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TABLE OF CONTENTS

HEADER	1
ABSTRACT	1
BACKGROUND	2
OBJECTIVES	3
METHODS	3
ACKNOWLEDGEMENTS	9
REFERENCES	10
APPENDICES	13
CONTRIBUTIONS OF AUTHORS	16
DECLARATIONS OF INTEREST	16
SOURCES OF SUPPORT	17
NOTES	17

[Intervention Protocol]

Workplace interventions to reduce the risk of SARS-CoV-2 infection outside of healthcare settings

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ABSTRACT

Objectives

This is a protocol for a Cochrane Review (intervention). The objectives are as follows:

To assess the benefits and harms of interventions in non-healthcare-related workplaces to reduce the risk of SARS-CoV-2 infection relative to other interventions or no intervention.

BACKGROUND

Description of the condition

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by the novel coronavirus, SARS-CoV-2 (severe acute respiratory syndrome coronavirus-2), which first appeared in late 2019. Its development was declared a global health emergency on 31 January 2020 and a pandemic on 11 March 2020 (WHO 2020a).

The principal mode of SARS-CoV-2 transmission is through exposure to respiratory fluids carrying this virus. Generally, exposure occurs in these three, not mutually exclusive, ways:

- inhalation of very fine respiratory droplets and aerosol particles;
- deposition of respiratory droplets and particles on exposed mucous membranes in the mouth, nose, or eye by direct splashes and sprays; or
- touching mucous membranes with hands that have been soiled either directly by virus-containing respiratory fluids, or indirectly by touching surfaces with the virus on them (CDC 2021a; CDC 2021b).

While around a third of people remain asymptomatic (BCCDC 2021; Byambasuren 2020), most others experience a mild form of the disease with cough, fever, headache, fatigue, and other nonspecific symptoms (Gandhi 2020). However, some individuals can develop severe illness and die, particularly older people and those with underlying medical problems, such as cardiovascular disease, diabetes, chronic respiratory disease, or cancer. More severe cases generally suffer from dyspnoea, and may require critical care due to respiratory failure, sepsis, or multi-organ failure (Berlin 2020). In addition, some adults and children can develop long-term debilitating effects after the disease, resulting in so-called post-acute sequelae of SARS-CoV-2 infection (PASC, also known as 'long COVID') (Bruchfeld 2020; Osmanov 2021). On average, it takes five to six days from infection to the development of symptoms, but it has been reported to take up to 14 days (Lauer 2020; Yu 2020). The median time from symptom onset to diagnosis ranges between four to eight days, with hospital admission around day six for those with more severe disease (Chotirmall 2021). The infection fatality rate has been estimated to be around 0.68% (Meyerowitz-Katz 2020), but preliminary testing means any such estimate is uncertain.

The pandemic is having profound impacts on the nature and availability of work across the world (Semple 2020; Sim 2020). As part of the public health response to SARS-CoV-2, governments and the private sector across the world have temporarily closed non-essential workplaces; that is, workplaces that do not operate or provide services that are typically essential to continue critical infrastructure viability (CISA 2021). This has resulted in large numbers of workers moving to remote work, while others have lost their jobs or had their hours significantly reduced. As societies begin to re-open following widespread vaccination of parts of their populations, it is essential to identify workplace strategies that will allow this reintegration into the workplace in a way that is safe for individuals and society at large.

Since the advent of the pandemic, epidemiological studies have explored strategies to prevent or reduce infection rates among healthcare workers (Chou 2020; Nguyen 2020). However, many non-healthcare workers (non-HCWs) are also at increased risk (Kim 2020). These include police, workers providing social or home care

services, childcare, and education, cleaners, those in the hospitality industry, public transport workers and taxi drivers, and workers in meat processing industries, amongst others (Sim 2020).

Using the meat processing industry as an example, COVID-19 outbreaks have been reported in Germany, the UK, Ireland, Portugal, and the USA (Durand-Moreau 2020; Günther 2020; Herstein 2021; Price 2020). Studies also show that meat processing plants may be transmission vectors, playing a role in local community transmission (Althouse 2020; Taylor 2020). For example, data from Nebraska, USA, indicated that the total excess COVID-19 morbidity and mortality associated with proximity to livestock plants were 236,000 to 310,000 (6% to 8% of all US cases) and 4300 to 5200 (3% to 4% of all US deaths), respectively, during April to July 2020 (Herstein 2021).

Studies also report that essential workers in livestock processing plants are more likely to be from an ethnic minority compared to non-essential workers (Reid 2021; Waltenburg 2021). Migrant workers, in particular, have experienced a disproportionately high risk of adverse outcomes with COVID-19 infection (Roberts 2020). In some instances, meat processing workplaces may be crowded and social distancing is difficult. Yet ambient temperature, humidity, ventilation, air recirculation, and aerosolisation are significant factors facilitating SARS-CoV-2 dissemination and transmission in these environments (Donaldson 2020; Kumar 2021; Middleton 2020; Morris 2020; Ursachi 2021). Policy responses to the ongoing operational activity of meat processing industries have to find a balance between supporting essential supply chains and mitigating SARS-CoV-2 transmission (Taylor 2020). Face masks and partition barriers, for example, have shown a statistically significant reduction in COVID-19 incidence in some meat processing facilities (Herstein 2021). Other strategies to decrease transmission include screening workers for symptoms, appropriate sickness/absence policy changes, and disinfection of high-touch surfaces. As such, businesses and employers can play a key role in preventing or slowing the spread of SARS-CoV-2 within the workplace.

