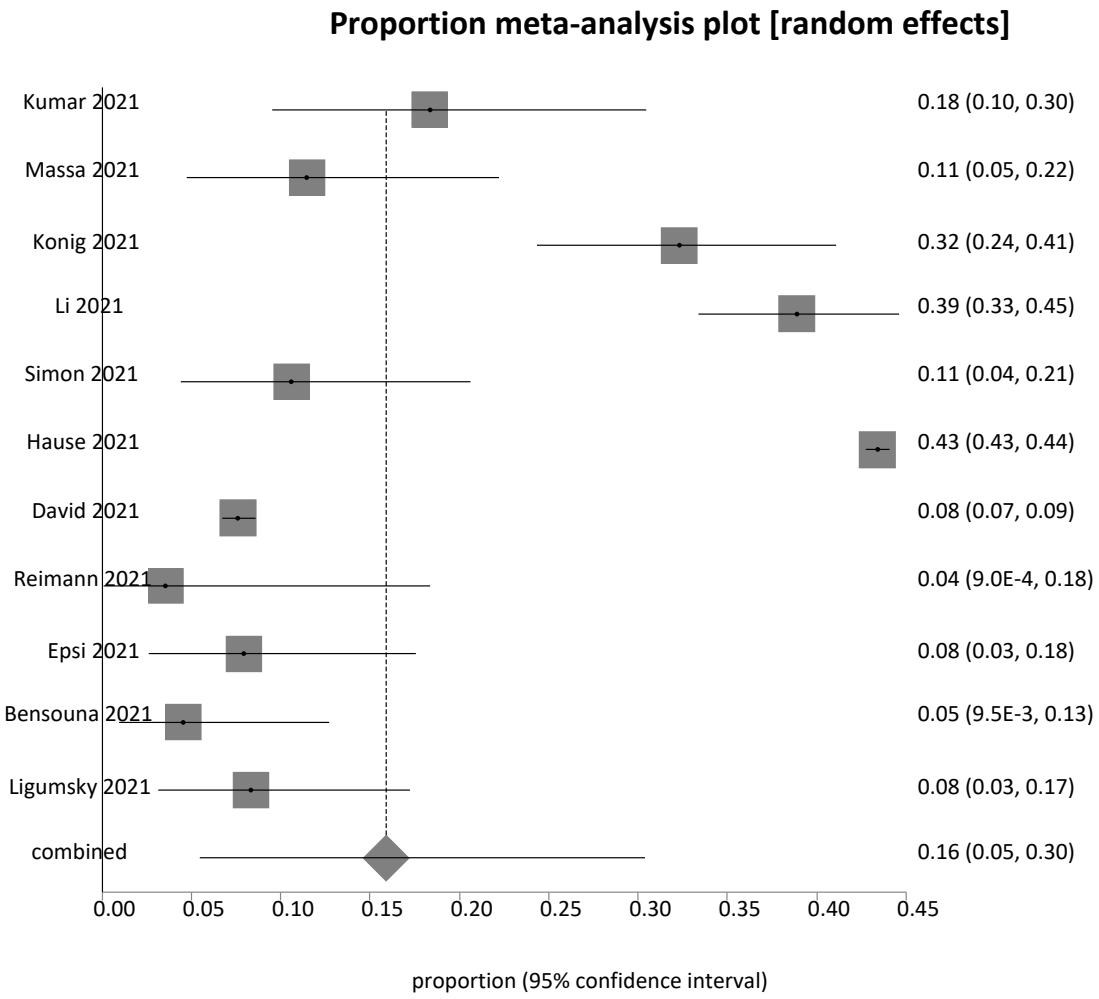


Figure 12. Headache in immunocompromised and dialysis patients receiving 3rd COVID-19 vaccination



Conclusion

Population studies suggest that a booster COVID-19 vaccination has about an 75% efficacy in protecting against the Delta variant of COVID-19 infection and symptoms in immunocompromised. This is slightly lower than the 94% protection seen in the healthy population. A third vaccination can increase seroconversion by 19% (95% CI = 14 to 24%) absolute increase in seroconversion rates. A third vaccination is more helpful in solid organ transplant patients increasing the absolute seroconversion rate by 27%. A fourth vaccine resulted in 56% seroconverting in those that had not seroconverted after three vaccinations. There is no major safety concern with COVID-19 vaccination symptoms in the immunocompromised and dialysis patients.

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