

## **ONLINE SUPPLEMENTARY DOCUMENT**

**Title: Differential COVID-19 infection rates in children, adults, and elderly: systematic review and meta-analysis of 38 pre-vaccination national seroprevalence studies**

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3 supplementary tables and supplementary references and PRISMA 2020 checklists.

**Supplementary Table 1:** Amendments/clarifications to protocol.

Manuscript section	Amendment/Clarification	Rationale
Eligibility for this subproject	For separating pediatric and non-elderly adult populations, we accepted cut-offs in the range 14-20, preferring the one available that was closest to 20. For separating non-elderly adults from elderly, we accepted cut-offs in the range of 54-70, preferring the one available that was closest to 60.	Clarification/specification needed for lower acceptable cut-off of pediatric group; for elderly cut-off accepted also one study (Portugal) with cut-off at 54 years (its exclusion gives similar results).
Analysis	The main analysis focused on the ratio of seroprevalence in the elderly versus non-elderly (non-elderly adults or non-elderly in general, if pediatric and adult population data were not offered separately). In sensitivity analyses, we examined the ratios of seroprevalence in the elderly versus any non-elderly, and elderly versus strictly non-elderly adults.	Clarification/specification needed
Analysis	Calculations were performed using the crude numbers (tested positive/tested) in each age stratum; when these were not available, we used the adjusted seroprevalence estimates and converted the adjusted proportion to an equivalent number of seropositives. When both crude numbers and adjusted estimates were available, we examined whether the latter changed results.	Clarification/specification needed; analyses were run with both crude and adjusted results and results are similar (as shown in the paper)
Analysis	The presented 95% confidence intervals for seroprevalence ratios are estimated using crude counts in a 2 by 2 table for each study. When only adjusted seroprevalence estimates were available without crude data, these were converted to equivalent of number positive (number positive = adjusted seroprevalence x number tested in the specific age group).	Clarification/specification needed

**Supplementary Table 2.** Details of excluded studies among reports manually assessed for eligibility (first search: 107 assessed, 72 excluded; search update: 9 assessed, 7 excluded).

URL/DOI	Country	Reason for exclusion
<i>First search</i>		
<a href="https://dx.doi.org/10.1038/s41598-021-92775-y">https://dx.doi.org/10.1038/s41598-021-92775-y</a>	Brazil	Several sampled (sub)regions not representative of country
<a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8225319/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8225319/</a>	Brazil	Several sampled (sub)regions not representative of country
<a href="https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3762489">https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3762489</a>	Cabo Verde	Seroprevalence < 1 - test specificity
<a href="https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3752659">https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3752659</a>	Canada	Duplicate
<a href="https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3933650">https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3933650</a>	Chile	Several sampled (sub)regions not representative of country
<a href="https://dx.doi.org/10.1016/j.lanwpc.2021.100094">https://dx.doi.org/10.1016/j.lanwpc.2021.100094</a>	China	Several sampled (sub)regions not representative of country
<a href="https://dx.doi.org/10.1007/s10654-021-00796-8">https://dx.doi.org/10.1007/s10654-021-00796-8</a>	Denmark	Duplicate
<a href="https://dx.doi.org/10.1007/s10654-021-00796-8">https://dx.doi.org/10.1007/s10654-021-00796-8</a>	Denmark	Duplicate
<a href="https://dx.doi.org/10.1007/s10654-021-00796-8">https://dx.doi.org/10.1007/s10654-021-00796-8</a>	Denmark	Duplicate
<a href="https://doi.org/10.1101/2021.05.07.21256725">https://doi.org/10.1101/2021.05.07.21256725</a>	Denmark	Not general population sample
<a href="https://www.medrxiv.org/content/10.1101/2021.08.10.21261777v1">https://www.medrxiv.org/content/10.1101/2021.08.10.21261777v1</a>	Denmark	Seroprevalence < 1 - test specificity
<a href="https://dx.doi.org/10.1371/journal.pat.1009413">https://dx.doi.org/10.1371/journal.pat.1009413</a>	Egypt	Several sampled (sub)regions not representative of country
<a href="https://ut.ee/et/sisu/koroonaviiruselevimuse-seireuringu-antikehade-analuusi-tulemused">https://ut.ee/et/sisu/koroonaviiruselevimuse-seireuringu-antikehade-analuusi-tulemused</a>	Estonia	News article
<a href="http://dx.doi.org/10.1016/j.ijid.2021.08.028">http://dx.doi.org/10.1016/j.ijid.2021.08.028</a>	Ethiopia	Several sampled (sub)regions not representative of country
<a href="https://dx.doi.org/10.1186/s12879-021-06973-0">https://dx.doi.org/10.1186/s12879-021-06973-0</a>	France	Duplicate of included study
<a href="https://www.medrxiv.org/content/10.1101/2021.10.25.21265456v1.full-text">https://www.medrxiv.org/content/10.1101/2021.10.25.21265456v1.full-text</a>	France	Duplicate (preprint of full paper)
<a href="https://drees.solidarites-sante.gouv.fr/sites/default/files/2021-01/er1167-en.pdf">https://drees.solidarites-sante.gouv.fr/sites/default/files/2021-01/er1167-en.pdf</a>	France	Duplicate (preprint of full paper)
<a href="https://dx.doi.org/10.1016/j.idnow.2020.12.007">https://dx.doi.org/10.1016/j.idnow.2020.12.007</a>	France	Several sampled (sub)regions not representative of country
<a href="https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3834300">https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3834300</a>	Germany	Several sampled (sub)regions not representative of country
<a href="https://www.ifo.de/en/publikationen/2020/monograph-authorship/die-deutschen-und-corona">https://www.ifo.de/en/publikationen/2020/monograph-authorship/die-deutschen-und-corona</a>	Germany	Not general population sample