Providing evidence-based interventions to prevent SARS-CoV-2 infection among non-HCWs has become more urgent with the opening of the economy, the spread of more infectious SARS-CoV-2 variants of concern (VoC), and the potential psychological toll imposed by the COVID-19 pandemic (Allen 2021). The lessons learned from the experience with the COVID-19 pandemic will likely inform the appropriate risk mitigation measures that need to be in place to reduce adverse societal impacts of possible future waves of the pandemic, and for any future pandemic of a similar nature.

Description of the intervention

This systematic review focuses on non-healthcare workers. It will attempt to include all workers in close contact with potentially infectious clients, such as public transportation personnel, cashiers in grocery stores, and staff in restaurants. It will also include workers without close contact with clients and the potential to be infected by colleagues, such as office workers. Adopting the classic epidemiological triad model of Agent, Host and Environment (Khan 2020), and employing a hierarchy of control concepts in occupational health and safety studies (as outlined in a Canadian Centre for Occupational Health and Safety document (CCOHS 2020)), we include any type of intervention to limit SARS-CoV-2 transmission that can be implemented in workplaces of interest.

Accordingly, the interventions to be included in our review are as follows.

- The elimination of procedures, or substitution of alternative procedures, or both, to achieve the same workplace outcomes but reduce the risk of SARS-CoV-2 exposure. This might include automating procedures, or providing education regarding COVID-19 symptoms and sickness absence policy for symptomatic individuals.
- Engineering controls; that is, the controls built into the design of the plant, equipment or process. These measures are effective and reliable since they are 'in place' at all times. In the case of COVID-19, engineering controls may reduce viral transmission, for example, by providing barriers or by reconfiguring workplaces to minimise contact with co-workers or clients, as well as by environmental measures such as reengineering of air ventilation and purification methods.
- Administrative controls, which are processes that limit a worker's exposure through rules or procedures. Administrative controls may reduce potential viral transmission in the workplace through health check declarations prior to coming to the workplace, flexible working hours, as well as accommodating appropriate spacing between workers at the workplace.

How the intervention might work

By employing the classic epidemiological concept of Agent, Host and Environment (Khan 2020), within the hierarchy of controls for SARS-CoV-2 in the workplace safety guide proposed by the Canadian Centre for Occupational Health and Safety (CCOHS 2020), our group considered that the interventions may work by: reducing or eliminating transmission of the agent to the host by reducing the duration of infectiousness after a person becomes infected; reducing or eliminating the likelihood of infection per contact between a susceptible person and an infectious person; and reducing or eliminating the contact rate of an infectious person (Delamater 2019). In addition to the use of personal protective equipment (PPE), a number of studies have reported that measures like social distancing, appropriate hand hygiene, addressing ventilation systems, addressing work procedures (such as self-administered health screening), minimising face-to-face contacts, and other endeavours helped to reduce transmissions (Baptista 2021; Clancy 2021; Faghri 2021; Haug 2020, US OSHA 2020; OSHA 2021).

Why it is important to do this review

Work is an integral part of life, and is central to individual identity, social roles, and social status, as well as to meeting financial and psychosocial needs. There is strong evidence that good work leads to better health, improving individuals' quality of life and well-being in many realms (Waddell 2006).

During this COVID-19 pandemic, there has been a massive decline in economic activities, manifested by sharp declines in states' gross domestic product and sharp increases in unemployment, beginning as early as March 2020 (Fomenko 2021). Further, measures to prevent and control infections implemented during the pandemic – such as physical distancing, quarantine, and restrictions on social contacts – have contributed to adverse mental health issues, including an increase in depression and anxiety (Rauschenberg 2021; Sigahi 2021). Much research has focused on

preventing or reducing infection among healthcare workers since the advent of the COVID-19 pandemic. At present, there are at least six Cochrane Reviews associated with COVID-19 interventions to prevent infection among healthcare workers (Burton 2020a; Burton 2020b; Burton 2020c; Houghton 2020; Kumbargere Nagraj 2020; Verbeek 2020). So far, non-healthcare workers have received less attention. However, providing evidence-based interventions to prevent workplace-related COVID-19 transmission among non-healthcare workers has become more urgent with the re-opening of the economy, the spread of more infectious SARS-CoV-2 variants, and the potential psychological toll imposed by the COVID-19 pandemic (Altmann 2021; Htay 2020; Moore 2021; Shaw 2020).

OBJECTIVES

To assess the benefits and harms of interventions in non-healthcare-related workplaces to reduce the risk of SARS-CoV-2 infection relative to other interventions or no intervention.

METHODS

Criteria for considering studies for this review

Types of studies

We will include any study that compares outcomes in the intervention group to outcomes in a control group that did not get the intervention. We will include randomised control trials and non-randomised studies of interventions (NRSI); that is, prospective experimental studies with a concurrent control where the allocation of participants to intervention and control groups was not random (e.g. participants chose by themselves).

We will not include observational studies, such as natural experiments, in which the researchers did not introduce the intervention. This is because it is difficult to predict if the effects can be translated to real experiments in which the intervention is introduced by stakeholders. We will not include cross-sectional studies because disease incidence can fluctuate rapidly and the temporal association is impossible to determine. We will not include mathematical modelling studies due to their limitations resulting from their many assumptions. We also assume that there is empirical evidence available, being more than one year into the pandemic.

We will include studies reported as full-text articles, those published as abstract only, and unpublished data. We will also include preprints. We will not impose any language or date restrictions.

