


BMJ Open Characteristics of registered and published systematic reviews focusing on the prevention of COVID-19: a meta-research study

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ABSTRACT

Objective We investigated characteristics of systematic reviews (SRs) assessing measures to prevent COVID-19 by (1) identifying SR registrations in Prospective Register of Systematic Reviews (PROSPERO), (2) identifying published SRs in COVID-19 Living Overview of the Evidence (L-OVE) and (3) estimating the proportion of PROSPERO registrations published as full SR between 8 and 16 months after registration.

Study design This meta-research study is part of the German CEOsys project, www.covid-evidenz.de. We searched PROSPERO entries registered between 1 January 2020 and 31 August 2020, and we searched COVID-19 L-OVE for published SRs (search date: 5 May 2021) focusing on measures to prevent COVID-19 and SARS-CoV-2 transmission. The two samples were screened for eligibility and key characteristics were extracted and summarised.

Results Of 612 PROSPERO registrations, 47 focused on prevention and were included. The preventive measures included public health interventions (20), followed by personal protective equipment (10), vaccinations (9) and others (8). In total, 13 of 47 (28%) PROSPERO registrations had been published as full SR (as preprint only (6), as peer-reviewed article only (6), as preprint and peer-reviewed article (1)). Median time between PROSPERO registration and publication was 5 months for peer-reviewed SRs and 2 months for preprints.

Of the 2182 entries identified in COVID-19 L-OVE, 51 published SRs focused on prevention and were included. Similar to the PROSPERO sample, most published SRs focused on public health interventions (21). The number of included primary studies ranged between 0 and 64 (median: 7). Nine published SRs did not include any studies because of a lack of primary studies.

Conclusion Considering the urgent information needs of policymakers and the public, our findings reveal the high-speed publication of preprints and lack of primary studies in the beginning of the COVID-19 crisis. Further meta-research on COVID-19 SRs is important to improve research efficiency among researchers across the world.

PROSPERO registration number CRD42021240423.

INTRODUCTION

The COVID-19 pandemic is still impacting almost all countries worldwide. By 21 March

Strengths and limitations of this study

- ⇒ We systematically described Prospective Register of Systematic Reviews (PROSPERO) registrations and published systematic reviews identified in COVID-19 Living Overview of the Evidence (L-OVE) focusing on COVID-19 prevention (the most important intervention at the beginning of the pandemic).
- ⇒ Although the focus of this research was on the beginning of the pandemic, the findings and methodological approaches are important regarding pandemic preparedness to next disease outbreaks.
- ⇒ We considered systematic reviews which are important to guide evidence-based clinical and health policy decision-making at different stages (as PROSPERO registration and published as full systematic review, including preprints and peer-reviewed articles).
- ⇒ We estimated the proportion of PROSPERO registrations published as full systematic review within 8 to 16 months after registration.

2022, approximately 6 100 000 (<https://www.worldometers.info/coronavirus/>) people died due to COVID-19. Since the beginning of the pandemic in early 2020, researchers are responding to the virus by conducting a wide range of research from basic research to clinical studies and systematic reviews—to identify both the most effective prevention and treatment strategies.

In the COVID-19 pandemic and beyond, the synthesis of clinical studies within systematic reviews is essential to guide evidence-based clinical and health policy decision-making. Prior to 2011, only a few organisations, including Cochrane and the Joanna Briggs Institute, disseminated protocols (to define the research question and methods) for the planned or ongoing systematic reviews and the majority of reviews have become ‘public’ only at the time when the review was completed, peer-reviewed and published.¹ To

facilitate the transparency, reproducibility and usability of conducted systematic reviews, the International Prospective Register of Systematic Reviews (PROSPERO) was launched in February 2011 and it is recommended that each systematic review is registered before conducting the full systematic review.^{1 2} A PROSPERO registration can be updated once the review is completed and the full citation for the final report should be provided (including the uniform resource locator (URL)). Besides the increasing transparency regarding the conduct of systematic reviews, PROSPERO is also a valuable source to investigate the quality of current research (ie, for meta-research, research on research).

There have been several investigations (meta-research projects) on PROSPERO registrations^{3–5} and also on published systematic reviews of COVID-19.^{6–10} These meta-research studies focused on different methodological aspects, including the external validity of the research questions. Moreover, they often revealed poor reporting in COVID-19 research, both at the protocol stage and of the published systematic review. However, to our knowledge, there has been no investigation on PROSPERO registrations focusing on epidemiological and methodological characteristics and publication rates of prevention research during the beginning of the COVID-19 pandemic in 2020.

We conducted a meta-research study to investigate the number and characteristics of PROSPERO registrations and published systematic reviews identified in COVID-19 Living Overview of the Evidence (L-OVE) (a web-based app which aims to capture the entirety of all published research addressing COVID-19) focusing on measures to prevent COVID-19 and SARS-CoV-2 transmission during the beginning of the pandemic. Moreover, we determined the proportion of PROSPERO registrations (registered up to 31 August 2020) that have been published either as preprint or peer-reviewed systematic review (by 5 May 2021) and we piloted an approach to evaluate whether there are methodological differences between the PROSPERO registration and the corresponding published systematic review.

METHODS

This meta-research study followed the methods of a systematic review and is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guideline.¹¹ This meta-research project was prospectively registered in PROSPERO and has been part of a larger research project (CEOsyst, <https://covid-evidenz.de/>) funded by the German Federal Ministry of Education and Research (BMBF, grant number 01Kx2021). The registered protocol for the current project refers to (1) research on preventive measures for COVID-19 and (2) research on treatment measures for COVID-19 (on the date of April 2022, the research focusing on treatment is still 'ongoing'). We decided to present both research questions in separate publications

taking into account that prevention research has been the first response to COVID-19 and SARS-CoV-2 transmission in the early phase of the pandemic. We believe that evaluating both samples (prevention and treatment) together would not allow us to point out the importance of prevention research under pandemic circumstances in detail. Furthermore, stakeholders related to prevention research and research on treatment measures may (partly) differ: while epidemiologists, the general population and different stakeholders involved in public health decisions are more interested in preventive measures, clinicians and/or stakeholders involved in clinical guideline development may be more interested in COVID-19 treatment.

Systematic literature searches

First, we searched the PROSPERO registry (<https://www.crd.york.ac.uk/prospero/>) for entries registered between 1 January 2020 and 31 August 2020 (including the beginning of the pandemic) focusing on measures to prevent COVID-19 and SARS-CoV-2 transmission. The PROSPERO COVID-19 filter was applied and the search was restricted to specific fields (prevention, treatment). The automatic search was supplemented by manual searches. The keywords used are displayed in online supplemental material S1. The search strategy used for the automatic search is displayed in online supplemental material S2.

Second, we searched for published systematic reviews in COVID-19 L-OVE (<https://app.iloveevidence.com/>). COVID-19 L-OVE contains entries from over 40 medical databases (including Medline, Embase, Cochrane Library, CINAHL and others) and registries (including different national trial registries, medRxiv, bioRxiv, Research Square and others). Our search made use of filters as implemented in COVID-19 L-OVE ('Prevention and Treatment' and 'Systematic Review' filters, see online supplemental material S3). We did not further restrict our search by using keywords. The search for published reviews in COVID-19 L-OVE was performed on 5 May 2021. Additionally, we performed manual searches in Google Scholar that included the Center for Reviews and Dissemination (CRD) numbers of eligible PROSPERO registrations to make sure that we did not miss any PROSPERO registration published as full systematic review by 5 May 2021.

Eligibility criteria and study selection

We included PROSPERO registrations and full published systematic reviews, which addressed any preventive measure in any human population confronted with the COVID-19 pandemic reporting at least one health-related outcome. Preventive measures were defined as any intervention to prevent the transmission of the virus or to prevent an infection and/or the outbreak of the disease. We did not apply any restrictions regarding the comparators. We excluded PROSPERO registrations and full systematic reviews if measures were evaluated in relation to other viruses (eg, influenza). Moreover, interventions

to prevent aggravation of clinical symptoms were not considered.

Considering the fact that PROSPERO registrations do not provide abstracts, screening for eligibility was based on the full registration entry. The records identified in COVID-19 L-OVE, on the other hand, were screened using a two-step approach: (1) title and abstract screening and (2) full-text screening. The screening process in PROSPERO was conducted by two reviewers independently (JN and JS). The screening process in COVID-19 L-OVE was conducted by one reviewer (JN) and checked by another reviewer (JS). Disagreements were resolved by discussion between both reviewers or by consulting a third reviewer (CS) to reach consensus.

Data extraction

The following main characteristics of the PROSPERO registrations and published systematic reviews (identified in COVID-19 L-OVE) were extracted: reference (eg, registration ID, CRD number or DOI), corresponding author, institutional affiliation, review type (eg, network meta-analysis, living systematic review, rapid systematic review), population, intervention and primary outcomes (as defined in the inclusion criteria both in the PROSPERO registration and the published systematic review). Furthermore, we collected information on study types predefined in the PROSPERO registration and study types included in the published systematic reviews.

For PROSPERO registrations, we additionally extracted the registration date and anticipated completion date. Furthermore, to assess deviations between the PROSPERO registration and the corresponding published systematic review, we additionally extracted methodological key data, including information on the database search, the risk of bias assessment and the outcomes of interest. These key data were compared between the PROSPERO registration and the published systematic review to explore possible deviations, which may impact the methodological quality of systematic reviews.

For published systematic reviews identified in COVID-19 L-OVE, we additionally extracted the number of included studies, type of publication (preprint, journal publication) and whether a published protocol was available (either additionally to the PROSPERO registration or only as publication (journal publication or published on a platform other than PROSPERO)). Data extraction was performed by one reviewer (JN) and checked by a second reviewer (JS). Any disagreements were resolved by discussion or by involving a third reviewer (CS) if no agreement could be reached.

Outcomes

Our main outcomes were (1) the number and characteristics of COVID-19 PROSPERO registrations with focus on prevention that were registered during the first pandemic wave (between 1 January 2020 and 31 August 2020), (2) the number and characteristics of published COVID-19 systematic reviews with focus on prevention

identified in COVID-19 L-OVE up to 5 May 2021 and (3) the proportion of PROSPERO registrations that have been completed and published as full systematic review by 5 May 2021 (including the time between registration and publication).

Data synthesis

Data analysis involved a combination of qualitative synthesis and descriptive statistics for the identified PROSPERO registrations and also for the published systematic reviews. To estimate the proportion of PROSPERO registrations that were published as full systematic reviews, we matched the PROSPERO registrations and the published systematic reviews based on (1) key characteristics (population, intervention, study design), (2) URLs provided in the PROSPERO registration, (3) registration (CRD) numbers provided in the published systematic reviews and (4) comparing corresponding and/or first authors in PROSPERO registration with corresponding and/or first authors in the published systematic review.