<a href="https://www.medrxiv.org/content/10.1101/2021.06.21.21259001v1.full-text">https://www.medrxiv.org/content/10.1101/2021.06.21.21259001v1.full-text</a>	Germany	Not general population sample
<a href="https://dx.doi.org/10.3390/vaccines9050504">https://dx.doi.org/10.3390/vaccines9050504</a>	Greece	Not general population sample: Leftover samples
<a href="https://revistas.ucr.ac.cr/index.php/psm/article/view/43261/46175">https://revistas.ucr.ac.cr/index.php/psm/article/view/43261/46175</a>	Honduras	Municipalities with no reported cases
10.1101/2021.03.19.21253429	India	Several sampled (sub)regions not representative of country
<a href="https://dx.doi.org/10.1016/S2214-109X(20)30544-1">https://dx.doi.org/10.1016/S2214-109X(20)30544-1</a>	India	Duplicate
<a href="http://dx.doi.org/10.4103/ijmr.IJMR_3290_20">http://dx.doi.org/10.4103/ijmr.IJMR_3290_20</a>	India	Duplicate of included study
<a href="https://www.bbc.com/news/world-asia-india-55945382">https://www.bbc.com/news/world-asia-india-55945382</a>	India	News article
<a href="https://www.medrxiv.org/content/10.1101/2021.02.05.21251118v2">https://www.medrxiv.org/content/10.1101/2021.02.05.21251118v2</a>	India	Several sampled (sub)regions not representative of country
<a href="http://dx.doi.org/10.1016/S1473-3099%2820%2930858-6">http://dx.doi.org/10.1016/S1473-3099%2820%2930858-6</a>	Iran	Several sampled (sub)regions not representative of country
<a href="http://dx.doi.org/10.1016/S1473-3099%2820%2930858-6">http://dx.doi.org/10.1016/S1473-3099%2820%2930858-6</a>	Iran	Several sampled (sub)regions not representative of country
<a href="https://www.google.com/url?rct=j&amp;sa=t&amp;url=https://www.timesofisrael.com/initial-antibody-tests-indicate-200000-israelis-have-had-covid-19-report/&amp;ct=ga&amp;cd=CAAYBjlaOTBkZWE5ODk5NGU5MTg1OTpjb206ZW46VVVM&amp;usg=AFQjCNHYeXqD2hEiNnZoH5qLiVlZKxQjg">https://www.google.com/url?rct=j&amp;sa=t&amp;url=https://www.timesofisrael.com/initial-antibody-tests-indicate-200000-israelis-have-had-covid-19-report/&amp;ct=ga&amp;cd=CAAYBjlaOTBkZWE5ODk5NGU5MTg1OTpjb206ZW46VVVM&amp;usg=AFQjCNHYeXqD2hEiNnZoH5qLiVlZKxQjg</a>	Israel	News article
<a href="https://dx.doi.org/10.1128/Spectrum.00870-21">https://dx.doi.org/10.1128/Spectrum.00870-21</a>	Israel	Seroprevalence < 1 - test specificity
<a href="https://www.istat.it/it/files//2020/08/ReportPrimiRisultatiIndagineSiero.pdf">https://www.istat.it/it/files//2020/08/ReportPrimiRisultatiIndagineSiero.pdf</a>	Italy	Duplicate
<a href="http://dx.doi.org/10.1016/j.onehlt.2021.100292">http://dx.doi.org/10.1016/j.onehlt.2021.100292</a>	Jordan	Duplicate
<a href="http://dx.doi.org/10.1016/j.onehlt.2021.100292">http://dx.doi.org/10.1016/j.onehlt.2021.100292</a>	Jordan	Duplicate
<a href="https://dx.doi.org/10.3390/jcm9123989">https://dx.doi.org/10.3390/jcm9123989</a>	Liechtenstein	Not general population sample
<a href="https://www.medrxiv.org/content/10.1101/2020.05.11.20092916v1">https://www.medrxiv.org/content/10.1101/2020.05.11.20092916v1</a>	Luxembourg	Seroprevalence < 1 - test specificity
<a href="https://www.gob.mx/salud/prensa/255-secretaria-de-salud-presenta-resultados-preliminares-de-la-encuesta-nacional-de-salud-y-nutricion-covid-19?idiom=es">https://www.gob.mx/salud/prensa/255-secretaria-de-salud-presenta-resultados-preliminares-de-la-encuesta-nacional-de-salud-y-nutricion-covid-19?idiom=es</a>	Mexico	News article
<a href="https://saludpublica.mx/index.php/spm/article/view/12847">https://saludpublica.mx/index.php/spm/article/view/12847</a>	Mexico	Not general population sample
<a href="https://saludpublica.mx/index.php/spm/article/view/12847">https://saludpublica.mx/index.php/spm/article/view/12847</a>	Mexico	Duplicate