Types of participants

We will include adults (> 18 years), both those who come into close contact with clients or customers (e.g. public-facing employees such as cashiers or taxi drivers), and those who do not, but who can be infected by co-workers. We will exclude studies involving healthcare workers (including dentists and other allied health professionals), as they are considered in separate Cochrane Reviews. We will include studies on workers at social care and home care services if they are not caring for people with SARS-CoV-2. We will exclude studies in children in primary and secondary school and students at universities. We will include studies in paid workers (i.e. employed workers) and exclude studies exclusively in people working on a volunteer basis.

We will include studies on severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS). We will then differentiate between direct evidence from SARS-CoV-2 studies and indirect evidence from SARS and MERS studies in subgroup analyses ([Subgroup analysis and investigation of heterogeneity](#)).

We will include any study if at least 80% of the participants meet the review criteria as defined above, or if there are data for the relevant subset of participants in whom we are interested. We will explore differences in subgroup analyses.

Types of interventions

We will include interventions that attempt to prevent or reduce workers' exposure to SARS-CoV-2 in the workplace. We will define categories of intervention according to the hierarchy of hazard controls. Consequently, the interventions to be included in our review are as follows.

Elimination (i.e. eliminating the source of SARS-CoV-2)

- Polymerase chain reaction (PCR) or rapid antigen testing with self-isolation policy and quarantining close-contact co-workers
- Education regarding COVID-19 symptoms and sickness absence policy for symptomatic individuals
- Automated processes (e.g. production lines)

Engineering controls

- Walk-through disinfection systems
- Air-purification systems (including, but not limited to, misting/fogging machines or high-efficiency particulate absorbing (HEPA) filters)
- Installation of or improvement to ventilation (including installation of new systems)
- Barriers to separate or distance co-workers and workers from members of the public (e.g. Perspex, glass, metal shield)
- Use of ultraviolet (UV) lighting
- Reconfiguration of workplace to minimise contact with the public (e.g. safe collection points for customers)
- Closing work areas to prevent groups of people assembling (including cafeterias)

Administrative controls

- Personal protective equipment (PPE)
- Vaccination of workers (where this exists specific to a workforce or workplace)
- Distancing between colleagues in the workplace (so-called social distancing), including details of distance used (e.g. 1 m, 2 m, etc.)
- Hand-washing protocols (including use of hand sanitisers)
- Working from home (WFH, where it is possible to do so). Also, allowing flexible working hours to facilitate home-schooling and other caring responsibilities.
- Checking temperature (i.e. thermal screening) on entering the workplace (could also include formal screening for symptoms)
- Workplace cleaning and disinfecting regimes (i.e. infection prevention and control (IPC) policies and standard operating procedures)

- Use of online, rather than face-to-face, meetings (i.e. remote working arrangements)
- Cancelling or curtailing of work-based travel
- Variation in start times, finish times, lunch and other work breaks to minimise contact with work colleagues (i.e. staggered rosters)
- Forming 'isolation bubbles' within the workplace to avoid mixing between different work teams (i.e. staffing bubbles)
- Facilitating travel to work in private cars, rather than having to use public transport (e.g. paying for parking)
- Cancelling work-related out-of-hour social activities
- Introducing one-way walk systems in workplaces
- Paid sick days

We will include interventions not listed here that also aim to reduce exposure to SARS-CoV-2 in the workplace.

We will include combinations of eligible interventions.

Eligible interventions may be compared to:

- standard IPC practices in the workplace prior to the COVID-19 pandemic (e.g. what deviation, if any, from pre-existing IPC standard operating procedures were initiated since the COVID-19 epidemic);
- no intervention to reduce exposure to SARS-CoV-2;
- a different intervention to reduce exposure to SARS-CoV-2; or
- different combinations of interventions to reduce exposure to SARS-CoV-2.

Types of outcome measures

Primary and secondary outcomes are listed below. Where applicable, we have specified relevant time frames and how the outcomes may be measured. However, we acknowledge that exact details are difficult to determine in a rapidly changing situation, and additional measures may appear important. We will consider the following follow-up times for outcome measurement: short term, defined as less than 3 months after the intervention started; medium term, defined as between 3 and 12 months; and long term, defined as 12 months or longer. In situations where multiple time points are reported, we will include the longest follow-up time from each study for analysis. All follow-up time data will be reported descriptively.

We are considering SARS-CoV-2 infections and other respiratory diseases (SARS, MERS) as a surrogate for exposure to SARS-CoV-2, (SARS-CoV-1, MERS-CoV). Development of a core outcome set (COS) for COVID-19 prevention interventions, the COS COVID-P study, is underway ([COMET 2021](#)). Work so far recommends that COVID-19 infection is an essential outcome to measure in prevention studies, but has found that a number of different definitions are used ([COMET 2021](#)).

Primary outcomes

- Incidence rate of SARS-CoV-2 (or other viruses) infection
- SARS-CoV-2-related mortality
- Adverse events, including but not limited to cutaneous and respiratory events, accidents, depression, anxiety

The denominator for all primary outcomes will be based on the number of workplace employees. This could be summarised at either the individual or the workplace level.

Note that the primary analysis from outcomes relating to COVID-19 will include all direct evidence, regardless of the risk of bias. Where SARS or MERS are targeted, outcome data will appear separately as a subgroup on forest plots and will not be combined with COVID-19 data.

We will accept any definition of a case of COVID-19 provided by the authors. In the case that both suspected and confirmed cases are given for the same study, we will use the most reliable measure (e.g. PCR test).

Secondary outcomes

- All-cause mortality
- Quality of life as defined by authors
- Absenteeism
- Hospitalisation
- Uptake, acceptability, or adherence to strategies (e.g. use of hand sanitiser, wearing of face masks, degree of social distancing), measured using ordinal (e.g. Likert scale) or dichotomous (e.g. yes/no) data measures

Search methods for identification of studies

Electronic searches

We will conduct a systematic literature search to identify all published and unpublished trials that can be considered eligible for inclusion in this review. We will adapt the search strategy we developed for Ovid MEDLINE (see [Appendix 1](#)) for use in the other electronic databases. We used the following search strategies to develop our search.

