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Masks and respirators for the prevention of respiratory infections: a mechanism-informed narrative synthesis

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ADMINISTRATIVE INFORMATION

Support - This study is supported by UKRI Cross Research Council Responsive Mode (CRCRM) grant 25130 for Interdisciplinary Research.

Review Stage at time of the first submission - Preliminary searches.

Conflicts of interest - JW developed the Evidential Pluralism methodology that is the basis for the proposed Systematic Review+ approach. TG led a previous narrative review on masks (on which MU was a coauthor) and is a member of Independent SAGE. MU has written critiques of mask RCTs. All other authors declare no conflicts of interest.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 11 May 2025 and was last updated on 28 September 2026. Amended 1 June 2026. The review is now conducted in two components (community settings; healthcare settings), reported separately. The method described as Systematic Review+ (SR+) was developed into mechanism-informed narrative synthesis (MINS). Bespoke design-specific appraisal tools replaced GRADE checklists; no meta-analysis was performed; quantitative bias analysis was used as a stress test; a large language model supported searching and appraisal; qualitative evidence is synthesised separately. The databases searched for the community component are listed under Search strategy. Two references to mask mandates in the synthesis section, carried over in error from the companion mandates protocol (INPLASY 202550024), have been corrected. The healthcare component will use the same methods; any component-specific details will be added by further amendment before appraisal of healthcare studies begins.

INTRODUCTION

Review question / Objective Empirical objectives (this protocol):

1. To determine the efficacy of face coverings (masks and respirators) in reducing the spread of respiratory infections, in community settings and in healthcare settings.

2. To identify the mechanisms through which this effect is achieved (or the mechanisms which explain why it is not achieved).

Methodological objective. Using this review as a worked example:

1. To produce a potentially generalisable methodology for combining associative and mechanistic evidence in systematic review,

originally described as Systematic Review+ (SR+) and now developed as mechanism-informed narrative synthesis (MINS).

2. To examine the extent to which this methodology mitigates key criticisms of orthodox systematic reviews, both epistemological and ethical.

Rationale The question of whether face masks and face mask mandates are effective in reducing transmission of respiratory diseases generated much controversy during the COVID-19 pandemic. An orthodox systematic review, analysing only randomised controlled trials (RCTs) and published in the Cochrane Library, concluded that the existing evidence on face mask efficacy was not definitive (i.e. the authors decided that they could not firmly conclude either that masks were effective or that they were ineffective).¹ One review which included non-RCT evidence, especially evidence of mechanism ('mechanistic evidence'), concluded that there was evidence of efficacy; it proposed explanations for why some RCTs demonstrated efficacy while others did not.² One key area of contestation is whether trials were testing masking itself or 'advice to mask'.

Accordingly, we are currently exploring both the efficacy of masks and the efficacy of mask mandates in separate reviews. This review addresses the former.

One contentious issue is whether (and if so, why) respirators are superior to medical masks or cloth masks. Another contentious issue is whether masks or respirators should be worn by healthcare workers a) only when in close vicinity of a patient with known or suspected respiratory infection, b) only when doing a so-called aerosol-generating medical procedure, or c) continuously when at work. To design optimal association studies that could answer these questions, we need to know how masks and respirators achieve any effect they may have. In other words, we need evidence of mechanism.

To demonstrate causality, we typically need two kinds of evidence: associative (to show that a change in one phenomenon is associated with a change in another) and mechanistic (to be confident that any observed association is genuinely causal). In biomedicine, the former is, ideally, obtained from RCTs but the latter may come from a wide range of study designs. Orthodox methods of evidence synthesis, such as those used for Cochrane reviews and informed by the GRADE criteria, classify mechanistic evidence as inherently lower quality than RCT evidence. But

this position can be challenged on both epistemological grounds (since mechanistic evidence can raise or lower confidence in a causal claim) and on ethical grounds (since dismissing certain forms of evidence may be a form of epistemic injustice). Furthermore, a poorly designed RCT, which tests an intervention but takes no account of mechanism and is hence sub-optimally designed, may mislead. This study, which seeks to extend the emerging scholarly tradition of 'EBM+' with 'SR+', will formally and systematically evaluate mechanistic evidence and use that evidence to complement and challenge findings from RCTs and other associative evidence.

The evidence pertaining to whether and how mask and respirators work is heterogeneous and comes from multiple disciplines. The associative evidence comprises RCTs and observational (non-randomised comparative) studies, but many are difficult to interpret because a) different studies tested different products; b) people received variable instruction on when and how to wear their face covering; c) compliance with these instructions varied (and was sometimes unmeasured); d) many of the associative studies did not engage adequate specialist expertise; and e) reviews of associative studies have tended to overlook the extensive body of work by topic experts in the field (e.g. of occupational health). Mechanistic evidence (e.g. on the behaviour of droplets and aerosols in indoor air, the physical and material properties of masks and respirators, the process by which particles are filtered, the impact of masking on physiological biomarkers, and the impact of different communication strategies in advice to mask) comes from a wide range of disciplines and study designs including aerosol science, engineering, and physiology.