Within our sample of PROSPERO registrations, we calculated the overall proportion of those registrations that were published as full systematic review by 5 May 2021. This analysis was based on dichotomous data (published vs not published). Additionally, we calculated the median time in months between the registration in PROSPERO and the publication of the systematic review (for PROSPERO registrations that were published by 5 May 2021) and stratified the published systematic reviews after publication type (preprint or peer-reviewed article or both).

Deviations from the PROSPERO registration and the corresponding published full systematic review were summarised descriptively.

Patient and public involvement

No patient involved.

RESULTS

Results of the literature searches

PROSPERO registrations

The searches in PROSPERO identified 612 registrations (figure 1, PRISMA flowchart). After screening (applying the eligibility criteria), 47 PROSPERO registrations were considered eligible.

Published systematic reviews identified in COVID-19 L-OVE

The search in COVID-19 L-OVE identified 2179 records (figure 2, PRISMA flowchart). From these, 25 were automatically identified as duplicates by the software Endnote, 1114 were excluded during title and abstract screening and 982 during full-text screening. In total, 58 records corresponding to 48 unique published systematic reviews met our inclusion criteria. Our manual searches identified three more systematic reviews. Finally, we included 51 published systematic reviews.

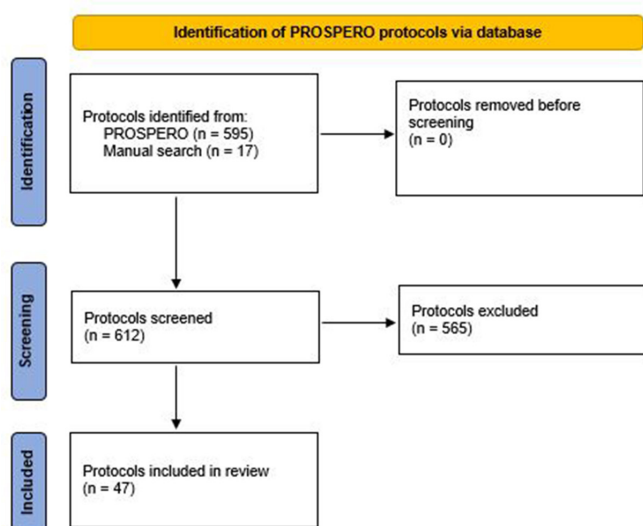


Figure 1 PRISMA flowchart¹¹ of PROSPERO registrations between 1 January 2020 and 31 August 2020. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; PROSPERO, Prospective Register of Systematic Reviews.

Characteristics of PROSPERO registrations

The key characteristics of the 47 PROSPERO registrations are presented in [table 1](#). Detailed characteristics are

Table 1 Characteristics of PROSPERO registrations

| Characteristics | N (%) |
|--|----------|
| Total | 47 (100) |
| Institutional affiliation: | |
| Asia | 13 (28) |
| Latin America | 12 (26) |
| Europe | 10 (21) |
| North America | 6 (13) |
| Africa | 4 (9) |
| Australia | 1 (2) |
| International cooperation | 1 (2) |
| Population: | |
| General population | 20 (43) |
| High-risk population* | 18 (38) |
| Mixed population | 7 (15) |
| Other population | 2 (4) |
| Intervention: | |
| Public health intervention | 20 (43) |
| Personal protective equipment | 10 (21) |
| Vaccination | 9 (19) |
| Pharmaceutical prevention | 4 (9) |
| Others | 4 (9) |
| Outcomes†: | |
| Incidence or prevalence of COVID-19 and/or SARS-CoV-2 transmission | 47 (100) |
| Mortality | 20 (43) |
| Disease severity | 16 (34) |
| Safety | 13 (28) |
| Others | 10 (21) |
| Review type: | |
| (Network) Meta-analysis | 23 (49) |
| Systematic review | 10 (21) |
| Rapid review | 10 (21) |
| Living systematic review | 4 (9) |
| Publication status of PROSPERO registrations (5 May 2021): | |
| Published as full systematic review | 13 (28) |
| No publication identified | 34 (72) |
| Anticipated completion date provided in PROSPEROs: | |
| Before 5 May 2021 | 35 (74) |
| After 5 May 2021 | 12 (26) |

*High-risk population: populations with a higher risk for COVID-19 (eg, healthcare workers).

†In some systematic reviews, more than one characteristic applies. PROSPERO, Prospective Register of Systematic Reviews.

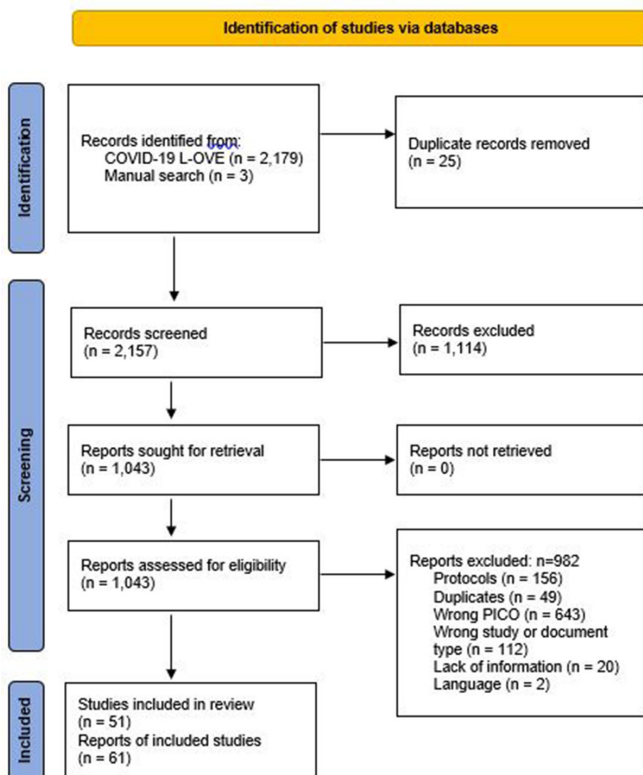


Figure 2 PRISMA flowchart¹¹ of published systematic reviews identified in COVID-19 L-OVE (search on 5 May 2021). L-OVE, Living Overview of the Evidence; PICO, Population Intervention Comparison Outcome; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

provided in online supplemental material S4.

Affiliation of main investigator

The institutional affiliation of the main investigator was based in Asia (13/47), Latin America (12/47), Europe (10/47), North America (6/47) and others.

Population, intervention and outcomes

Most PROSPERO registrations (38/47) set their focus on the general population and/or on high-risk populations (elderly, populations with morbidities, healthcare workers or others having contact with patients with COVID-19). Almost half of the PROSPERO registrations (20/47) focused on public health interventions (eg, mass screening, quarantine, boarder restrictions, hygiene or distance, or a combination of different strategies). The most frequently predefined outcomes were incidence or prevalence of COVID-19 and/or SARS-CoV-2 transmission (47/47), mortality rates (20/47) and disease severity (defined, eg, as severity of symptoms or hospitalisation, 16/47).

PROSPERO registrations published as full systematic reviews

Between 8 and 16 months after registration, 13/47 of the PROSPERO registrations were published as full systematic review. Therefrom, 6/13 were peer-reviewed articles (including n=1 Cochrane review), 6/13 were preprints and 1/13 was published as preprint and peer-reviewed article (online supplemental material S4).

When comparing the PROSPERO registrations with the corresponding published systematic review, we identified concerns regarding the methodology in 5/13 reviews. The concerns mainly refer to (1) the selection of the reported results (ie, predefined outcomes in the PROSPERO registration and reported outcomes in the published systematic review showed major differences (3/5 reviews)) and (2) the predefined risk of bias assessment, which was finally not conducted in the published systematic review (2/5 reviews). The remaining systematic reviews (8/13) showed no or only (very) minor deviations—mainly related to the fact that the systematic review authors searched less databases to identify primary studies than indicated in PROSPERO (see also online supplemental material S5).

Median time between PROSPERO registration and the date of the publication was 5 months for peer-reviewed articles (n=6, first quartile: 2.5, third quartile: 7.5, range: 1–9 months) and 2 months for preprints (n=7, first quartile: 1.5, third quartile: 4, range: 1–7 months).

Characteristics of published systematic reviews identified in COVID-19 L-OVE

The main characteristics of the 51 published systematic reviews identified in COVID-19 L-OVE are presented in table 2. Detailed characteristics are provided in Online supplemental material S6).

Affiliation of main investigator

The institutional affiliation of the investigating groups was mostly based in Europe (19/51), Asia (15/51), North America (9/51) and others (8/51).

Table 2 Characteristics of published systematic reviews identified in COVID-19 L-OVE

| Characteristics | N (%) |
|--|----------|
| Total | 51 (100) |
| Institutional affiliation: | |
| Europe | 19 (37) |
| Asia | 15 (29) |
| North America | 9 (18) |
| Latin America | 4 (8) |
| Africa | 4 (8) |
| Population: | |
| General population | 26 (51) |
| High-risk population* | 16 (31) |
| Mixed population | 8 (16) |
| Other population | 1 (2) |
| Intervention: | |
| Public health intervention | 21 (41) |
| Pharmaceutical prevention | 9 (18) |
| Personal protective equipment | 8 (16) |
| Vaccination | 8 (16) |
| Others | 5 (10) |
| Outcomes†: | |
| Incidence or prevalence of COVID-19 and/or SARS-CoV-2 transmission | 36 (71) |
| Effectiveness‡ | 20 (39) |
| Safety | 16 (31) |
| Disease severity | 5 (10) |
| Mortality | 4 (8) |
| Others | 8 (16) |
| Review type: | |
| Systematic review | 18 (35) |
| Rapid review | 17 (33) |
| (Network) Meta-analysis | 13 (28) |
| Living systematic review | 3 (6) |
| Publication status: | |
| Preprint | 13 (25) |
| Peer-reviewed publication | 28 (55) |
| Both | 10 (20) |
| Study types identified in the systematic reviews†: | |
| Non-randomised studies of interventions | 29 (57) |
| Randomised controlled trials | 12 (24) |
| Modelling studies | 12 (24) |
| Published protocol or PROSPERO registration†: | |
| No protocol published | 29 (57) |
| PROSPERO registration | 17 (33) |

Continued

Table 2 Continued

| Characteristics | N (%) |
|--|--------|
| Only protocol published | 5 (10) |
| Protocol published + PROSPERO registration | 3 (6) |

*High-risk population: population with a higher risk for COVID-19 (eg, healthcare workers).
†In some systematic reviews, more than one characteristic applies.
‡General effectiveness in terms of preventing the disease or transmission of the virus (with a wide range of definitions).
L-OVE, Living Overview of the Evidence; PROSPERO, Prospective Register of Systematic Reviews.