- COVID-19 terms for the MEDLINE strategy were modified from the CADTH Respiratory Pandemics (including COVID-19, SARS, and MERS) - MEDLINE filter ([covid.cadth.ca/literature-searching-tools/cadth-covid-19-search-strings/#covid-19-medline](https://www.cadth.ca/literature-searching-tools/cadth-covid-19-search-strings/#covid-19-medline)).
- The study design filter was modified from the CADTH Randomised Controlled Trials / Controlled Clinical Trials - OVID Medline, Embase and PsycINFO filter (www.cadth.ca/resources/finding-evidence/strings-attached-cadths-database-search-filters#rand).
- The text words for occupational categories in the workplace were informed by the Centers for Disease Control and Prevention Interim List of Categories of Essential Workers (www.cdc.gov/vaccines/covid-19/categories-essential-workers.html).

We will impose no restriction on language of publication. We will arrange for the translation of key sections of potentially eligible non-English language papers, or we will arrange for people who are proficient in the publications' languages to fully assess them for potential inclusion in the review as necessary.

We will search the following electronic databases from their inception to the present for identifying potential studies.

- Cochrane Central Register of Controlled Trials (CENTRAL) (Cochrane Library).

- MEDLINE (Ovid) ([Appendix 1](#)).
- Embase (Ovid) ([embase.com](https://www.embase.com)).
- NIOSHTIC-2 (OSH-UPDATE) (National Institute for Occupational Safety and Health bibliographic database).
- HSELINE (OSH-UPDATE) (Health and Safety Executive Library and Information Service).
- CISDOC (OSH-UPDATE) (International Labor Organization occupational safety and health bibliographic database).
- CISILO (International Occupational Safety and Health Information Centre bibliographic database).
- Web of Science Core Collections.
- Cochrane COVID-19 Study Register (covid-19.cochrane.org/); via the Cochrane Register of Studies (crsweb.cochrane.org/).
- World Health Organization (WHO) COVID-19 Global literature on coronavirus disease (search.bvsalud.org/global-literature-on-novel-coronavirus-2019-ncov/).

We will also conduct a search of unpublished and ongoing trials in ClinicalTrials.gov (www.clinicaltrials.gov/), the WHO International Clinical Trials Registry Platform (www.who.int/clinical-trials-registry-platform), and medRxiv (www.medrxiv.org/).

If studies are published in languages other than those our review team can accommodate (Danish, Dutch, English, French, German, Italian, Portuguese, Spanish, and Swedish), we will consider involving Cochrane TaskExchange to identify people within Cochrane to translate these studies.

Searching other resources

We will check the reference lists of all primary studies and review articles for additional references. We will contact experts in the field to identify additional unpublished materials.

Data collection and analysis

Selection of studies

We will screen titles and abstracts using Covidence ([Covidence](#)). Review authors (ABP, KN, SR, KS, EP, BNS, JEV, OS, SD, DM, TF, MVT, CG, MB) will screen titles and abstracts independently and in duplicate, and exclude studies that clearly do not fulfil the criteria for inclusion.

We will retrieve the full texts of potentially eligible records and a pair of review authors (ABP, KN, SR, KS, EP, BNS, JEV, OS, DM, MVT, MB) will assess these to identify studies for inclusion. We will resolve any disagreements through discussion or, if required, through consulting a third review author (SD or CM).

We will record reasons for exclusion of studies assessed at the full-text screening stage and report this in a PRISMA flow chart and in the 'Characteristics of excluded studies' table.

We will identify and exclude duplicates, and collate multiple reports of the same study so that each study is the unit of interest.

Should our systematic searches identify studies conducted by authors of this review, we will make sure to avoid conflict of interest by having all decisions concerning inclusion and exclusion, data extraction, and risk of bias assessment, made by review authors who were not involved with the study.

Because of the breadth of the review, review authors will communicate regularly whilst conducting screening to monitor the process and to avoid leaving numerous discrepancies to resolve at the end of the process.

Studies will be included regardless of language of publication.

We will document the details of the search strategy used and the number of records retrieved from each database (total number retrieved) or Internet search performed (total number screened) in accordance with PRISMA guidance ([Page 2021](#)).

Data extraction and management

We will use a data collection form for study characteristics and outcome data which has been piloted on 20 studies representing different intervention types. Review authors (ABP, KN, EP, BNS, SD, JEV, SR, KS) will extract the following study characteristics from included studies independently and in duplicate.

- Publication details: author, study source (e.g. journal publication, preprint, peer-reviewed).
- Methods: study design, total duration of study, study location (e.g. country, city), study setting (e.g. type of workplace), withdrawals/missing data and how they were handled.
- Participants: number included/randomised, mean age or age range, sex/gender, severity of condition, diagnostic criteria if applicable, inclusion criteria, and exclusion criteria.
- Interventions: description of intervention (category and type), comparison, duration (including date of implementation), intensity, and co-interventions.
- Outcomes: description of primary and secondary outcomes and measures specified and collected, and time points for reporting.
- Notes: funding, ethical approval and notable conflicts of interest of trial authors.

We will note in the 'Characteristics of included studies' tables if outcome data were not reported in a usable way. We will resolve disagreements by consensus or by involving a third review author (SD, MB, or CM). One review author (ABP) will transfer data into RevMan Web ([RevMan Web 2020](#)). A second review author (EP) will check study characteristics for accuracy against the primary study.