<a href="https://dx.doi.org/10.1136/jech-2020-215678">https://dx.doi.org/10.1136/jech-2020-215678</a>	Netherlands	Duplicate of included study
<a href="https://dx.doi.org/10.1016/j.ijid.2021.09.062">https://dx.doi.org/10.1016/j.ijid.2021.09.062</a>	Oman	Duplicate
<a href="https://dx.doi.org/10.1016/j.ijid.2021.09.062">https://dx.doi.org/10.1016/j.ijid.2021.09.062</a>	Oman	Duplicate
<a href="https://dx.doi.org/10.1016/j.ijid.2021.09.062">https://dx.doi.org/10.1016/j.ijid.2021.09.062</a>	Oman	Duplicate
<a href="https://dx.doi.org/10.1007/s15010-021-01629-2">https://dx.doi.org/10.1007/s15010-021-01629-2</a>	Pakistan	Several sampled (sub)regions not representative of country
<a href="https://world.kbs.co.kr/service/news_view.htm?lang=e&amp;Seq_Code=157801">https://world.kbs.co.kr/service/news_view.htm?lang=e&amp;Seq_Code=157801</a>	Republic of Korea	News article
<a href="https://www.google.com/url?rct=j&amp;s a=t&amp;url=http://www.koreaherald.com/view.php%3Fud%3D20200709000787&amp;ct=ga&amp;cd=CAAYEDlaOTBkZWE5ODk5NGU5MTg1OTpj206ZW46VV M&amp;usg=AFQjCNG8AlCeBcx2rR4FfgC726ll5TtgUw">https://www.google.com/url?rct=j&amp;s a=t&amp;url=http://www.koreaherald.com/view.php%3Fud%3D20200709000787&amp;ct=ga&amp;cd=CAAYEDlaOTBkZWE5ODk5NGU5MTg1OTpj206ZW46VV M&amp;usg=AFQjCNG8AlCeBcx2rR4FfgC726ll5TtgUw</a>	Republic of Korea	News article
<a href="https://www.themoscowtimes.com/2020/06/10/1-in-7-russians-have-coronavirus-immunity-official-a70540">https://www.themoscowtimes.com/2020/06/10/1-in-7-russians-have-coronavirus-immunity-official-a70540</a> ; <a href="https://www.interfax.ru/russia/712617">https://www.interfax.ru/russia/712617</a>	Russia	News article
<a href="https://www.medrxiv.org/content/10.1101/2021.01.28.21250598v1">https://www.medrxiv.org/content/10.1101/2021.01.28.21250598v1</a>	Saudi Arabia	Not general population sample
<a href="https://dx.doi.org/10.1016/j.cmi.2021.03.009">https://dx.doi.org/10.1016/j.cmi.2021.03.009</a>	Slovenia	Duplicate
<a href="https://www.nicd.ac.za/wp-content/uploads/2021/03/COVID-19-Special-Public-Health-Surveillance-Bulletin-9-12-March-2021.pdf">https://www.nicd.ac.za/wp-content/uploads/2021/03/COVID-19-Special-Public-Health-Surveillance-Bulletin-9-12-March-2021.pdf</a>	South Africa	Several sampled (sub)regions not representative of country
<a href="https://www.medrxiv.org/content/10.1101/2021.02.26.21252512v1">https://www.medrxiv.org/content/10.1101/2021.02.26.21252512v1</a>	United Kingdom of Great Britain and Northern Ireland	Duplicate
<a href="https://www.medrxiv.org/content/10.1101/2021.02.26.21252512v1">https://www.medrxiv.org/content/10.1101/2021.02.26.21252512v1</a>	United Kingdom of Great Britain and Northern Ireland	<90% by Jan 31, 2021
<a href="https://www.ukbiobank.ac.uk/media/x0nd5sul/ukb_serologystudy_report_revised_6months_jan21.pdf">https://www.ukbiobank.ac.uk/media/x0nd5sul/ukb_serologystudy_report_revised_6months_jan21.pdf</a>	United Kingdom of Great Britain and Northern Ireland	Not general population sample: Biobank
<a href="https://www.gov.uk/government/publications/national-covid-19-surveillance-reports">https://www.gov.uk/government/publications/national-covid-19-surveillance-reports</a>	United Kingdom of Great Britain and Northern Ireland	Not general population sample
<a href="https://www.gov.uk/government/publications/national-covid-19-surveillance-reports">https://www.gov.uk/government/publications/national-covid-19-surveillance-reports</a>	United Kingdom of Great Britain and Northern Ireland	Not general population sample
<a href="https://www.medrxiv.org/content/10.1101/2020.10.26.20219725v1.full.pdf">https://www.medrxiv.org/content/10.1101/2020.10.26.20219725v1.full.pdf</a>	United Kingdom of Great Britain and Northern Ireland	Duplicate (preprint of full paper)