Condition being studied Face masks and respirators in reducing transmission in the context of respiratory infection outbreaks. (See also separate protocol, INPLASY 7685, on mask mandates).

Examining the relationship between mask wearing and incidence of respiratory infections requires integration of both associative evidence (i.e. whether and to what extent masking can be determined to affect incidence of new cases in particular disease outbreaks and settings) and mechanistic evidence (i.e. whether and how masks and respirators interfere with essential steps in respiratory disease transmission).

Masks are hypothesised to work, or fail, at four interdependent levels. Each level must be at least

partly activated for mask wearing to prevent infection; failure at any one can negate the others.

1. Physical and material. Masks reduce emission and inhalation of infectious particles by filtration. Respirators filter efficiently across the sub-micron range; surgical and cloth masks filter less and more variably. In practice, protection depends more on leakage around the face seal than on the filter material.

2. Biological and dose-response. Respiratory infections spread mainly through exhaled particles, including aerosols that remain suspended in poorly ventilated spaces. Reducing the inhaled dose lowers the probability of infection in a graded way, so partial protection is biologically meaningful, and masks on infectious people reduce the dose received by others.

3. Behavioural. Masks protect only when worn consistently, correctly and during the relevant exposures. Adherence depends on motivation, comfort and social norms.

4. Epidemiological. Individual protection reduces transmission in a population only with sufficient coverage. Source control and wearer protection combine, and benefits depend on who is masked, contact networks and epidemic phase. The effect of masking on an individual is therefore not the same as the effect of a mask policy on a population.

The review is conducted in two components, reported separately: community settings, and healthcare settings (including the comparison of respirators with medical masks, and when healthcare workers should wear them).

METHODS

Search strategy Searching will be iterative and use multiple methods. These will include

- for the community component, key word searches of five databases: PubMed (Medline), Web of Science Core Collection (which includes SSCI), Embase, Cochrane Library and PsycINFO. CINAHL, Scopus, JSTOR and Annals of Work Exposure and Health will be searched for the healthcare component;
- author search (authors of seminal papers will be name-searched in relevant databases to identify additional papers by them);
- citation-tracking (via Google Scholar);
- mining previous systematic reviews;
- relevant engineering standards and the references on which they are based, including British/European (e.g. EN14683, EN149), American (e.g. National Institute for Occupational Safety and Health, NIOSH), and Canadian (e.g. Canadian Standards Association, CSA);

- asking experts in relevant fields e.g. occupational health and safety;

- AI-assisted searching using a large language model, with all results checked by the review team.

Key words and database search strings:

Related to masks: masks, respirators, face coverings, non-pharmaceutical interventions (NPIs), respiratory protective devices.

Related to respiratory outbreaks: respiratory outbreak, respiratory pandemic, epidemic control, public health intervention.

Specific respiratory illness keywords: COVID-19, SARS-CoV-2, influenza, SARS (Severe Acute Respiratory Syndrome), MERS (Middle East Respiratory Syndrome).

Outcome and Effect Keywords: transmission rate, infection rate, disease spread, hospitalization rate, mortality rate, community transmission, effectiveness, impact, efficacy.

Mechanism keywords: aerosols, air filtration, filtration efficiency, adsorption, absorption, breathability, fit factor, mask efficiency, mask coatings, antibacterial.

Database Search Strategies:

Combine keywords using Boolean operators (AND, OR, NOT).

Example: (mask*) AND (COVID-19 OR influenza) AND transmission rate

Use truncation (*) to capture variations of words.

Example: mask* will find masks, masking, etc.

Use phrase searching (quotation marks) to find exact phrases.

Example: "public health intervention"

Use MeSH terms (Medical Subject Headings) in PubMed/MEDLINE for more precise results.

Example Search Strings:

PubMed: (mask*[Title/Abstract] OR face covering[Title/Abstract]) AND (COVID-19[MeSH Terms] OR influenza[MeSH Terms]) AND (transmission[Title/Abstract] OR infection[Title/Abstract])

Google Scholar: mask* AND (respiratory outbreak OR pandemic) AND (transmission OR effectiveness)

These keywords and search strategies were piloted in the specific databases and modified in response to emerging findings. Searching was iterative and continued to saturation. The full search strategies used for the community component, with search dates, are reported in the supplementary material to the review.

