COVID-19 Living Evidence Synthesis 15.1: Effectiveness of ventilation for reducing transmission of COVID-19 and other respiratory infections in non-health care community-based settings

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This living evidence synthesis (LESs) is part of a suite of LESs of the best-available evidence about the effectiveness of six PHSMs (masks, quarantine and isolation, ventilation, physical distancing and reduction of contacts, hand hygiene and respiratory etiquette, cleaning, and disinfecting), as well as combinations of and adherence to these measures, in preventing transmission of COVID-19 and other respiratory infectious diseases in non-health care community- based setting. This first full version was developed after two interim versions, which are available upon request. The next update to this and other LESs in the series is to be determined, but the most up-to-date versions in the suite are available on the COVID-END website. We provide context for synthesizing evidence about public health and social measures in Box 1 and an overview of our approach in Box 2.

Questions

Effectiveness

1. What is the effectiveness of different ventilation strategies in reducing transmission of COVID-19 and other viral respiratory illnesses (e.g. influenza, respiratory syncytial virus (RSV)) in community-based settings (i.e., not clinical or healthcare settings)? Ventilation strategies include ventilation rates (air changes per hour, flow rates), air flow patterns, and the ratio of outdoor air to re-used air.
2. What is the effectiveness of different filter ratings (within ventilation systems) in reducing transmission of COVID-19 or other viral respiratory illnesses in community-based settings?
3. What is the effectiveness of different combinations of ventilation and filtration strategies in reducing transmission of COVID-19 or other viral respiratory illnesses in community-based settings?
4. What is the effectiveness of portable air cleaners in reducing transmission of COVID-19 or other viral respiratory illnesses in community-based settings?

Negative outcomes

5. What are the negative impacts of improving ventilation or filtration (e.g., costs, increased inequity in COVID-19 transmission)?
6. What are the negative impacts of introducing portable air cleaners (e.g., costs, increased inequity in COVID-19 transmission)?

Executive summary

Background

- Airborne (or aerosol) transmission is recognized as a route of transmission of the SARS-CoV-2 virus which causes COVID-19 illness.[1] Airborne transmission occurs when the virus is released by an infected individual in small particles or droplets; aerosol droplets tend to follow air flow patterns instead of travelling on their own trajectory. The aerosol droplets travel with the air and may be inhaled by other individuals. Inhalation of these droplets may or may not result in infection and subsequent illness based on various factors, such as viral load and characteristics of the individual. Aerosol droplets can remain airborne, sometimes indefinitely, and can travel long distances. Environmental conditions such as ventilation rates and airflow patterns affect the routes and distances that aerosols travel.
- Heating, ventilation and air conditioning (HVAC) systems within the built environment can increase or mitigate the risk of airborne transmission of aerosols. A number of principles regarding ventilation are well-established and supported by organizations that set standards for the HVAC industry such as the American Society of Heating, Refrigerating and Air Conditioning Engineers (ASHRAE). These include maintaining minimum outdoor airflow rates, using combinations of filters and air cleaners that achieve a minimum efficiency, promoting mixing of space air while avoiding strong air currents, and balancing exposure reduction with energy expenditures. Given these recognized standards, this review focused on comparative effectiveness in terms of: ventilation rates (often quantified as air changes per hour, ACH); air flow patterns (i.e., where air flows within a space, influenced by various factors including the nature and placements of inlet and outflow of air from a space); the ratio of outdoor (e.g., fresh) air to re-used air (outdoor air is introduced by mechanical HVAC systems as well as by opening doors or windows); and filters within HVAC systems. Updates (versions 2 and 3) of this review also added questions about effectiveness and negative impacts of portable air cleaners (questions 4 and 6).
- Recent systematic reviews (SRs) have investigated ventilation,[2] filtration,[3] humidity,[4] and ultraviolet irradiation[5] within mechanical HVAC systems and the impact of these features on aerosol transmission. The SR of ventilation (32 studies published between 2004 and 2021; majority modelling studies) confirmed a number of well-understood principles, including increasing ventilation rate is associated with decreased virus transmission. However, multiple factors need to be considered simultaneously "such as ventilation rate, airflow patterns, air balancing, occupancy, and feature placement." The SR of filtration (23 studies published between 1966 and 2021; animal studies n=17, aerosolized virus studies n=7, modelling studies n=9) also confirmed several well-understood principles, including decreased virus transmission with increasing filter efficiency. The review authors concluded that "filtration is one factor offering demonstrated potential for decreased transmission."
- ASHRAE sets standards for testing and application of HVAC features that guide practices in North America. A statement from ASHRAE in April 2021 acknowledged that airborne transmission of SARS-CoV-2 is significant and provided guidance on changes to building operations including HVAC systems.[6]