Assessment of risk of bias in included studies

Review authors (ABP, SR, KS, EP, BNS, JEV., SD) will independently and in duplicate assess the risk of bias for each study, using the Cochrane risk of bias 2 tool (RoB2) ([Sterne 2019](#)), and the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* for each study design ([Higgins 2021](#), hereafter referred to as the *Cochrane Handbook*). We will resolve any disagreements through discussion or by involving another author (MB or CM).

As we anticipate a wide array of included study designs, we have elaborated on multiple, potentially applicable tools below, in accordance with a recent comparable Cochrane Review on SARS-CoV-2 ([Burns 2021](#)).

For randomised controlled trials (RCTs), we will use the Cochrane RoB 2 tool, which assesses the risk of bias according to these domains:

- bias arising from the randomisation process (random sequence generation, allocation concealment, blinding of participants and personnel);
- bias due to deviations from intended interventions; we are interested in the 'intention-to-treat effect';
- bias due to missing outcome data;
- bias in measurement of the outcome; and
- bias in selection of the reported result.

We will use the appropriate RoB2 Excel tool to assess cluster-RCTs and cross-over trials.

We will grade each potential risk of bias as high, low, or some concerns, and provide a quote from the study report, together with a justification for our judgment, in the risk of bias tables. We will add additional domains for other study designs to the risk of bias tables. We will summarise the risk of bias judgements across different studies for each of the domains listed. We will consider blinding separately for different key outcomes where necessary (e.g. for unblinded outcome assessment, risk of bias for all-cause mortality may be very different from a quality of life assessment). Where information on the risk of bias relates to unpublished data or correspondence with a trial author, we will note this in the risk of bias table.

For assessing the risk of bias in NRSIs, we will use the Risk of Bias in Non-Randomised Studies of Interventions (ROBINS-I) tool ([Sterne 2016](#)). Our target trial against which we will assess the risk of bias would be a trial in which adults are assigned to a group with interventions in place that aim to reduce COVID-19 infection at the workplace or standard practice or alternative interventions. We will consider the following variables as potential confounders: age, sex, ethnicity, comorbidities, and socioeconomic status. We will first use the signalling questions as prescribed in the ROBINS-I tool and then assess the risk of bias if these questions indicate a potential risk of bias.

We will assess these risk of bias domains:

- bias due to confounding;
- bias due to selection of participants into the study;
- bias in the classification of interventions;
- bias due to deviation of intended interventions;
- bias due to missing data;
- bias due to outcome measurement;
- bias in selection of the reported result.

We will judge the risk of bias of NRSIs in all the above domains to be low, moderate, serious, or critical.

We will assess the risk of bias for these key outcomes, which will be included in the summary of findings tables:

- incidence rate of SARS-CoV-2 (or other viruses) infection;
- SARS-CoV-2-related mortality;
- adverse events, including but not limited to cutaneous and respiratory events, accidents, depression, anxiety;
- all-cause mortality;
- quality of life as defined by authors;
- hospitalisation;

- adherence to strategies (e.g. use of hand sanitiser, wearing of face masks, degree of social distancing), measured using an ordinal scale (e.g. Likert).

Overall risk of bias at the study level

We will judge a study to have a high risk of bias overall when we judge one or more domains to have a high risk of bias. Conversely, we will judge a study to have a low risk of bias overall when we judge the risk of bias to be low for all domains.

When considering treatment effects, we will take into account the risk of bias for the studies that contribute to that outcome.

Assessment of bias in conducting the systematic review

We will conduct the review according to this published protocol, and report any deviations from it in the 'Differences between protocol and review' section of the systematic review.

Measures of treatment effect

We will enter the outcome data for each study into the data tables in RevMan Web to calculate the treatment effects ([RevMan Web 2020](#)). Where possible, we will convert these effect estimates to a common format to allow meta-analysis. We will use odds ratios for binary outcomes, and mean differences or standardised mean differences for continuous outcomes, or other types of data as reported by the authors of the studies. Where binary measures of effect estimates have been reported using an alternative format to an odds ratio, we will convert alternative effect estimates (risk ratios, risk differences, rate ratio) into odds ratios using available information (e.g. baseline or control group risk).

If only effect estimates and their 95% confidence intervals or standard errors are reported in studies, we will enter these data into RevMan Web using the generic inverse variance method ([RevMan Web 2020](#)). We will ensure that higher scores for continuous outcomes have the same meaning for the particular outcome, explain the direction to the reader, and report where the directions were reversed if this was necessary. When the results cannot be entered, we will describe them in the 'Characteristics of included studies' table, or enter the data into Additional tables.

For interrupted time series (ITS) studies, we will extract data from the original papers and re-analyse them according to the recommended methods for the analysis of ITS designs for inclusion in systematic reviews ([Ramsay 2003](#)). We will use the standardised change in level and change in slope as effect measures. For other non-randomised studies, we will extract the estimate of intervention effect together with a measure of precision (confidence interval or standard error) and information about the method of analysis and adjustment for confounders. If both unadjusted and adjusted intervention effects are reported, then adjusted effects will be chosen in preference. Some non-randomised studies report multiple adjusted estimates from analyses, including different sets of covariates. If multiple adjusted estimates of intervention effect are reported, we will choose the one that is judged to minimise the risk of bias due to confounding, after discussion between review authors (see [Chapter 25, Section 25.2.1](#)). We will present randomised and non-randomised studies as separate subgroups, without aggregation.