Population, intervention and outcomes

The focus in terms of population and intervention was comparable to the PROSPERO registrations. Most published systematic reviews set their focus on the general population and/or high-risk populations (50/51) and almost half of the publication (21/51) evaluated public health interventions (eg, wearing masks, social distancing, handwashing, screening for the virus). The most frequent-reported outcomes focused on the incidence or prevalence of COVID-19 or SARS-CoV-2 transmission (36/51), effectiveness (with a wide range of definitions, 20/51) and safety (16/51).

Publication status

In total, 13/51 systematic reviews were published as preprints, both as preprint and peer-reviewed publication (10/51) or as peer-reviewed publication (28/51).

Studies identified in systematic reviews

The published systematic reviews included mostly non-randomised studies of interventions (29/51) and/or randomised controlled trials (12/51) and/or modelling studies (12/51). In 9/51 systematic reviews, no clinical studies were included. Overall, the total number of included studies ranged between 0 and 64 (figure 3).

Protocol published prior to publication of systematic review

In total, 17/51 published systematic reviews were registered in PROSPERO and 3/17 of the registered PROSPERO registries were additionally published in a peer-reviewed journal, including one Cochrane protocol. Furthermore, for 5/51 systematic reviews, we identified a protocol on a platform other than PROSPERO (on the Open Science Framework platform (OSF.io) or on the website of the affiliated institution). For the remaining 29/51 published systematic reviews, neither a PROSPERO entry nor a published protocol exists.

DISCUSSION

Main findings

In contrast to the PROSPERO registrations where most prevention research was initiated in Asia (mainly India and China), followed by Latin America (mainly Brazil)

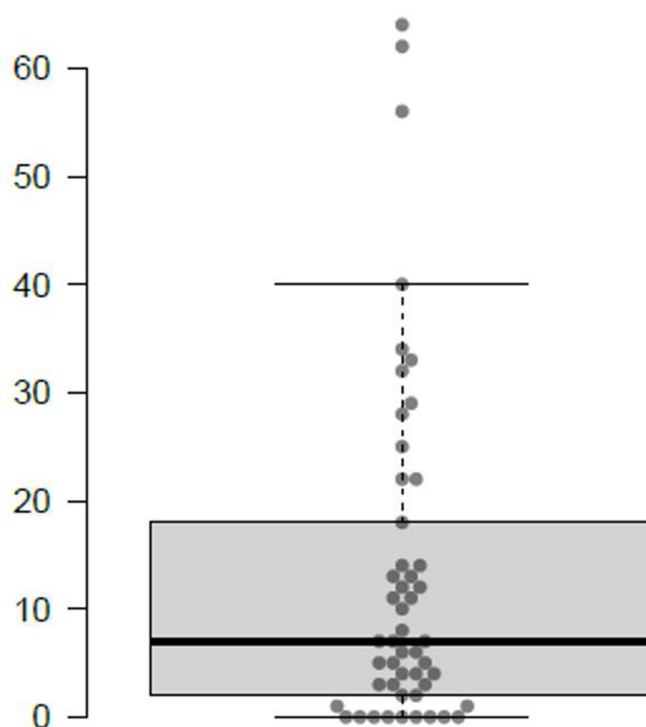


Figure 3 Boxplot for number of included studies within published systematic reviews identified in COVID-19 L-OVE. Upper whisker (40) and lower whisker (0) extend 1.5 times the IQR from the third and first quartile. Box height represents third quartile (75%)=18 and first quartile (25%)=3; IQR=15; Centre line inside the box represents median=7. Each dot represents one sample point. n=50 sample points. Boxplot was created with <http://shiny.chemgrid.org/boxplotr/> based on R statistics software. L-OVE, Living Overview of the Evidence

and Europe (mainly UK), published systematic reviews identified in COVID-19 L-OVE were affiliated with European countries (mainly UK) followed by Asia (mainly India and China) and North America (USA and Canada). Similar to the PROSPERO registrations, most of the published systematic reviews focused on public health interventions and on the general or high-risk population. Outstanding, at the beginning of the pandemic preventive measures particularly in school populations were not adequately considered (n=2 PROSPERO registrations, n=1 published systematic review).

Approximately, 20% (9/51) of the published systematic reviews identified in COVID-19 L-OVE did not include any primary clinical study addressing the research question of interest. The reason for these 'empty reviews' may be associated with restrictions regarding the predefined eligible study design such as randomised controlled trials or a general lack of studies. While it is obvious that these 'empty reviews' may not be useful for decision-making¹² they reveal important research gaps to initiate primary studies.

Of the systematic reviews identified in COVID-19 L-OVE, 45% (23/51) were published as preprints. Preprints have played an important role in the COVID-19

pandemic. For example, postings on the preprint server MedRxiv have increased by over 400%: from over 580 in the last 4 months in 2019 to over 2500 in the first 4 months in 2020. Additionally, views of preprint have increased by 100%.¹³ Besides bypassing the often-delaying peer-review process, preprint studies also benefit from immediate open access dissemination and facilitate collaborations between researchers worldwide. However, the increasing adoption of preprint studies is also associated with pitfalls: for example, even before the pandemic, up to 85% of research was ‘wasted’ and/or biased due to poor research questions, poor study designs and study methodology, poor reporting and selective publication.^{14–16} Taking into account the time pressure and often an inadequate research infrastructure, many of these problems have been amplified in COVID-19 research.^{6–10} Moreover, a lacking critically scientific validation by peer review may particularly impact the large number of preprint publications.¹⁷

Comparison with other meta-research

To our knowledge, there is no other meta-research project published or ongoing that describes the characteristics of systematic reviews of COVID-19 prevention measures at the protocol stage (ie, when registered in PROSPERO) and for published systematic reviews. For example, Andersen *et al*¹⁸ searched for published meta-analyses indexed in the PubMed database (<https://pubmed.ncbi.nlm.nih.gov/>) and for corresponding *a priori* registered PROSPERO entries focusing on any clinical intervention—but before the COVID-19 crisis. In this meta-research, one-third of the 2475 meta-analyses identified were affiliated with institutions in England or China, followed by another third from USA, Canada, Australia and Brazil. These are basically the same countries we also identified as the ‘leaders in the pandemic’—except for Australia, where the COVID-19 incidence was very low during the early phase of the pandemic.¹⁹ Furthermore, approximately 20% of the meta-analyses in Andersen *et al*¹⁸ were published within 0 to 9 months after registration in PROSPERO. Considering that our meta-research focused on preventive measures in COVID-19 and also included preprint publications, it is difficult to compare our findings with the results of Andersen *et al*. It further remains unclear how many of the PROSPERO registrations in our sample have been stopped before completion or rejected for publication or where still under ‘peer review’, whereas in Andersen *et al*,¹⁸ the study sample consisted only of meta-analyses that have all been published successfully.

Strengths and limitations

The current meta-research study represents characteristics of PROSPERO registrations and published systematic reviews on preventive measures—the most important intervention—at the beginning of the COVID-19 crisis. Although this meta-research project is based on small samples (owing to the first phase of the COVID-19 crisis and the fact that adequate prevention research

had to be ‘established’ at this stage) and a limited external validity (owing to the dynamic of the COVID-19 pandemic) concealing these findings would be contra productive regarding pandemic preparedness to next disease outbreaks, particularly by ‘other’ viruses causing epidemics or pandemics. We also believe that the established methodology related to meta-research studies within this publication will be beneficial for other researchers, epidemiologists and/or different stake holders when conducting research on research (meta-research) to investigate the quality and characteristics of current evidence synthesis and to support evidence-based clinical and health policy decision-making.

CONCLUSION

Most research on preventive measures in form of evidence synthesis was conducted in Asia, Europe and South America and addressed public health interventions. Furthermore, we found that almost 20% (9/51) of the published systematic reviews on prevention identified in COVID-19 L-OVE were empty, implicating the lack of primary studies at this early stage of the pandemic.

To improve cooperation strategies among research groups and also between policymakers worldwide, our meta-research indicated that it is important to investigate reasons for not publishing initiated research projects in more detail. Moreover, we would like to stress the importance of investigating deviations between what was originally predefined and planned by using, for example, data from the PROSPERO register and/or other platforms or published review protocols and what was finally reported in the published systematic review (ie, investigating reporting bias and dissemination bias) using larger samples.

Although preprints allow fast dissemination particularly in pandemic situations, such form of publication need to be handled cautiously owing to the lacking peer review and authors need to be strongly encouraged to publish their findings also in a peer-reviewed journal.

Overall, PROSPERO is a platform that enables communication among authors of systematic reviews worldwide. Therefore, we feel it is important to encourage authors of systematic reviews to register their research in PROSPERO, to keep the PROSPERO entry updated and clearly describe potential deviations between the PROSPERO entry (or any other published protocol) and the published full systematic review.

Contributors JN, JJM and CS conceptualised the aim of this meta-research project and designed the methodology. JN, JS and CS were involved in screening, data extraction and data synthesis. JN prepared the original draft. JS, WS, JJM and CS contributed to the refinement (review and editing) of the draft. CS supervised all steps of this meta-research project. JJM obtained the financial support supporting this study. All the authors reviewed and agreed to the final version being submitted. CS is guarantor.

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Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

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Provenance and peer review Not commissioned; externally peer reviewed.

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S1. Search strategy used for manual search in PROSPERO

Search string:

(prevention OR transmission OR prophyla*) AND (covid-19 OR sars-cov-2 OR coronavirus OR sars-cov OR sars OR mers)

AND (

(BCG OR vaccine OR vaccines OR vaccination)

OR (personal protective equipment OR gloves OR mask OR PPE)

OR (public health OR social distancing OR physical distancing OR screening)

)

S2. Search strategy used for automatic search in PROSPERO

((coronavirus or corona-virus) AND (wuhan or beijing or shanghai or Italy or South-Korea or korea or China or Chinese or 2019-nCoV or nCoV or COVID-19 or Covid19 or SARS-CoV* or SARSCov2 or ncov)) OR (pneumonia AND Wuhan) or "COVID-19" or "2019-nCoV" or "SARS-CoV" or SARSCOV2 or 2019-nCov or "2019 coronavirus" or "2019 corona virus" or covid19 or ncov OR "novel corona virus" or "new corona virus" or "nouveau corona virus" or "2019 corona virus" OR "novel coronavirus" or "new coronavirus" or "nouveau coronavirus" or "2019 coronavirus")

AND (Intervention OR Prevention):RT

NOT Animal:DB

WHERE CD FROM 01/01/2020 TO 31/08/2020

S3. Search strategy used for automatic search in COVID-19 L-OVE

The following search string is used as the main Boolean strategy by the repository COVID-19 L-OVE to identify articles that address any issue concerning COVID-19. According to the repository providers,[1] it is adapted to the syntax of each source and complemented by manual searches.

```
*COVID* OR *coronavir* OR *coronovir* OR *betacoronavir* OR *beta-coronavirus* OR "corona virus" OR "virus corona" OR "corono virus" OR "virus corono" OR *neocoronavir* OR hcov* OR *2019-ncov* OR *cv19* OR *cv-19* OR "cv 19" OR n-cov* OR ncov* OR (wuhan* AND (virus OR viruses OR viral)) OR *cv-19* OR sars* OR sari OR "severe acute respiratory syndrome" OR antisars* OR anti-sars* OR "corona patients" OR *pandemi*
```