<a href="https://www.medrxiv.org/content/10.1101/2020.10.26.20219725v1.full.pdf">https://www.medrxiv.org/content/10.1101/2020.10.26.20219725v1.full.pdf</a>	United Kingdom of Great Britain and Northern Ireland	Duplicate (preprint of full paper)
<a href="https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3764198">https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3764198</a>	United Kingdom of Great Britain and Northern Ireland	Not general population sample
<a href="https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3764198">https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3764198</a>	United Kingdom of Great Britain and Northern Ireland	Duplicate
<a href="https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3764198">https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3764198</a>	United Kingdom of Great Britain and Northern Ireland	Duplicate
<a href="https://www.gov.uk/government/publications/national-covid-19-surveillance-reports">https://www.gov.uk/government/publications/national-covid-19-surveillance-reports</a>	United Kingdom of Great Britain and Northern Ireland	Seroprevalence < 1 - test specificity
<a href="https://dx.doi.org/10.1126/scitranslmed.abh3826">https://dx.doi.org/10.1126/scitranslmed.abh3826</a>	United States of America	Duplicate
<a href="https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2777502?utm_source=For%20The%20Media&amp;utm_medium=referral&amp;utm_campaign=facebook_links&amp;utm_term=031621">https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2777502?utm_source=For The Media&amp;utm_medium=referral&amp;utm_campaign=facebook_links&amp;utm_term=031621</a>	United States of America	Not general population sample: Life insurance
<a href="https://www.croiconference.org/abstract/us-population-based-survey-of-vaccine-willingness-and-sars-cov-2-antibody-prevalence/">https://www.croiconference.org/abstract/us-population-based-survey-of-vaccine-willingness-and-sars-cov-2-antibody-prevalence/</a>	United States of America	Meeting abstract
<a href="https://dx.doi.org/10.1136/bmjopen-2021-048778">https://dx.doi.org/10.1136/bmjopen-2021-048778</a>	United States of America	Not general population sample
<a href="https://pubmed.ncbi.nlm.nih.gov/33532807/">https://pubmed.ncbi.nlm.nih.gov/33532807/</a>	United States of America	Duplicate (report of full paper)
<a href="https://dx.doi.org/10.1016/j.ejim.2021.01.029">https://dx.doi.org/10.1016/j.ejim.2021.01.029</a>	Vatican City	Not general population sample
<a href="http://dx.doi.org/10.3390/ijerph18126353">http://dx.doi.org/10.3390/ijerph18126353</a>	Viet Nam	Not general population sample: High-risk communities
<a href="http://dx.doi.org/10.3390/ijerph18126353">http://dx.doi.org/10.3390/ijerph18126353</a>	Viet Nam	Duplicate
<a href="http://dx.doi.org/10.3390/ijerph18126353">http://dx.doi.org/10.3390/ijerph18126353</a>	Viet Nam	Duplicate
<a href="https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(21)00053-X/fulltext">https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(21)00053-X/fulltext</a>	Zambia	Several sampled (sub)regions not representative of country
<b>Search update</b>		
<a href="https://dx.doi.org/10.1001/jamanetworkopen.2021.46798">https://dx.doi.org/10.1001/jamanetworkopen.2021.46798</a>	Canada	Duplicate of included study
<a href="https://dx.doi.org/10.1186/s12879-022-07045-7">https://dx.doi.org/10.1186/s12879-022-07045-7</a>	Chile	Several sampled (sub)regions not representative of country
<a href="https://doi.org/10.1038/s43856-022-00080-0">https://doi.org/10.1038/s43856-022-00080-0</a>	Czechia	Overlapping with included study
<a href="https://dx.doi.org/10.1038/s41467-022-28232-9">https://dx.doi.org/10.1038/s41467-022-28232-9</a>	Mexico	Duplicate of included study
<a href="https://dx.doi.org/10.2807/1560-7917.ES.2022.27.13.2100376">https://dx.doi.org/10.2807/1560-7917.ES.2022.27.13.2100376</a>	Norway	Duplicate of included study
<a href="https://dx.doi.org/10.1016/j.jcv.2022.105130">https://dx.doi.org/10.1016/j.jcv.2022.105130</a>	Spain	Duplicate of included study