Unit of analysis issues

For studies that employ a cluster-randomised design and that report sufficient data to be included in the meta-analysis but do not make an allowance for the clustering, we will inflate the standard errors using the design effect. We will calculate the design effect based on a fairly large assumed intra-cluster correlation coefficient. We base this assumption of 0.10 being a realistic estimate by analogy with studies about implementation research ([Campbell 2001](#)). We will explore this assumption using sensitivity analysis, as clustering may be high in the context of COVID-19. We will follow the methods described in the *Cochrane Handbook* for the calculations ([Higgins 2021](#)). Note that cluster-randomisation could be at the level of the workplace (e.g. a factory), a subset of the workplace (e.g. department or shift) or a larger unit (e.g. a geographical area), and we will take care to ensure that the analysis makes appropriate adjustment for clustering at the correct level.

When cross-over trials report continuous outcomes with which the authors have not reported a paired analysis, we will perform a paired analysis based on a reported or imputed correlation between the outcomes of the intervention and the control condition, as advised in Chapter 16 of the *Cochrane Handbook* ([Higgins 2021](#)). For dichotomous outcomes, we will adjust the confidence intervals for the paired analysis according to [Elbourne 2002](#).

Dealing with missing data

We will contact investigators or study sponsors in order to verify key study characteristics and obtain missing numerical outcome data where possible (e.g. when a study is identified as abstract only). Where this is not possible, and the missing data are thought to introduce serious bias, we will explore the impact of including such studies in the overall assessment of results by a sensitivity analysis.

If numerical outcome data are missing, such as standard deviations or intra-cluster correlation coefficients and they cannot be obtained from the authors, we will calculate them from other available statistics such as P values, according to the methods described in the *Cochrane Handbook* ([Higgins 2021](#)).

Assessment of heterogeneity

We will assess the clinical homogeneity of the results of included studies based on similarity of population, intervention, outcome and follow-up.

- We will consider any workplace populations as similar enough to combine.
- We will consider interventions as similar when they are from the same sub-category within the hierarchy of controls (as listed in [Types of interventions](#)).
- We will consider any outcome measure relating to the rate of SARS-CoV-2 as similar enough to combine. We will not combine data on SARS-CoV2 with data on SARS or MERS.
- We have categorised follow-up times as follows: short term as less than 3 months after the intervention has begun; medium term as between 3 and 12 months; and long term as 12 months or longer. We will consider short- and long-term follow-up times as different, whereas we will combine short- and medium-term outcomes or medium- and long-term outcomes where relevant.

Despite the aforementioned points, we recognise that we cannot anticipate all of the various populations, interventions, outcomes, and follow-up times that the included studies will report on and their potential comparability and compatibility. As such, we will perform our full assessment of heterogeneity and definition of follow-up times after evaluating the included studies. We will reach decisions after consulting the entire author team to consider both Cochrane and occupational medicine viewpoints.

As well as visual inspection of forest plots, we will use the I^2 statistic to assess heterogeneity amongst the trials in each analysis. If we identify substantial heterogeneity, we will report it and explore possible causes by prespecified subgroup analysis. We will consider heterogeneity as substantial if I^2 is above 50%.

Assessment of reporting biases

If we are able to pool more than 10 trials in any single meta-analysis, we will create and examine a funnel plot to explore possible small study biases.

Data synthesis

We will pool data from studies we judge to be clinically homogeneous, as defined in the section [Assessment of heterogeneity](#), using RevMan Web ([RevMan Web 2020](#)). If more than one study provides usable data in any single comparison, we will perform meta-analysis. We will use a random-effects model because we believe that the type of intervention and study designs included will always lead to heterogeneity.

For ITS studies, we will perform separate meta-analyses for level and slope using the generic inverse variance method.

Where multiple trial arms are reported in a single trial, we will include only the relevant arms. If two comparisons (e.g. intervention A versus no intervention, and intervention B versus no intervention) are combined in the same meta-analysis, we will halve the no intervention group to avoid double-counting.

We will refer to SWiM guidelines for synthesis without meta-analysis if this is the case in this review ([Campbell 2020](#)).

Subgroup analysis and investigation of heterogeneity

We plan to carry out the following subgroup analyses.

- Dose (intensity, duration of the intervention).
- Sector (e.g. transportation, agriculture, tourism, manufacturing, construction, forestry and fishing, mining and quarrying, electricity, gas, steam and air conditioning supply, water supply; sewerage, waste management and remediation activities, wholesale and retail trade; repair of motor vehicles and motorcycles, transportation and storage, accommodation and food service activities, information and communication, financial and insurance activities, real estate activities, professional, scientific and technical activities, administrative and support service activities, public administration and defence; compulsory social security, education, human health and social work activities, arts, entertainment and recreation, other service activities, activities of households as employers; undifferentiated goods- and services-producing activities of households for own use, activities of extraterritorial organisations and bodies) ([UNIDO 2015](#)).

- Geographic region (Africa, Asia, Caribbean, Central America, Europe, North America, Oceania, and South America).
- Country income-level (high, upper-middle, lower-middle, low-income).
- The time frame of the pandemic during which the study was conducted (early and late based upon the median).
- Studies in which both intervention and control groups use PPEs.
- Studies that include only a subset of relevant participants,
- SARS-CoV-2 studies versus indirect evidence from SARS and MERS studies.
- Funding (public/governmental vs industry/commercial).
- Public-facing versus non-public-facing workplaces.

We will use the three primary outcomes in subgroup analyses. We will use the χ^2 test to test for subgroup interactions in RevMan Web ([RevMan Web 2020](#)).

Sensitivity analysis

We will perform sensitivity analysis defined a priori to assess the robustness of our conclusions. This will involve:

- studies with low risk of bias versus studies with high risk of bias;
- excluding studies with estimated presumably intra-cluster correlation co-efficient (ICC) (or using alternative ICCs);
- non-peer-reviewed publications (preprints, abstracts only) versus peer-reviewed publications.