The following sources are used for the automated searches:

- Pubmed/medline (updated several times a day)
- EMBASE (updated weekly)
- CINAHL (updated weekly)
- PsycINFO (updated weekly)
- LILACS (Latin American & Caribbean Health Sciences Literature) (updated weekly)
- Wanfang Database (updated every 2 weeks)
- CBM - Chinese Biomedical Literature Database (updated every 2 weeks)
- CNKI - Chinese National Knowledge Infrastructure (updated every 2 weeks)
- VIP - Chinese Scientific Journal Database (updated every 2 weeks)
- IRIS (WHO Institutional Repository for Information Sharing) (updated weekly)
- IRIS PAHO (PAHO Institutional Repository for Information Sharing)) (updated weekly)
- IBECS - Índice Bibliográfico Español en Ciencias de la Salud (Spanish Bibliographic Index on Health Sciences) (updated weekly)
- Microsoft Academic (last searched: 23 August 2021)
- ICTRP Search Portal (updated daily)
- Clinicaltrials.gov (updated daily)
- ISRCTN registry (updated daily)
- Chinese Clinical Trial Registry (updated daily)
- IRCT - Iranian Registry of Clinical Trials (updated daily)
- EU Clinical Trials Register: Clinical trials for covid-19 (updated daily)
- NIPH Clinical Trials Search (Japan) - Japan Primary Registries Network (JPRN) (JapicCTI, JMACCT CTR, jRCT, UMIN CTR) (updated daily, via ICTRP search portal)
- UMIN-CTR - UMIN Clinical Trials Registry (updated daily, via ICTRP search portal)
- JRCT - Japan Registry of Clinical Trials (updated daily, via ICTRP search portal)
- JAPIC Clinical Trials Information (updated daily, via ICTRP search portal)
- Clinical Research Information Service (CRIS), Republic of Korea (updated daily, via ICTRP search portal)
- ANZCTR - Australian New Zealand Clinical Trials Registry (updated daily, via ICTRP search portal)
- ReBec - Brazilian Clinical Trials Registry (updated daily, via ICTRP search portal)
- CTRI - Clinical Trials Registry - India (updated daily, via ICTRP search portal)
- RPCEC - Cuban Public Registry of Clinical Trials (updated daily, via ICTRP search portal)
- DRKS - German Clinical Trials Register (updated daily, via ICTRP search portal)
- LBCTR - Lebanese Clinical Trials Registry (updated daily, via ICTRP search portal)
- TCTR - Thai Clinical Trials Registry (updated daily, via ICTRP search portal)

- NTR - The Netherlands National Trial Register (updated daily, via ICTRP search portal)
- PACTR - Pan African Clinical Trial Registry (updated daily, via ICTRP search portal)
- REPEC - Peruvian Clinical Trial Registry (updated daily, via ICTRP search portal)
- SLCTR - Sri Lanka Clinical Trials Registry (updated daily, via ICTRP search portal)
- medRxiv (updated several times a day)
- bioRxiv (updated several times a day)
- SSRN Preprints (updated several times a day)
- ChinaXiv (updated every 2 weeks)
- SciELO Preprints (updated weekly)
- Research Square (updated daily)

We used the database as follows:

| | |
|---|---|
| Filters: | "Prevention and treatment", "Systematic reviews" |
| Date of the search: | 05/05/2021 |
| Number of hits imported into Endnote: | 2,179 |
| After automatic deduplication in Endnote: | 2,154 |

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S4. Characteristics of systematic review protocols identified in PROSPERO for prevention of COVID-19

Table 1 Characteristics of systematic review protocols identified in PROSPERO for prevention of COVID-19

| Corresponding author | Country of affiliation of the review ^a | Review type | Population | Intervention | Outcomes | Study type included | Registration date | Anticipated completion date | Link ^b | Publication (date of publication) |
|------------------------------------|---|------------------------|--|---|---|---------------------|-------------------|-----------------------------|------------------------|-----------------------------------|
| Public health interventions (n=20) | | | | | | | | | | |
| Ahmed | USA | SR, MA | persons working in non-healthcare or non-school settings (general population) | workplace Non-pharmaceutical measures | COVID-19 incidence, hospitalizations, COVID-19 mortality | RCT, NRSI, MS | 04/05/2020 | 31/07/2020 | 182660 | no |
| Ayouni | Tunisia | SR | general population | PHIs | effectiveness of mitigation of the spread of COVID-19 | RCT, NRSI | 30/06/2020 | 17/08/2020 | 196018 | no |
| Cuadrado | Chile | living SR | school population | school practices to promote social distancing | all-cause/COVID-19 mortality, COVID-19 infection rate, reproduction number | RCT, NRSI, MS | 21/04/2020 | 17/05/2020 | 180701 | no |
| Delgrange | UK, England | rapid SR | high-income countries or economies (general population) | PHIs | mortality, COVID-19 incidence, COVID-19 reproduction number, | n.r. | 19/05/2020 | 31/07/2020 | 183989 | no |
| Elchall | Cochrane France | living SR, MA, NMA | high risk patients, close contacts of COVID-19 patients, healthcare workers, healthy volunteers (mixed population) | vaccination, prophylactic interventions, PPE, movement control strategies | COVID-19 incidence, hospital or ICU admissions or death, all-cause mortality, clinical efficacy | RCT, NRSI | 28/04/2020 | 31/12/2021 | 182600 | no |
| Frazer | UK, Ireland | SR | adults in long term care facilities (residents, employees, visitors) (high risk population) | any intervention to reduce COVID-19 transmission | COVID-19 morbidity, symptoms, mortality | any type | 02/07/2020 | 31/08/2020 | 191569 | yes, preprint (03/11/2020) |
| Fuentealba-Torres | Chile | rapid SR | countries in COVID-19 pandemic (general population) | quarantine restrictions | COVID-19 incidence, prevalence, mortality | NRSI, MS | 05/05/2020 | 31/01/2021 | 183701 | no |
| Iezadi | USA | SR, realist review, MA | general population | PHIs | COVID-19 incidence, basic reproduction number, mortality | NRSI | 20/05/2020 | 28/02/2021 | 186855 | no |
| Juneau | Canada | SR | general population | contact tracing | COVID-19 transmission | RCT, NRSI, MS | 14/07/2020 | 13/08/2020 | 198462 | yes, preprint (25/07/2020) |
| Khatib | India | rapid SR, MA | individuals at risk for COVID-19 (most likely high risk population) | WASH (Water, sanitation and Hygiene) interventions | COVID-19 incidence, hospitalisations, COVID-19 mortality, safety | NRSI, MS | 16/04/2020 | 11/05/2020 | 179663 | no |

| | | | | | | | | | | |
|--------------------------------------|---------------------------|----------|--|--|---|---------------|------------|------------|------------------------|--|
| Li | China | SR, MA | people at risk of infection from COVID-19, MERS or SARS (high risk population) | physical interventions (PI, e.g., hand hygiene, PPE, isolation, social distancing) | mortality, COVID-19 incidence and severity, hospital admissions, safety | any type | 15/04/2020 | 15/08/2020 | 178638 | no |
| Mbakaya | Malawi | SR | any community setting (workplace, market, school settings, family, neighbourhood) (general population) | any community-based measures to prevent COVID-19 | COVID-19 incidence, transmission | NRSI, MS | 18/08/2020 | 30/10/2020 | 204984 | yes, preprint (30/10/2020) |
| Milanese | Australia | rapid SR | general population | screening tools | COVID-19 infections | NRSI, MS | 21/08/2020 | 15/10/2020 | 205274 | no |
| Oliveira | Brazil | SR | general population | any intervention (based on health promotion) | effectiveness (universal health and social protection coverage) | RCT, NRSI | 20/04/2020 | 30/06/2020 | 180066 | no |
| Pearce-Smith | Public Health England, UK | rapid SR | persons in school setting (children and staff) | school measures during COVID-19 pandemic (re-openings, limited closures, other control measures) | SARS-CoV-2 infection rate in children and staff, transmission of SARS-CoV-2 within school settings, COVID-19 outbreaks in schools | RCT, NRSI, MS | 15/06/2020 | 24/07/2020 | 191867 | yes, online document (09/04/2021) |
| Pintel Ramos | Brazil | SR | health care workers (high risk population) | recommendations for prevention (e.g., using PPE) | COVID-19 infections in healthcare workers | NRSI | 12/08/2020 | 11/12/2020 | 190491 | no |
| Schuneman n | Canada | rapid SR | close contacts of COVID-19 patients (high risk population) | distance (1m+) with or without mask and/or eye protection | disease transmission, COVID-19 infection, acceptability, disease severity | any type | 16/04/2020 | 28/04/2020 | 177047 | yes, journal (01/06/2020), preprint (26/05/2020) |
| Shah | India | SR, MA | general population | PHIs | COVID-19 infection rate, recovery rate, mortality, rate of growth of cases | any type | 20/04/2020 | 31/07/2020 | 180528 | no |
| Silva | Brazil | SR | elderly (60+) in home care (high risk population) | measures to prevent COVID-19 | COVID-19 prevalence | RCT, NRSI, QS | 12/06/2020 | 28/05/2021 | 188952 | no |
| Wangge | Indonesia | rapid SR | asymptomatic population in COVID-19 pandemic (general population) | mass screening | COVID-19 incidence, mortality, transmission (basic reproduction number), resource use | NRSI, MS | 29/06/2020 | 06/07/2020 | 190546 | yes, journal (18/12/2020) |
| Personal protective equipment (n=10) | | | | | | | | | | |
| Al-Moraissi | Saudi Arabia | rapid SR | adult dental health care workers (high risk population) | enhanced PPE | effectiveness against COVID-19 infection | RCT NRSI | 25/06/2020 | 30/09/2020 | 192912 | yes, preprint (23/11/2020) |
| Conceição de Jesus | Brazil | SR, MA | healthcare workers assisting COVID-19 patients (high risk population) | PPE | COVID-19 infections in healthcare workers | RCT, NRSI | 20/04/2020 | 31/12/2020 | 180264 | yes, journal, but not included ^c (05/09/2020) |
| Ekwaro | Uganda | rapid SR | general population, healthcare workers in low- and middle | masks (medical or non-medical) | COVID-19 infections | RCT, NRSI | 20/08/2020 | 30/11/2020 | 205136 | no |