- ASHRAE[7] and the United States Environmental Protection Agency[8] (EPA) suggest using portable (or in-room, stand-alone, plug-in) air cleaners (or air purifiers) when existing HVAC systems do not meet ASHRAE standards. Portable air cleaners use one or a combination of technologies (e.g., filters, ultraviolet light in the germicidal wavelengths [UV-C]) to remove particles from the air and/or kill or inactivate infectious agents.[9] ASHRAE advises that portable air cleaners using some technologies such as ionisers and photocatalytic oxidation [UV-PCO]) are considered emerging without proven efficacy, and may convert contaminants to other potentially harmful compounds.[9]
- Two recent SRs examined the effectiveness of portable air cleaners. One SR focused on HEPA (high efficiency particulate air) purifiers and included 11 experimental studies. Results showed that HEPA filters were effective in reducing particles that are similar in size to SARS-COV-2.[10] A second SR found no studies examining the effect of air filters on incidence of respiratory infections, but identified two studies showing that filters can capture airborne bacteria.[11]

Key points

- Airborne transmission is a route for COVID-19 infection and involves transmission through aerosols. Ventilation and filtration can affect movement of aerosols within a space, including the patterns and distances that aerosols travel.
- Eight studies[12-19] examined ventilation in different community-based settings (4 in schools, 2 at industrial worksites, and 2 in private homes). Studies in schools found that improving ventilation could reduce COVID-19 infection; however, two studies did not provide quantitative estimates of effect. Studies of different industrial worksites found different impacts of ventilation. Studies in homes also found different effects for ventilation: a study that only investigated a few environmental factors found an effect while the other study that examined numerous personal and household practices (e.g., mask use, disinfection and social distancing) in addition to physical features of the home found no effect of ventilation in multivariable analyses.
- Five studies[20-24] used modelling to investigate outbreaks of COVID-19. Three studies demonstrated an association between ventilation rates and infection risk or attack rates. A fourth study showed that a number of factors including ventilation influenced transmission (i.e., duration of exposure and emission rate from the infected source). The fifth study did not show consistently lower infection rates with higher ventilation rates; authors attributed differences in infection rate to mask use.
- One study[25] examined the effectiveness of portable air cleaners in reducing transmission of COVID-19 or risk of infection; authors attributed different secondary attack rates at two restaurants (at different times during the pandemic) to UV-C air purifiers. However, other public health measures were not considered (notably one outbreak occurred prior to availability of vaccines).
- We found no studies reporting on negative outcomes of improving ventilation, which may be due to the focus of the review on comparative studies and COVID-19. One study[26] surveyed students and teachers about acceptance of portable HEPA air purifiers in classrooms, and found that noise levels could be disturbing and affect communication in class. Acceptance improved when noise levels were reduced (i.e., by lowering flow rate of air purifiers).
- Overall, existing studies show some differences in terms of the role of ventilation in transmission of SARS-CoV-2 and incidence of COVID-19. Comparisons across studies are difficult due to: different research methods; definitions, measurements, and categorization of ventilation and other variables; and analytic approaches (in particular control for confounding).

Many existing studies are of low quality (high risk of bias) due to issues with selection, measurement, and/or confounding. Comparisons within and across studies are complicated by different time periods during the pandemic when new variants appeared and diverse public health measures were available and enforced. Some findings may not be applicable to a Canadian context due to the influence of environmental factors on ventilation strategies and their effects.

- Many modelling and simulation studies of ventilation and filtration have been published since the start of the COVID-19 pandemic. Some include risk or probability of transmission or infection; however, many others focus on airflow patterns, dispersion of particles, or concentration of potentially infectious particles (i.e., outcomes that are upstream in the transmission/infection chain). These studies may be challenging to apply to 'real world' scenarios due to the complex interactions of variables related to ventilation parameters themselves as well as other factors in the space (e.g., occupancy, characteristics and movement of infected and non-infected individuals, etc.).
- ASHRAE and similar organizations support a number of well-established principles regarding ventilation such as maintaining minimum outdoor airflow rates, using combinations of filters and air cleaners, and promoting mixing of space air. They also provide recommendations for HVAC system operation and commissioning. These principles contribute to indoor air quality and also provide health benefits independent of COVID-19 (illnesses or irritation caused by viruses, bacteria, pollutants, allergens, and other agents).
- ***Key points from citizen partners:***
    - Public facilities should ensure that recommended standards (i.e., from ASHRAE) for HVAC systems are implemented. This will contribute to improved indoor air quality and lessen other respiratory illnesses, negative health effects, and potential future outbreaks.
    - Knowledge translation for the public and those working in public spaces (e.g., teachers) about ventilation principles and parameters should be considered. Further, posting ventilation conditions and adherence to standards in public facilities would help the public make informed decisions about visiting or not.
    - More research about the effectiveness of commercially available portable air cleaners in non-healthcare community-based settings is urgently needed to guide decision-making.