We will also perform sensitivity analyses to check how our assumptions influence the conclusions of the review.

Summary of findings and assessment of the certainty of the evidence

We will create summary of findings tables for all comparisons of workplace interventions with no intervention or standard practices.

For these comparisons, we will report the following outcomes.

- Incidence rate of SARS-CoV-2 (or other viruses) infection.
- SARS-CoV-2-related mortality.
- Adverse events, including but not limited to cutaneous and respiratory events, accidents, depression, anxiety.
- All-cause mortality.
- Quality of life as defined by authors.
- Hospitalisation.
- Adherence to strategies (e.g. use of hand sanitiser, wearing of face masks, degree of social distancing), measured using an ordinal scale (e.g. Likert).

We will use the five GRADE considerations (study limitations, consistency of effect, imprecision, indirectness, and publication bias) to assess the quality of a body of evidence as it relates to the studies that contribute data to the meta-analyses for the prespecified outcomes. We will use methods and recommendations described in the *Cochrane Handbook* ([Higgins 2021](#)), using GRADEpro software ([GRADEpro GDT](#)) We will justify all decisions to down- or upgrade the quality of studies using footnotes.

We will prioritise the evidence from RCTs. Because of the inclusion of non-randomised studies, if necessary, we will compile an additional summary of findings table showing all our GRADE decisions about the quality of evidence and their justifications. If we include RCTs and non-RCTs for the same outcome, we will base our GRADE assessments on the evidence from RCTs. If only a non-RCT reports a key outcome, we will assess it using GRADE.

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APPENDICES
Appendix 1. Search strategy - MEDLINE
Search strategy

Source: MEDLINE Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE® Daily and Ovid MEDLINE® 1946-Present (Ovid SP)

Search results (16 August 2021): 1806

Search strategy
COVID block

1. (coronavirus/ or betacoronavirus/ or coronavirus infections/) and (disease outbreaks/ or epidemics/ or pandemics/)
2. COVID-19/ or SARS-CoV-2/ or COVID-19 Vaccines/ or Severe Acute Respiratory Syndrome/ or Middle East Respiratory Syndrome Coronavirus/

3. (nCoV* or 2019nCoV or 19nCoV or COVID19* or COVID or 2019 nCoV or nCov 2019 or SARS-CoV2 or SARS CoV-2 or SARS-COV-2 or SARSCOV-2 or SARSCOV2 or Severe Acute Respiratory Syndrome Coronavirus 2 or Severe Acute Respiratory Syndrome Corona Virus 2).ti,ab,kf,nm,ot,ox,rx,px.
4. ((new or novel or "19" or "2019" or Wuhan or Hubei or China or Chinese) adj3 (coronavirus* or corona virus* or betacoronavirus* or CoV or HCoV)).ti,ab,kf,ot.
5. ((coronavirus* or corona virus* or betacoronavirus* or SARS or MERS) adj3 (pandemic* or epidemic* or outbreak* or crisis)).ti,ab,kf,ot.
6. ((Wuhan or Hubei) adj5 pneumonia).ti,ab,kf,ot.
7. (Severe Acute Respiratory Syndrome* or sudden acute respiratory syndrome* or SARS like or MERSCoV* or Middle East Respiratory or camel flu or EMC 2012).ti,ab,kf.
8. or/1-7

Workplace/personnel block

9. exp Occupational Health/ or Occupational Diseases/ or Occupational Exposure/ or Occupational Medicine/
10. Work/ or Workplace/ or Employment/ or Manpower/
11. (work or job or jobs).kf,kw.
12. (works* or worka* or worke* or workg* or worki* or worlk* or workp* or occupat* or company* or offic* or busines* or laborer* or labourer* or manpower or employee*).ti,ab,kf,ot.
13. (community* or population-base* or office-base* or household or retail* or restaurant* or manufacturing or meat processing or administrators or bartenders or cashiers or chefs or cleaners or dishwashers or drive-thru operators or cooks or baker* or waiter* or supervisor* or manager* or supplier* or machine operators or tradespeople or material handlers or painters or finishers or architects or engineers or contractors or customers or visitors or driver* or passenger* or clients or vendors or builder* or shipper* or plumber* or electrician* or technician* or police or cafe* or hotel* or accommodation or couriers or messengers or garden* or laundry or park* or sport*).ti,ab,kf,ot.
14. ((transport* or commut* or deliver* or transit or air or bus or train or rail or motor or vehicle or ship or car or taxi) adj5 (employ* or work* or people or crew* or pilot or staff or team* or service or driver* or passenger* or sector*)).ti,ab.
15. ((maintenance or trade or market* or retail* or shop* or store* or restaurant* or construction* or on-shore or outdoor or office or domestic or sanitation or social care or public or home or secur* fire or gym* or fitness or postal or repair or packaging or labeling or gasoline or legal or court or librar* or technical or television or film) adj5 (employ* or work* or people or crew* or staff or team* or service or sector or enterprise* or entrepreneur* or dealer*)).ti,ab.
16. ((firstline or first-line or frontline or public or customer* or coworker* or first responder*) adj3 (contact* or expos*)).ti,ab,kf,ot.
17. (((crowd* or close* or share*) adj3 (place* or space* or room*)) or (lunchroom* or changeroom* or breakroom* or break room)).ti,ab,kf.
18. or/9-17

Intervention block

19. Protective Devices/ or Ear Protective Devices/ or Eye Protective Devices/ or exp Gloves, Protective/ or Masks/ or Personal Protective Equipment/ or Protective Clothing/ or Respiratory Protective Devices/
20. (personal protect* or PPE or PPEs or protective device* or protective layer*).ti,ab,kf.
21. ((protect* or safe*) adj3 (glasses or eyeglasses or eyewear or cap or caps or equipment or garment* or clothing or clothes or apron* or suit or suits or shoe* or attire or shield* or gear)).ti,ab,kf.
22. (protect* adj2 (head or heads or face or faces or facial or foot or feet or hand or hands or eye or eyes or mouth or mouths or skin)).ti,ab,kf.
23. (facepiece* or face piece* or mask or masks or facemask* or faceshield* or face shield* or respirator or respirators or FFP1 or FFP2 or FFP3).ti,ab,kf.