| | | | | | | | | | | |
|-------------------|--|-------------|--|--|---|-------------------|------------|------------|------------------------|----------------------------|
| | | | income countries (mixed population) | | | | | | | |
| Griswold | UK, England | rapid SR | healthcare workers in hospital setting during COVID-19 pandemic (esp. emergency neurosurgical care) (high risk population) | use of PPE, rapid testing, chest CT for patients | COVID-19 incidence | RCT, NRSI | 30/07/2020 | 31/08/2020 | 198267 | no |
| Gupta | India | SR | general population | face mask (any type) | COVID-19 transmission: contacts/secondary attack ratio | RCT, NRSI | 06/05/2020 | 10/06/2020 | 183807 | no |
| Kurniawan | Indonesia | SR | general population | face mask (any type) | COVID-19 infections, COVID-19 mortality | RCT, NRSI | 11/05/2020 | 01/09/2020 | 184371 | no |
| Ortiz-Muñoz | Chile | SR, MA | healthy population at risk of COVID-19, MERS, SARS (mixed population) | gloves (any type) | COVID-19 infections, hospitalizations, all-cause mortality, safety | RCT, NRSI | 27/05/2020 | 29/06/2020 | 188674 | yes, preprint (26/01/2021) |
| Schmölzer | International Liaison Committee on Resuscitation | SR, MA | healthcare workers attending deliveries (high risk population) | PPE | transmission of COVID-19 infection to healthcare workers, quality of neonatal resuscitation | RCT, NRSI | 16/04/2020 | 05/05/2020 | 178250 | no |
| Silveira | Brazil | SR, MA | healthcare workers assisting COVID-19 patients (high risk population) | techniques of using of PPE | COVID-19 infections in healthcare workers | RCT, NRSI | 15/07/2020 | 30/11/2020 | 198631 | no |
| Teoh | China | SR, MA | healthcare workers performing surgical, endoscopic and anaesthetic procedures on patients with COVID-19, SARS or MERS (high risk population) | use of PPE | transmission of SARS-CoV-2, SARS-CoV and MERS-CoV, risk of infection | RCT, NRSI | 28/04/2020 | 24/05/2020 | 182298 | no |
| Vaccination (n=9) | | | | | | | | | | |
| Adhikari | Illinois, USA | SR, MA | adults (18+) with or without comorbidities (mixed population) | BCG vaccine | COVID-19 incidence and severity at 6 (9, 12) months | RCT | 24/04/2020 | 31/05/2021 | 182122 | no |
| Alhassane | France | SR, NMA | healthy adults (general population) | COVID-19 vaccine | COVID-19 incidence, immunogenicity, safety | RCT (phase I-III) | 23/07/2020 | 31/08/2021 | 200012 | no |
| Azhir | Canada | SR, MA, NMA | healthy adults (18-60) not previously infected (general population) | COVID-19 vaccine | all-cause mortality, COVID-19 incidence, safety | RCT, NRSI | 26/08/2020 | 31/10/2021 | 204881 | no |
| Baliga | India | SR, MA | health care workers with or without comorbidities (high risk population) | BCG vaccine | COVID-19 mortality, COVID 19 incidence and severity | RCT | 08/06/2020 | 10/06/2021 | 189394 | no |

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|------------------------------------|-------------|------------------------|---|--|--|-----------------|------------|------------|------------------------|-----------------------------------|
| Henriques | Portugal | SR, MA | adults (18+) with or without comorbidities, healthcare professionals (mixed population) | BCG vaccine | COVID-19 incidence and severity | RCT, NRSI | 02/06/2020 | 31/07/2021 | 188486 | no |
| Kwasi Korang | Denmark | living SR, NMA, IPD-MA | people not previously infected (general population) | COVID-19 vaccine | all-cause mortality, COVID-19 incidence, safety | RCT | 01/07/2020 | 01/06/2021 | 196492 | no |
| Remón Torres | Peru | SR, MA | healthy adults (18+) not previously infected with SARS-CoV-2 (general population) | COVID-19 vaccine | COVID-19 incidence | RCT (phase III) | 28/08/2020 | 31/01/2022 | 206390 | no |
| Singh | India | SR, MA | healthy people without pre-exposure or infection with COVID-19 (general population) | BCG vaccine | COVID-19 mortality, COVID-19 incidence, safety | RCT, NRSI | 18/08/2020 | 15/10/2020 | 204466 | yes, preprint (28/10/2020) |
| Trunk | Switzerland | SR, MA | children and adults (0-80) (general population) | BCG vaccine, MCV, OPV, SPV, DTP vaccine | COVID-19 incidence and severity | RCT, NRSI | 01/05/2020 | 30/06/2021 | 183428 | no |
| Pharmaceutical interventions (n=4) | | | | | | | | | | |
| Lenza | Brazil | SR, MA | adults (18+) with household or occupational exposure (high risk population) | CQ, HCQ | COVID-19 incidence and severity, hospitalisation, antibodies, mortality, clinical efficacy, safety | RCT, NRSI | 10/07/2020 | 31/12/2020 | 197070 | no |
| Meremikwu | Nigeria | SR, MA | peoples at high risk of exposure to COVID-19 (high risk population) | CQ, HCQ (+/- azithromycin or clarithromycin) | COVID-19 incidence and severity; safety | RCT, NRSI | 02/06/2020 | 30/06/2020 | 184020 | no |
| Quintanilla Sánchez | Mexico | SR, MA | asymptomatic adults (18+) with exposure to COVID-19 (high risk population) | CQ, HCQ | COVID-19 incidence, safety, hospitalisation | RCT, NRSI | 14/04/2020 | 30/04/2021 | 177993 | no |
| Singh | UK | SR, MA | people at risk of exposure or with exposure to SARS-CoV-2 (high risk population) | CQ, HCQ (+/- other treatments) | COVID-19 incidence and severity, infections in close contacts, antibodies, mortality, clinical efficacy, safety, | RCT | 19/05/2020 | 08/06/2020 | 185220 | yes, Cochrane review (12/02/2021) |
| Other interventions (n=4) | | | | | | | | | | |
| El-Hajj Fuleihan | Lebanon | SR, MA | adults (18+) (general population) | vitamin D (supplementation, vitamin D deficiency) | COVID-19 seropositivity, risk of positive seroconversion to family members | RCT, NRSI | 14/08/2020 | 12/11/2020 | 203960 | yes, journal (24/03/2021) |
| Hernández Vásquez | Peru | SR | Individuals of all ages (healthy, pre-exposure, post-exposure to COVID-19, MERS or SARS) (mixed population) | chlorine dioxide, chlorine derivatives | clinical efficacy and safety | RCT, NRSI | 27/07/2020 | 27/08/2020 | 200641 | yes, journal (07/09/2020) |
| Wang | China | living SR, MA | asymptomatic people with/without exposure (pre-/ post-exposure) to COVID-19 (mixed population) | Western medicine, TCM agents; each alone or in combination | COVID-19-free survival, COVID-19 incidence, hospitalization, mortality, safety | RCT, NRSI | 08/06/2020 | 31/12/2021 | 190210 | no |

| | | | | | | | | | | |
|----|-------|---------|--|---------------------------|---|-----|------------|------------|------------------------|----|
| Xu | China | SR, NMA | hospital workers and laboratory technicians in high-risk virus laboratories (high risk population) | TCM (extracts from herbs) | COVID-19 infections, time and rate of disappearance of symptoms | RCT | 20/04/2020 | 01/06/2021 | 179399 | no |
|----|-------|---------|--|---------------------------|---|-----|------------|------------|------------------------|----|

BCG=Bacillus Calmette-Guérin; COVID-19=Corona-Virus Disease 2019; CQ=Chloroquine; CT=Computer Tomography; DTP=Diphtheria-Tetanus-Pertussis; HCQ=Hydroxychloroquine; ICU=Intensive Care Unit; IPD=Individual Participant Data; MA=Meta-Analysis; MCV=Measles Containing Vaccine; MERS = Middle East Respiratory Syndrome; MS=Modelling Studies; NMA=Network Meta-Analysis; n.r.=not reported; NRSI=Non-Randomized Studies of Interventions including, cohort studies, case-control-studies, cross-sectional studies and case series/reports; OPV=Oral Polio Vaccine; PHI=Public Health Intervention; PPE=Personal Protective Equipment; QS=Qualitative Studies; RCT=Randomized Controlled Trials; SARS =Severe Acute Respiratory Syndrom; SPV=Smallpox Vaccine; SR=Systematic Review; TCM=Traditional Chinese Medicine.

^acountry of institutional affiliation of corresponding and/or first author

^bLink to the PROSPERO protocol: https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=>>Record-ID<<

^cPublication found, but population, intervention, outcomes did not meet our inclusion criteria.

S5. Comparison of the methodologies described in PROSPERO and in the published systematic reviews

Table 4: Comparison of the methodology between protocols in our PROSPERO sample for which we also identified a full text publication by 05/05/2021 with their assigned full text publication

| | Author, Year | PROSPERO registration | Published systematic review | Differences between PROSPERO registration and published systematic review* |
|----|---|---|--|--|
| 1. | Frazer, 2020 Link to the PROSPERO: https://dx.doi.org/10.1101/2020.10.19.20222182 Link to the fulltext: https://dx.doi.org/10.1101/2020.10.19.20222182 | <u>Review type</u> : Systematic review <u>Predefined databases to be searched</u> : PubMed, EMBASE, CINAHL and the Cochrane Library, MedRxiv and Google Scholar <u>Predefined risk of bias</u> : Narrative summary of methodological quality (first version: Cochrane RoB tool and CASP) <u>Predefined main outcomes</u> : Not specified | <u>Review type/methodology</u> : Rapid systematic review (preprint) <u>Databases searched</u> : Medline, EMBASE, CINAHL, Cochrane Library, MedRxiv <u>Risk of bias</u> : MMAT <u>Main outcomes</u> : Morbidity data, case fatality rates, reductions in reported transmission rates, and facility characteristics associated with COVID-19 incidence | 1) Rapid review methodology (instead of predefined systematic review) 2) Risk of bias assessment tool changed => no impact because it's a reliable tool 3) Main outcomes: Outcomes were not predefined in the protocol Overall: Some concerns regarding the selection of the reported results |
| 2. | Juneau, 2020 Link to the PROSPERO: https://dx.doi.org/10.1101/2020.07.23.20160234 Link to the fulltext: https://dx.doi.org/10.1101/2020.07.23.20160234 | <u>Review type</u> : Systematic review <u>Predefined databases to be searched</u> : Medline, EMBASE, Global Health, EBM Reviews <u>Predefined risk of bias</u> : Grouping of studies based on design into higher quality (randomized trials) and lower quality (other designs) <u>Predefined main outcomes</u> : R ₀ and other measures of transmission | <u>Review type/methodology</u> : Systematic review (preprint) <u>Databases searched</u> : Medline, EMBASE, Global Health, EBM Reviews <u>Data synthesis</u> : Tabular description of study characteristics and main findings <u>Risk of bias</u> : Risk of bias was not assessed <u>Main outcomes</u> : Contact tracing effectiveness in the context of COVID-19 | 1) Risk of bias was not assessed as indicated in the PROSPERO registration => Impacts the validity of the review results 2) Main outcomes differed slightly in their definition => most likely has no impact on the published systematic reviews Overall: Some concerns regarding missing risk of bias assessment. |
| 3. | Chisale, 2020 Link to the PROSPERO: https://dx.doi.org/10.21203/rs.3.rs-98441/v1 Link to the fulltext: https://dx.doi.org/10.21203/rs.3.rs-98441/v1 | <u>Review type</u> : Systematic review <u>Predefined databases to be searched</u> : PubMed, EMBASE, PsycINFO, AMED, CINAHL, DOAJ, Medline and Google Scholar <u>Predefined risk of bias</u> : MMAT <u>Predefined main outcomes</u> : Reduction in the incidence of COVID-19 | <u>Review type/methodology</u> : Systematic review (preprint) <u>Databases searched</u> : PubMed, EMBASE, PsycINFO, AMED, CINAHL, DOAJ, Medline and Google Scholar <u>Risk of bias</u> : MMAT <u>Main outcomes</u> : To identify community-based interventions used to prevent COVID-19 in low- and middle-income countries | Main outcomes: Outcomes changed Overall: Some concerns regarding the selection of the reported result |