<a href="https://dx.doi.org/10.1186/s12916-022-02286-4">https://dx.doi.org/10.1186/s12916-022-02286-4</a>	United Kingdom of Great Britain and Northern Ireland	Not general population sample
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**Supplementary Table 3:** Adjustments used in the adjusted seroprevalence estimates

Country	Adjustments made
Afghanistan	NA
Andorra	NA
Canada	NA
Czech Republic	NA
Denmark	Test sensitivity and specificity using the Rogan-Gladen estimator
England	Test performance, and weighted to account for sample design and for variation in response rate (age, sex, ethnicity, region and deprivation) to be representative of the England population over 18 years
Faroe Islands	NA
France (Warszewski)	Sample design, non-response, census calibration
France (Carrat)	NA
Germany	Non-response, test performance and seroreversion
Hungary	Design weighted. Response sample calibrated to known population counts by region, sex, and age categories.
Iceland	NA
India	Cluster sampling, sensitivity, specificity
Iran	Measurement error of the laboratory test, non-response bias and sampling design.
Ireland	Weighted to adjust for varying response rates in age-sex strata
Israel	Age, sex, time period, RT-PCR status, municipal strata, sampling
Italy	Non-response, region, age, sex, working status, province
Japan	NA
Jersey	NA
Jordan	NA
Lao PDR	Weighted for complex survey sample design, age and sex
Lebanon	Sex, age and area of residence, test performance