24. ((surgical or procedure or respiratory or protect* or facial or face or N99 or N95 or N 99 or N 95) adj2 mask*).ti,ab,kf.
25. ((N99 or N95 or N 99 or N 95 or FFP or P100) adj3 respirator*).ti,ab,kf.
26. ((protect* or filter*) adj2 respirator*).ti,ab,kf.
27. (coverall* or boot or boots or donning or donned or doff or doffing or doffed or face cover* or facial cover* or glove or gloves or gloving or gown or gowns or gowning or goggle* or head cover* or headwear or hood or hoods or overshoe* or shoe cover* or smock or smocks or visor or visors).ti,ab,kf.
28. ((physical* or social) adj3 (distanc* or contact*)).ti,ab,kf.
29. (stagger* or barrier* or bubble* or hazard* or marking* or schedule* or reschedule* or adjust* or adapt* or ((work or traffic) adj3 flow*)).ti,ab,kf.
30. (hand* adj3 (sanit* or disinfect* or wash* or clean* or hygiene*)).ti,ab,kf.
31. (HVAC or HEPA or heat* or ventilat* or (air adj3 (condition* or purificat* or filter*))) or fresh air or mist* or fog*).ti,ab,kf.
32. (UV light* or ultraviolet light* or clean* or disinfect*).ti,ab,kf.
33. ((telework* or telecommut* or (tele or remote or mobile or distant* home)) adj3 (work* or office or job)).ti,ab,kf.
34. Vaccination/
35. (vaccin* or train* or screen* or policy or sick* or absent* or audit or surveillance).ti,ab,kf.
36. (((rapid or antigen or home-based or PCR or molecular-based) adj3 test*) or self-test*).ti,ab,kf.
37. (quarant* or self-isolat* or isolat* or outbreak or contact tracing).ti,ab,kf.
38. (close* or open* or reopen* or return or return-to-work).ti,ab,kf.
39. (((protect* or control) adj3 measure*) or ((source or engineering or administrative) adj3 control*)).ti,ab,kf.
40. or/19-39

Study design block

41. (Randomized Controlled Trial or Controlled Clinical Trial or Pragmatic Clinical Trial or Equivalence Trial or Clinical Trial, Phase III).pt.
42. Randomized Controlled Trial/
43. exp Randomized Controlled Trials as Topic/
44. Controlled Clinical Trial/
45. exp Controlled Clinical Trials as Topic/
46. Randomization/
47. Random Allocation/
48. Double-Blind Method/ or Double-Blind Studies/ or Single-Blind Method/ or Single-Blind Studies/
49. Placebos/ or Placebo/
50. Control Groups/ or Control Group/
51. (random* or sham or placebo*).ti,ab,hw,kf,kw.
52. ((singl* or doubl*) adj (blind* or dumm* or mask*)).ti,ab,hw,kf,kw.
53. ((tripl* or trebl*) adj (blind* or dumm* or mask*)).ti,ab,hw,kf,kw.
54. (control* adj3 (study or studies or trial* or group*)).ti,ab,kf,kw.

55. (Nonrandom* or non random* or non-random* or quasi-random* or quasirandom*).ti,ab,hw,kf,kw.
56. allocated.ti,ab,hw.
57. ((open label or open-label) adj5 (study or studies or trial*)).ti,ab,hw,kf,kw.
58. ((equivalence or superiority or non-inferiority or noninferiority) adj3 (study or studies or trial*)).ti,ab,hw,kf,kw.
59. (pragmatic study or pragmatic studies).ti,ab,hw,kf,kw.
60. ((pragmatic or practical) adj3 trial*).ti,ab,hw,kf,kw.
61. ((quasiexperimental or quasi-experimental) adj3 (study or studies or trial*)).ti,ab,hw,kf,kw.
62. (phase adj3 (III or "3") adj3 (study or studies or trial*)).ti,hw,kf,kw.
63. Interrupted Time Series Analysis/
64. exp Controlled Before-After Studies/
65. Comparative Study/
66. (controlled before-after stud* or time series).ti,ab,kf,kw,pt.
67. or/41-66

Combined search

68. 8 and 18 and 40 and 67

CONTRIBUTIONS OF AUTHORS

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Coordinating the protocol: ABP, MB

Writing the protocol: ABP, KN, OS, EP, JEV, CG, KJJ, CM, DM, BNS, MTV, SR, KS, TF, SD, MB

Providing general advice on the protocol: SD

DECLARATIONS OF INTEREST

ABP has no interest to declare.

MB has no interest to declare.

KN has no interest to declare.

OS has no interest to declare.

EP has no interest to declare.

JEV has no interest to declare.

CG has no interest to declare.

KJJ has no interest to declare.

DM has no interest to declare.

BNS has no interest to declare.

MVT has no interest to declare.

CM has no interest to declare.

KS has no interest to declare.

SR has no interest to declare.

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NOTES

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