| | | | | |
|----|--|--|---|---|
| 4. | <p>Public Health England, 2021</p> <p>Link to the PROSPERO: 191867</p> <p>Link to the fulltext (Update 2): https://phe.koha-ptfs.co.uk/cgi-bin/koha/opac-retrieve-file.pl?id=9adedb17d5622f9cd7e42febcbadb19ad</p> <p>original version: https://ukhsa.koha-ptfs.co.uk/cgi-bin/koha/opac-de-tail.pl?biblionumber=62728&query_desc=covid%20school</p> | <p><u>Review type</u>: Rapid Review</p> <p><u>Predefined databases to be searched</u>: Medline, EMBASE, MedRxiv, WHO COVID-19 Research Database and Google Scholar</p> <p><u>Predefined risk of bias</u>: Evaluation of papers based on study design and main sources of bias, validated tools will not be used for primary studies</p> <p><u>Predefined main outcomes</u>: SARS-CoV-2 infection rate in children and staff, transmission of SARS-CoV-2 within school settings, COVID-19 outbreaks in schools.</p> | <p><u>Review type/methodology</u>: Rapid review (Online document without external peer-review)</p> <p><u>Databases searched</u>: Medline, EMBASE, MedRxiv, WHO COVID-19 Database (2-weekly updates) and Google Scholar (first version only)</p> <p><u>Risk of bias</u>: Quality criteria checklist for primary research</p> <p><u>Main outcomes</u>: SARS-CoV-2 infection rate in children and staff, transmission of SARS-CoV-2 within school settings, COVID-19 outbreaks in schools</p> | <p>No changes in the review methodology were identified.</p> <p>Overall: No major concerns.</p> |
| 5. | <p>Chu, 2020</p> <p>Link to the PROSPERO: 177047</p> <p>Link to the fulltext: https://dx.doi.org/10.1016/S0140-6736(20)31142-9</p> | <p><u>Review type</u>: Rapid systematic review</p> <p><u>Predefined databases to be searched</u>: PubMed, Medline, EMBASE, CINAHL, and the Cochrane Library, three Chinese databases and four COVID-19 specific databases (e.g., COVID-19 WHO, COVID-19 L-OVE), two platforms for trial registries</p> <p><u>Predefined risk of bias</u>: Cochrane RoB tool for RCTs and Newcastle-Ottawa Scale for non-RCTs</p> <p><u>Predefined main outcomes</u>: Transmission (confirmed or probable), acceptability, harms, COVID-19 infection, ICU admission and other main outcomes</p> | <p><u>Review type/methodology</u>: Systematic review with meta-analysis (peer-reviewed journal publication)</p> <p><u>Databases searched</u>: PubMed, Medline, EMBASE, CINAHL, and the Cochrane Library, four COVID-19 specific databases, WHO ICTRP, ClinicalTrials.gov</p> <p><u>Risk of bias</u>: Newcastle-Ottawa Scale was used for non-RCTs</p> <p><u>Main outcomes</u>: Risk of transmission (confirmed or probable; COVID-19, SARS or MERS), hospitalization, ICU admission, death, time to recovery, and other main outcomes (similar to the PROSPERO entry)</p> | <p>The review type changed (improved) from Rapid review to Systematic review.</p> <p>Overall: No major concerns.</p> |
| 6. | <p>Johanna, 2020</p> <p>Link to the PROSPERO: 190546</p> <p>Link to the fulltext: https://dx.doi.org/10.4081/jphr.2020.2011</p> | <p><u>Review type</u>: Rapid systematic review</p> <p><u>Predefined databases to be searched</u>: Medline, EMBASE, CINAHL, Cochrane Library, ScienceDirect, ProQuest, WHO SEARO database, Scopus, Wiley Library, Sage Journals, Taylor&Francis, SpringerLink, Hindawi, DOAJ</p> <p><u>Predefined risk of bias</u>: EPHPP tool</p> <p><u>Predefined main outcomes</u>: Incident cases, onward transmission, mortality, resource use</p> | <p><u>Review type/methodology</u>: Systematic review (peer-reviewed journal publication)</p> <p><u>Databases searched</u>: Medline, Cochrane Library, CINAHL, DOAJ, ProQuest, Sage Journals, Science Direct, Pubmed, Scopus, WHO Global Index Mediscus, Wiley Library, clinical trial registries</p> <p><u>Risk of bias</u>: EPHPP tool</p> <p><u>Main outcomes</u>: Incident cases, onward transmission, mortality, resource use</p> | <p>1) The review type changed (improved) from rapid review to systematic review.</p> <p>2) The number of databases for the literature search was slightly reduced, but main databases covered.</p> <p>Overall: No major concerns.</p> |

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| 7. | <p>Al-Moraissi, 2020 Link to the PROSPERO: 192912 Link to the fulltext: https://dx.doi.org/10.1101/2020.11.20.20235333</p> | <p><u>Review type:</u> Systematic review <u>Predefined databases to be searched:</u> Medline, EMBASE, CINAHL, CENTRAL, and Scopus <u>Predefined risk of bias:</u> Authors only referred to the GRADE assessment. <u>Predefined main outcomes:</u> Effectiveness of PPE against COVID-19 (not further predefined)</p> | <p><u>Review type/methodology:</u> Systematic review (preprint) <u>Databases searched:</u> Medline, EMBASE, CINAHL, CENTRAL, and Scopus <u>Risk of bias:</u> Because there was extreme heterogeneity among the included studies, RoB assessment was not conducted <u>Main outcomes:</u> Effectiveness of PPE against COVID-19 (not further defined)</p> | <p>No changes in the methodology were identified.</p> <p>Overall: No major concerns.</p> |
| 8. | <p>Bertoncello, 2020 Link to the PROSPERO: 180264 Link to the fulltext: https://www.researchgate.net/publication/346967846 <i>Personal Protective Equipment to Prevention of COVID-19 in Health Workers A Review</i> (Note: The CRD was not provided in the fulltext. However, by a comparison of PICO, methodology and authors, we could assign this review to the PROSPERO entry)</p> | <p><u>Review type:</u> Systematic review <u>Predefined databases to be searched:</u> PubMed, Virtual Health Library, SciELO Brasil, Web of Science, Google Scholar (three first pages), CAPES portal <u>Predefined risk of bias:</u> Authors only referred to the GRADE assessment, ROBINS-I for observational studies <u>Predefined main outcomes:</u> COVID-19 infection</p> | <p><u>Review type/methodology:</u> Review (peer-reviewed journal publication) <u>Databases searched:</u> Pubmed, Virtual Health Library, SciELO Brazil, Scopus, Web of Science, Google Scholar (three first pages) <u>Risk of bias:</u> Not assessed <u>Main outcomes:</u> an outcome in the safety of health workers</p> | <p>1) The review type changed from systematic review to a (non-systematic) "Review" in a peer-reviewed journal article. 2) GRADE assessment of certainty of the evidence was not conducted (meta-analysis was not deemed possible) 3) The outcome changed substantially</p> <p>Overall: Some concerns regarding the selection of the reported result</p> |
| 9. | <p>Morales Ferrer, 2020 Link to the PROSPERO: 188674 Link to the fulltext: https://dx.doi.org/10.31219/osf.io/uz4rs</p> | <p><u>Review type:</u> Systematic review <u>Predefined databases to be searched:</u> COVID-19 L-OVE, Medline, CENTRAL, EMBASE, WHO ICTRP <u>Predefined risk of bias:</u> RoB 2.0 for RCTs, ROBINS-I for non-RCTs <u>Predefined main outcomes:</u> COVID-19 cases</p> | <p><u>Review type/methodology:</u> Living systematic review (preprint) <u>Databases searched:</u> COVID-19 L-OVE <u>Risk of bias:</u> Joanna Briggs Institute Checklist for Analytical Cross Sectional Studies <u>Main outcomes:</u> COVID-19 cases</p> | <p>1) The review type changed (improved) to Living systematic review, 2) CENTRAL (not included in COVID-19 L-OVE) was not searched</p> <p>Overall: No concerns</p> |
| 10. | <p>Khera, 2020 Link to the PROSPERO: 204466 Link to the fulltext: https://dx.doi.org/10.21203/rs.3.rs-97073/v1</p> | <p><u>Review type:</u> Systematic review and meta-analysis <u>Predefined databases to be searched:</u> CENTRAL, Medline, ClinicalTrials.gov, preprint servers <u>Predefined risk of bias:</u> Cochrane RoB-2 for RCTs, ROBINS-I for observational studies <u>Predefined main outcomes:</u> Mortality, number of cases</p> | <p><u>Review type/methodology:</u> Systematic review and meta-analysis (preprint) <u>Databases searched:</u> Medline, Cochrane Library, ClinicalTrials.gov <u>Risk of bias:</u> Not reported <u>Main outcomes:</u> Mortality, number of cases</p> | <p>1) Risk of bias was not assessed, neither using RoB-2 nor ROBINS-I as was the plan.</p> <p>Overall: Some concerns regarding missing risk of bias assessment.</p> |