Lithuania	NA
Maldives	NA
Mexico	Test performance, and used sampling weights to adjust for selection probabilities and non-response rates (with post-stratification on region, sex and age group)
Mongolia	Test sensitivity and weighted prevalence rates according to age, sex, and provincial or district population size
Nepal	Survey design weights, age
Netherlands	Adjusted for survey design, weighted to match the distribution of the general Dutch population (based on sex, age, ethnic background, and degree of urbanization) and controlled for test characteristics
Norway	Rake weighting for population estimates of seroprevalence by age, sex, place of birth and county based on individual-level data for the invited sample (participants and non-responders) together with the corresponding distributions from the source population, provided by the Norwegian Population Register. Applied propensity scores for nonresponse adjustment and jackknife replicate weights for the raking procedure. Estimates subsequently corrected for test performance
Oman	Age group, sex, nationality
Pakistan	NA
Portugal	Adjusted for test performance, used sample weights and post-stratified by sex to adjust the seroprevalence extrapolating from the strata to the whole population
Russia	NA
Senegal	Weighted according to the age and sex distribution of the general population and adjusted test performance
Slovenia	NA
Spain	Characteristics of the random subsample of the fourth round
USA (Sullivan)	Test performance, design weights

USA (Kalish)	Age, region, sex, urban/rural, race, Hispanic, BRFSS survey response, sensitivity, specificity
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NA, not available

## Supplementary References

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**Appendix. PRISMA 2020 checklists (Main article and Abstract)**

Section and Topic	Item #	Checklist item	Location where item is reported (page)
<b>TITLE</b>			
Title	1	Identify the report as a systematic review.	1
<b>ABSTRACT</b>			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	3
<b>INTRODUCTION</b>			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	5
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	5,6
<b>METHODS</b>			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	6
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	6
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	6
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.	6,7
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.	7
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	7,8
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	7,8
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.	6
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	8
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	8,9
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	8,9
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	8,9
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	8,9
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	9
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	9

Section and Topic	Item #	Checklist item	Location where item is reported (page)
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	-
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	-
<b>RESULTS</b>			
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.	9,27,30,31
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	30,31
Study characteristics	17	Cite each included study and present its characteristics.	38-44
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	9
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	9,24,28,29
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	-
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	10,11
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	11,12
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	11
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	-
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	-
<b>DISCUSSION</b>			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	12
	23b	Discuss any limitations of the evidence included in the review.	12-15
	23c	Discuss any limitations of the review processes used.	13
	23d	Discuss implications of the results for practice, policy, and future research.	15
<b>OTHER INFORMATION</b>			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	6
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	6
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	29
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	1,2
Competing	26	Declare any competing interests of review authors.	2

Section and Topic	Item #	Checklist item	Location where item is reported (page)
interests			
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.	-

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71. doi: 10.1136/bmj.n71

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Section and Topic	Item #	Checklist item	Reported (Yes/No)
<b>TITLE</b>			
Title	1	Identify the report as a systematic review.	Yes
<b>BACKGROUND</b>			
Objectives	2	Provide an explicit statement of the main objective(s) or question(s) the review addresses.	Yes
<b>METHODS</b>			
Eligibility criteria	3	Specify the inclusion and exclusion criteria for the review.	Yes
Information sources	4	Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched.	Yes
Risk of bias	5	Specify the methods used to assess risk of bias in the included studies.	Yes
Synthesis of results	6	Specify the methods used to present and synthesise results.	Yes
<b>RESULTS</b>			
Included studies	7	Give the total number of included studies and participants and summarise relevant characteristics of studies.	Yes
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 (i.e. which group is favoured).	Yes
<b>DISCUSSION</b>			
Limitations of evidence	9	Provide a brief summary of the limitations of the evidence included in the review (e.g. study risk of bias, inconsistency and imprecision).	Yes
Interpretation	10	Provide a general interpretation of the results and important implications.	Yes
<b>OTHER</b>			
Funding	11	Specify the primary source of funding for the review.	Yes

Section and Topic	Item #	Checklist item	Reported (Yes/No)
Registration	12	Provide the register name and registration number.	Yes

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