Participant or population Any setting where masks or respirators are tested.

Intervention Mask (cloth, medical, surgical) or respirator.

Comparator For associative studies, either no mask/respirator or a different kind of mask/respirator.

Study designs to be included No restriction in study design. We anticipate that a wide range of designs including a preponderance of laboratory and occupational health studies for the mechanistic component.

Eligibility criteria Empirical research studies (including evidence syntheses as a source of such studies) which contribute to establishing both the association between masking and reduction of respiratory disease transmission, and examining specific mechanism hypotheses underlying this association. Peer reviewed literature will be prioritised but if there is insufficient evidence on important aspects of the review question, publicly available preprints will be considered. Inconsistencies between study outcomes will be elucidated by exploring the cause of the inconsistency.

Information sources Electronic databases, sources known to the authors, topic experts in the field.

Main outcome(s) Whether, to what extent and why the introduction of mask wearing affects the incidence of respiratory infections. Whether existing studies—both associative and mechanistic—are adequate to answer these questions.

Additional outcome(s) These will be added as appropriate as the review unfolds.

Data management Data will be stored on University of Manchester, University of Oxford and University of Exeter computers. Eligible papers will be stored, organised and coded on an Endnote database. Data extraction will occur using summaries on Microsoft Office packages (e.g. Word, Excel). Specialist data management packages compliant with university data policies will be used if needed.

A large language model (Claude, Anthropic) was used to supplement searching, stress-test the explanatory account, and draft structured appraisals and tables; all outputs were checked by the review team. The knowledge documents that instructed the AI tool, and the appraisals of all included studies, are deposited on Zenodo (<https://doi.org/10.5281/zenodo.23005151>).

Quality assessment / Risk of bias analysis The study seeks to draw upon, challenge and extend the GRADE criteria and methodology for ranking and evaluating empirical evidence. Because GRADE assesses certainty across a body of evidence rather than appraising individual studies, primary studies were appraised with bespoke design-specific tools informed by GRADE guidance and standard risk-of-bias tools. The appraisal assessed whether the conditions needed for the protective mechanism to operate were present, and the likely direction and magnitude of each bias. Each study was classified as above the line (contributes to causal inference), below the line (null result mechanistically expected) or uninformative. As planned, input from topic experts was sought (e.g. clinicians, occupational health and safety, engineers, aerosol scientists, statisticians).

Strategy of data synthesis Tables were prepared of key studies, including author/year, study design, methods, sample, findings, strengths/limitations and comments.

An initial explanatory account of how masks work, and how studies can fail to detect an effect, was drawn from state-of-the-science reviews of mask mechanisms. Primary studies were grouped by design into cognate groups and synthesised narratively against this account, using the hermeneutic cycle, in which each new data source is used to refine and enrich the understanding of the whole. Formal meta-analysis was considered but not performed, because the studies were too heterogeneous for pooling; instead, disaggregated data are presented and differences in study protocol and conditions are used to explain differing outcomes.

Mechanistic evidence was combined with associative evidence to produce an emerging synthesis of causality in mask efficacy, contributing further insights into the overall strength of evidence and to estimates of the generalisability (external validity) of particular empirical findings. Qualitative evidence is being synthesised separately.

The findings from this review are being used to inform the methodological objective of developing MINS as a generalisable method for combining associative and mechanistic evidence; this aspect of the study is described in a separate protocol.

Subgroup analysis Hypotheses about subgroup effects will be tested as appropriate if and when they emerge as the review unfolds.

Sensitivity analysis Quantitative bias analysis was used as a stress test of selected findings, not as a primary analysis.

Language restriction No restriction. Studies published in languages not spoken by the review authors will be translated.

Country(ies) involved United Kingdom (University of Oxford).

Keywords See search strategy above.

Dissemination plans Dissemination plans include preparation of academic papers, including methods and publication guidance for SR+ to be submitted to the EQUATOR network. In addition, we will produce training materials, build links with policymakers and advocacy groups, and hold a series of workshops for academic reviewers, evaluators and lay (e.g. advocacy) groups.

Other relevant information Review stage at time of this submission: Community component completed; manuscript under submission. Healthcare component not yet started.

Contributions of each author

Author 1 - Trisha Greenhalgh - TG conceptualised the study along with JW and RH. She will be involved in all aspects of the review including searching, data extraction, data synthesis and writing up.

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Author 2 - Jon Williamson - JW is a philosopher who has worked on Evidential Pluralism. He conceptualised this study along with TG and RH. He will lead the methodological work package on the methodology of SR+, with input from all other authors.

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Author 3 - Sahanika Ratnayake - SR has a background in philosophy and systematic review. She will undertake searching, data extraction, data synthesis and writing up.

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