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| 11. | Singh, 2021 Link to the PROSPERO: 185220 Link to the fulltext: https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013587.pub2/full | <u>Review type</u> : Systematic review <u>Predefined databases to be searched</u> : CENTRAL, Medline, EMBASE, controlled-trials.com, COVID-NMA.com, Cochrane COVID-19 Study register <u>Predefined risk of bias</u> : Cochrane RoB tool <u>Predefined main outcomes</u> : Cases (confirmed), production of antibodies to SARS-CoV-2 | <u>Review type/methodology</u> : Cochrane review <u>Databases searched</u> : CENTRAL, Medline, EMBASE, controlled-trials.com, WHO ICTRP, COVID-NMA.com, Cochrane COVID-19 Study Register <u>Risk of bias</u> : No eligible trials were identified <u>Main outcomes</u> : Cases (confirmed), production of antibodies to SARS-CoV-2 | No changes in the methodology were identified. For the second objective of this systematic review (prevention of COVID-19), no eligible trials were identified. Therefore, no data synthesis or risk of bias assessment was conducted. Overall: No major concerns. |
| 12. | Bassatne, 2021 Link to the PROSPERO: 203960 Link to the fulltext: https://dx.doi.org/10.1016/j.metabol.2021.154753 | <u>Review type</u> : Systematic review and meta-analysis <u>Predefined databases to be searched</u> : Medline, EMBASE, CINAHL, Cochrane Library, ClinicalTrials.gov, WHO primary trial registries <u>Predefined risk of bias</u> : Cochrane RoB tool (version 1) for clinical trials, Newcastle-Ottawa quality scale for observational studies <u>Predefined main outcomes</u> : Mortality | <u>Review type/methodology</u> : Systematic review and meta-analysis (peer-reviewed journal publication) <u>Databases searched</u> : Medline, EMBASE, CINAHL, Cochrane Library, ClinicalTrials.gov, WHO primary trial registries, Australian New Zealand Clinical Trial Registry (ANZCTR), Iranian Registry of Clinical Trials (IRCT) <u>Risk of bias</u> : Cochrane RoB tool (version 1) for clinical trials, Newcastle-Ottawa quality scale for observational studies <u>Main outcomes</u> : Mortality rate from COVID-19 infection | 1) Four databases providing trial registries were additionally searched and 2) The main outcome was clearer defined in the final manuscript than was the case in the protocol. Overall: No major concerns. |
| 13. | Burela, 2020 Link to the PROSPERO: 200641 Link to the fulltext: https://dx.doi.org/10.17843/rmpesp.2020.374.6330 | <u>Review type</u> : Systematic review <u>Predefined databases to be searched</u> : Medline, EMBASE, CINAHL, Cochrane Library, Web of Science, LILACS, SciELO, Google Scholar, clinical trial registries, pre-print server <u>Predefined risk of bias</u> : Cochrane RoB tool for RCTs, Newcastle-Ottawa Scale for observational studies <u>Predefined main outcomes</u> : Any type of outcome measures that could reflect the prevention and clinical efficacy | <u>Review type/methodology</u> : Systematic review <u>Databases searched</u> : Medline, EMBASE, CINAHL, Cochrane Library, Web of Science, LILACS, SciELO, Google Scholar, clinical trial registries, preprint repositories <u>Risk of bias</u> : No study was identified <u>Main outcomes</u> : Any type of outcome measures that could reflect the prevention and clinical efficacy | No changes in the methodology were identified. As no primary study was deemed eligible for inclusion, no data synthesis and no risk of bias assessment were conducted. Overall: No major concerns. |

AMED=Allied and Complementary Medicine Database; CASP=Critical Appraisal Skills Programme; CENTRAL=Cochrane Central Register of Controlled Trials; CINAHL=Cumulative Index to Nursing and Allied Health Literature; COVID-19=Corona Virus Disease 2019; DOAJ=Directory of Open Access Journals; EBM=Evidence-Based Medicine; EPHPP=Effective Public Health Practice Project; GRADE=Grading of Recommendations, Assessment, Development and Evaluation; ICU=Intensive Care Unit; LILACS=Scientific health information from Latin America and the Caribbean countries

(translated abbreviation); MMAT=Mixed Methods Appraisal Tool; RCTs=Randomized Controlled Trials; RoB=Risk of Bias; ROBINS-I=Cochrane Risk of Bias In Non-Randomised Studies of Interventions; SARS-CoV-2=Severe Acute Respiratory Syndrome Corona Virus 2; SciELO=Scientific Electronic Library Online; SWiM=Synthesis without meta-analysis (reporting guideline for narrative data synthesis); WHO=World Health Organization; WHO ICTRP=World Health Organization International Clinical Trials Registry Platform; WHO SEARO=World Health Organization South-East Asia Regional Office

* Differences that may have impact on the validity of the published report are indicated.

S6. Characteristics of Published Systematic Reviews identified in COVID-19 L-OVE for prevention

Table 5 Characteristics of Published Systematic Reviews identified in COVID-19 L-OVE for prevention of COVID-19

| Author, Year | Country of affiliation of the review ^a | Review type | Population | Intervention | Main Outcome(s) reported | N studies for COVID-19 included (study types) | Protocol published prior to publication? | Type of publication, Comments (e.g. DOI, Link, PROSPERO registration) |
|------------------------------------|---|----------------------|---|---|---|---|--|--|
| Public health interventions (n=21) | | | | | | | | |
| Ayouni, 2021 | Tunisia | SR | general population | PHI (e.g., social distancing, lockdown, travel restrictions, etc.) | transmission of COVID-19 (effectiveness in preventing and controlling the spread of COVID-19) | 18 (2 ITS, 16 NRSI) | Yes, PROSPERO | journal publication 10.1186/s12889-021-11111-1 CRD42020196018 |
| Burns, 2020 | Germany | rapid SR | travellers (general population) | travel-related control measures during the COVID-19 pandemic, or SARS, MERS | effectiveness | 13 (NRSI), 49 (MS) | Yes, peer-reviewed Cochrane protocol | Cochrane review https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013717.pub2/full |
| Chetty, 2020 | South Africa | rapid SR | travelling populations (general population) | travel screening practices (e.g., body temperature measures, airport screening,...) | effectiveness | 0; 4 (MS) | No | journal publication 10.7196/SAMJ.2020.v110i1.1.14959 |
| Chisale, 2020 | Malawi | SR | population in low- and middle-income countries (general population) | community-based interventions to prevent COVID-19 transmission | COVID-19 transmission | 6 (NRSI) | Yes, PROSPERO | preprint 10.21203/rs.3.rs-98441/v1 CRD42020204984 |
| Chu, 2020 | Canada | SR, MA | people in healthcare or non-healthcare settings (mixed population) | social distancing, face mask, eye protection | person-to-person transmission of COVID-19, SARS, MERS | 64 (NRSI) | Yes, PROSPERO | journal publication and preprint 10.1016/S0140-6736(20)31142-9 CRD42020177047 |
| Chung, 2020 | UK | rapid SR, case study | n.r. (most likely general population) | testing, contact tracing, isolation policies | COVID-19 prevention and control | n.r. (48 with SR, guidelines also included) | No | preprint 10.1101/2020.06.04.20122614 |
| Frazer, 2020 | Ireland | rapid SR | older people in long term care facilities, employees, visitors | any intervention to reduce transmission, e.g., facility | transmission of COVID-19, SARS, MERS | 34 (NRSI) | Yes, PROSPERO | preprint 10.1101/2020.10.29.20222182 |

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|-----------------------------|---------------------------|----------|---|---|--|--------------------|---------------|---|
| | | | (high risk population) | measures, PPE, hygiene, social distancing | | | | CRD42020191569 |
| Girum, 2020 | Ethiopia | SR | persons after exposure to COVID-19 or at high risk or living in areas with an outbreak (high risk population) | contact tracing, screening, quarantine, isolation | effectiveness for COVID-19 prevention (incidence, transmission, ...) | 9 (NRSI), 13 (MS) | No | journal publication 10.1186/S41182-020-00285-W |
| Grépin, 2020 | China | rapid SR | travelling populations during COVID-19 pandemic (general population) | travel-related measures (e.g. travel advice, entry and exit screening, ...) | no restrictions (e.g. epidemiological, non-epidemiological outcomes) | 3 (NRSI), 26 (MS) | No | journal publication and preprint 10.1136/bmjgh-2020-004537 |
| Johanna, 2020 | Indonesia | SR, MA | general population during COVID-19 pandemic | mass screening, lockdown, combination of both | COVID-19 prevention (transmission, incidence, ...) | 4 (NRSI), 10 (MS) | Yes, PROSPERO | journal publication 10.4081/jphr.2020.2011 CRD42020190546 |
| Juneau, 2020 | USA, COVID-19 Work Group | SR | n.r. (most likely general population) | contact tracing | effectiveness | 14 (NRSI), 18 (MS) | Yes, PROSPERO | preprint 10.1101/2020.07.23.20160234 CRD42020198462 |
| Marasingh, 2020 | USA | SR | individuals not medically diagnosed with COVID-19 (general population) | public health recommendation for face masks | effectiveness in limiting the spread of COVID-19 | 0 | No | journal publication and preprint 10.14202/IJOH.2020.109-117 10.21203/rs.3.rs-16701/v3 |
| Mayr, 2020 | Austria | rapid SR | contacts of infected cases; travellers, general population (COVID-10, SARS, MERS) (mixed population) | quarantine with or without other public health measures | effectiveness in suppression of COVID-19 outbreak | 0; 10 (MS) | No | journal publication 10.1055/A-1164-6611 |
| Mbwogge, 2021 | UK | rapid SR | general population | mass testing with contact tracing vs testing of symptomatic individuals and contact tracing | effectiveness in suppression of COVID-19 outbreak | 1 (NRSI), 11 (MS) | No | journal publication and preprint 10.2196/27254 |
| Muhammed, 2020 | Iraq | rapid SR | n.r. (most likely general population) | school closure | transmission of COVID-19 in the general population | 3 (NRSI), 5 (MS) | No | journal publication 10.24017/COVID.12 |
| Public Health England, 2021 | Public Health England, UK | rapid SR | individuals in school setting (school population) | school based interventions (e.g., cohorting, distancing) | transmission of COVID-19 | 41 (NRSI), 15 (MS) | Yes, PROSPERO | update https://phe.koha-ptfs.co.uk/cgi-bin/koha/opac-retrieve-file.pl?id=9adedb17d5622f9cd7e42febcbdb19ad CRD42020191867 |
| Putri, 2020 | Indonesia | SR | healthcare workers, not infected (high risk population) | preventive actions (social distancing, using PPE, handwashing, screening, etc.) | transmission of COVID-19 | 7 (n.r.) | No | journal publication 10.19106/JMEDSCISI005203202013 |

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|-------------------------------------|---------|----------|---|---|--|--|--|--|
| Regmi, 2021 | UK | SR | any population during COVID-19 pandemic (mixed population) | PHI (isolation, social distance, quarantine) | COVID-19 incidence, risk of transmission reduction | 33 (NRSI) | Yes, PROSPERO and peer-reviewed protocol | journal publication 10.3390/ijerph18084274 CRD42020207338 |
| Viner, 2020 | UK | rapid SR | population during COVID-19, SARS, MERS outbreaks (general population) | school closure | effectiveness in limiting the spread of COVID-19 | 4 (NRSI), 1 (MS) | No | journal publication and preprint 10.1016/S2352-4642(20)30095-X |
| Viswanathan, 2020 | USA | rapid SR | general populations with unknown prevalence of SARS-CoV-2 | universal screening (mass screening) for SARS-CoV-2 infection vs no screening | effectiveness and screening test accuracy | 2 (MS, effectiveness); 17 (NRSI or DTA studies), 3 (MS, DTA studies) | Yes, OSF.io | Cochrane Review 10.1002/14651858.CD013718 |
| Walsh, 2021 | UK | SR | general population | school closures, reopening, school holidays | transmission of COVID-19 | 40 (NRSI) | Yes, PROSPERO | preprint 10.1101/2021.01.02.21249146 CRD42020213699 |
| Personal protective equipment (n=8) | | | | | | | | |
| Al-Moraissi, 2020 | Yemen | rapid SR | adult dental health care workers (high risk population) | respirators vs surgical masks | effectiveness against transmission of COVID-19, SARS, MERS | 0 | Yes, PROSPERO | preprint 10.1101/2020.11.20.20235333 CRD42020192912 |
| de Camargo, 2020 | Brasil | rapid SR | general population; SARS, MERS, COVID-19 | non-woven face mask (surgical masks, N95, FFP) vs no use | prevention of coronavirus infections (efficacy of protection) | 0 | No | journal publication and preprint 10.1590/1413-81232020259.13622020 |
| Dehaghi, 2020 | Iran | SR | patients with COVID-19, individuals with high risk or exposure (high risk population) | face masks (N95, surgical, cotton) | different (transmission) | 5 (NRSI) | No | journal publication 10.17533/UDEA.IEE.V38N2 E13 |
| Gross, 2021 | Germany | rapid SR | healthcare workers, not infected (high risk population) | any preventive measures (e.g. PPE, hand hygiene) | benefits (in terms of COVID-19 infection) and risks (e.g. headache or facial skin lesions due to N95 respirators) of preventive measures in the healthcare setting | 13 (NRSI) | No | journal publication 10.1136/bmjopen-2020-042270 |
| Li, 2020 | USA | SR, MA | Any population (mixed population) | face masks | transmission of COVID-19 | 6 (NRSI) | Yes, PROSPERO | journal publication and preprint 10.1016/j.ajic.2020.12.007 CRD42020211862 |

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|---|---------|----------------|--|---|--|-----------------------------|--|--|
| Morales Ferrer, 2021 | Chile | living SR | healthy population (general population) | gloves | COVID-19 infections, hospitalisation, safety | 1 (NRSI) | Yes, PROSPERO and peer-reviewed protocol | preprint 10.31219/osf.io/uz4rs CRD42020188674 |
| Rohde, 2020 | Ireland | rapid SR | community and household setting (general population) | face masks | effectiveness in prevention of SARS-CoV-2 transmission | 7 (NRSI) | No | preprint 10.12688/HRBOPENRES.13161.1 |
| Tabatabaei zadeh, 2021 | Iran | SR, MA | asymptomatic individuals without COVID-19 and COVID-19 patients (high risk population) | face masks | transmission of COVID-19 (risk of COVID-19 infection) | 4 (n.r.) | No | journal publication 10.1186/s40001-020-00475-6 |
| Vaccination (n=8) | | | | | | | | |
| Alimehmeti, 2021 | Albania | SR | n.r. (phase III clinical trials) (most likely general population) | COVID-19 vaccines | clinical efficacy and safety | 3 (phase III) | No | journal publication 10.32391/AJTES.V5i1.178 |
| Del Riccio, 2020 | Italy | SR | general population | influenza vaccination | risk of SARS-CoV-2 infection, severity, death | 12 (NRSI) | No | journal publication and preprint 10.3390/ijerph17217870 |
| Kaur, 2021 | India | SR | any population during COVID-19 pandemic (mixed population) | COVID-19 vaccines | safety | 11 (RCT, NRSI) | No | journal publication 10.1007/s12291-021-00968-z |
| Khera, 2020 | India | SR, MA | countries with universal BCG vaccination policy vs. countries without (general population) | BCG vaccination | protection against COVID-19 infection, incidence, mortality | 28 (NRSI) | Yes, PROSPERO | preprint 10.21203/rs.3.rs-97073/v1 CRD42020204466 |
| Pormoham mad, 2021 | Canada | SR, MA | n.r. (most likely general population) | COVID-19 vaccines | efficacy, safety | 25 (RCT, phase I-III) | No | journal publication https://pubmed.ncbi.nlm.nih.gov/34066475/ |
| Sathian, 2021 | Qatar | SR, MA | healthy adults (18+) (general population) | COVID-19 vaccines | safety, immunogenicity | 14 (RCT, NRSI, phase I-III) | Yes, OSF.io | journal publication 10.3126/nje.v11i1.36163 |
| Xing, 2021 ^b | China | SR | healthy adults (18+) (general population) | COVID-19 vaccines | efficacy, safety | 13 (RCT) | No | journal publication 10.7499/j.issn.1008-8830.2101133 |
| Yuan, 2021 | China | SR, MA | healthy adults (18+), without history of SARS or COVID-19 (general population) | COVID-19 vaccines | safety, tolerability, immunogenicity | 5 (RCT) | No | preprint 10.2139/ssrn.3746259 |
| Pharmaceutical interventions (n=9) | | | | | | | | |
| Bartoszeko, 2021 | Canada | living SR, NMA | people at risk of COVID-19 (pre-, post-exposure status and risk groups) (mixed population) | drugs for prophylaxis (HCQ, CQ, ivermectin, etc.) | effectiveness on COVID-19 (e.g. incidence, mortality) and SARS-CoV-2 infection | 11 (RCT) | No | journal publication and preprint 10.1136/bmj.n949 |

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|---------------------------|--|---------------|---|--|--|---|---|---|
| Bryant, 2021 | UK | SR, MA | patients with COVID-19, individuals with exposure or high risk (high risk population) | ivermectin | clinical efficacy and safety, incidence | post-exposure/high risk: 3 (RCT) | Yes, self-published (via tinyurl.com) | journal publication and preprint 10.1097/MJT.0000000000001402 |
| Ford, 2020 | Switzerland, World Health Organization | SR | patients with COVID-19, SARS or MERS, individuals with exposure (high risk population) | antiretroviral drugs (lopinavir/ritonavir, and others) | clinical efficacy and safety, incidence, transmission rate, ... (any clinical outcome) | post-exposure: 1 NRSI | No | journal publication 10.1002/JIA2.25489 |
| García-Albéniz, 2020 | USA; Spain | SR, MA | pre- or post-exposure, PCR-negative individuals (mixed population) | HCQ | COVID-19 infections (Risk Ratio) | 5 (RCT) | No | preprint 10.1101/2020.09.29.20203869 |
| Lewis, 2021 | Canada | SR, MA | adults with exposure or high risk (high risk population) | HCQ | prophylaxis efficacy and safety; transmission, mortality, hospitalization | 4 (RCT) | No | journal publication: 10.1371/journal.pone.0244778 |
| Rodríguez-Gutiérrez, 2021 | Mexico | living SR, MA | patients with COVID-19 (>16), individuals with exposure (high risk population) | ivermectin | clinical efficacy and safety | 2 (RCT) | Yes, PROSPERO | preprint 10.2139/ssrn.3802499 CRD42021235402 |
| Shah, 2020 | India | SR | n.r. (most likely high risk population) | HCQ, CQ | prophylactic effect | 0 | No | journal publication 10.1111/1756-185X.13842 |
| Singh, 2021 | UK; Cochrane Infectious Diseases Group | SR, MA | patients with COVID-19, individuals at risk of exposure or post-exposure (high risk population) | CQ, HCQ | clinical efficacy and safety, incidence, antibodies, transmission (e.g. to household contacts), disease severity | pre-exposure: 0; post-exposure: 2 (RCT) | Yes, PROSPERO and peer-reviewed Cochrane protocol | https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013587.pub2/full CRD42020185220 |
| Smit, 2021 | Switzerland | SR | any human population (e.g., high-risk older individuals, healthcare workers, healthy subjects) (mixed population) | pre- or post-exposure prophylaxis for COVID-19 (drug- or biologic-based; dietary supplements, herbal extracts) | impact on SARS-CoV-2 or COVID-19 incidence or prevalence | 7 (RCT, NRSI) | No | journal publication 10.1016/j.cmi.2021.01.013 |
| Other interventions (n=5) | | | | | | | | |
| Bassatne, 2020 | Lebanon | SR, MA | family members of adults with SARS, MERS, COVID-19 (high risk population) | vitamin D | clinical efficacy and safety, SARS-coV-2 positivity, transmission (to family members), disease severity | 3 (NRSI) | Yes, PROSPERO | journal publication 10.1016/j.metabol.2021.154753 CRD42020203960 |
| Burela, 2020 | Peru | SR | people of all ages (general population) | chlorine dioxide, chlorine derivatives | clinical efficacy and safety in preventing or treating COVID-19, SARS, MERS | 0 | Yes, PROSPERO | journal publication 10.17843/rpmesp.2020.374.6330 CRD42020200641 |

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|----------------------|-------------|----------|--|--|--|----------|--------------------------------------|---|
| Burton, 2020 | Cochrane UK | SR | healthcare workers, not infected (high risk population) | antimicrobial mouthwashes and nasal sprays | incidence, safety | 0 | Yes, peer-reviewed Cochrane protocol | Cochrane review 10.1002/14651858.CD013626.PUB2 |
| Flores-Genuino, 2020 | Philippines | rapid SR | individuals at risk of exposure to COVID-19 (high risk population) | oral fatty acid supplementation | any clinical outcome | 0 | No | journal publication 10.47895/AMP.V54I0.2443 |
| Gbinigie, 2020 | UK | rapid SR | people of all ages (general population) | zinc | clinical efficacy and safety (prophylaxis) | 1 (NRSI) | No | preprint 10.12688/wellcomeopenres.16173.1 |

BCG=Bacillus Calmette-Guérin; COVID-19=Corona-Virus Disease 2019; CQ=Chloroquine; CS=Case Studies (case series, case report); DTA=Diagnostic Test Accuracy; HCQ=Hydroxychloroquine; ITS=Interrupted Time-Series; MA=Meta-Analysis; MERS=Middle East Respiratory Syndrome; NMA=Network Meta-Analysis; n.r.=not reported; NRSI=Non-Randomized Studies of Interventions (including, cohort studies, case-control-studies, cross-sectional studies); PPE=Personal Protective Equipment; RCT=Randomized Controlled Trial; SARS (CoV-2)=Severe Acute Respiratory Syndrome (Corona-Virus 2); SR=Systematic Review; UK=United Kingdom; vs.=versus

^acountry of institutional affiliation of corresponding and/or first author

^bExtraction is based solely on data presented in the abstract, as the full text is only available in Chinese