Overview of evidence and knowledge gaps

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- Eight studies[12-19] examined ventilation in different community-based settings. Two studies in schools found associations between improved ventilation and reduced COVID-19 illness. A third study of a school outbreak concluded that poor ventilation was a contributing factor but did not provide quantitative estimates of effect. In the final school-based study there was no self-reported transmission of COVID-19 in classrooms with protocols of natural ventilation through regular window opening. Two studies of different industrial worksites (meat and chicken processing plants in Germany, oilfield in Kazakhstan) found different impacts of ventilation.[16, 18] The study of meat processing plants found an association between ventilation and COVID-19 illness. The oilfield study found that ventilation was not a significant factor; the authors concluded that individual factors (hand sanitizer use, social interactions) were main drivers of transmission with little contribution by environmental factors. Two studies examined transmission in homes of individuals with COVID-19.[17, 19] One study examining a large number of variables found no significant effect for ventilation (opening windows ≤1 vs >1 hour/day); authors concluded that mask use, disinfection and social distancing were more influential in reducing transmission. Study limitations included self-reporting exposure, categorization of

exposure variable, and unclear method of outcome ascertainment (secondary transmission). A second study found ventilation was significantly associated with transmission rate; however, analyses were not adjusted for other personal or behavioural variables.

- Five studies[20-24] used modelling to investigate outbreaks of COVID-19. Three studies demonstrated an association between ventilation rates and infection risk or attack rates. A fourth study showed that probability of infection was lower with higher ventilation rates; however, other factors also influenced transmission, specifically duration of exposure and emission rate from the infected source. The fifth study did not show consistently lower infection rates with higher ventilation rates; authors attributed differences in infection rates to mask wearing habits.
- One study[25] examined the effectiveness of portable air cleaners in reducing transmission of COVID-19 or risk of infection: the study compared outbreaks in two restaurants before and after mandatory ventilation requirements. The secondary attack rate was significantly lower in the second restaurant that had installed UV-C air purifiers (resulting in higher air changes per hour). Authors concluded that the air purifiers significantly reduced the secondary attack rate; however, other public health measures (e.g., availability of vaccines) were not considered.
- We found no studies reporting on negative outcomes of improving ventilation, which may be due to the focus of the review on comparative studies and COVID-19. We identified one study[26] that surveyed students and teachers twice (summer and winter) about acceptance of portable HEPA air purifiers that had been installed in German schools. Survey responses varied based on the sound pressure of the devices (operating at ~55 vs ~47 decibels for several months prior to each survey, respectively). Authors concluded that noise levels need to be considered and acceptance can be improved when noise level is reduced.
- We found only one study examining the effectiveness of portable air cleaners in terms of reducing transmission of COVID-19 or risk of infection. A recent SR noted the "important absence of evidence regarding the effectiveness" of portable air cleaners for reducing transmission of COVID-19 and other respiratory infections, and highlighted the urgent need for randomized controlled trials.[11] Most of the existing experimental studies of portable air cleaners assess the ability of devices to remove particles (e.g., surrogates reflecting the size of SARS-COV-2 or aerosol droplets) from the air (or reduce particulate matter concentration, i.e., filter efficiency).
- The methodological quality of most studies included in this review is low due to concerns about selection bias, measurement bias, and/or confounding. Conflicting results seen across studies may be attributable to differences in: research methods; analytic approaches (e.g., control for confounding; dichotomization or categorization of continuous variables); and definitions, measurement, and categorization of ventilation and other variables.
- Much of the scientific literature on these topics is in the form of modelling or simulation studies. It can be challenging to apply results from these studies to practical applications for various reasons. For instance, modelling or simulation studies may be based on assumptions that vary across specific 'real world' settings. They may focus on specific configurations that change continuously in real world scenarios (e.g., occupancy, movement, and specific activities of people within a space; presence and characteristics of infected individuals; susceptibility of other individuals). And often they focus on specific steps within the chain of transmission: many modelling or simulation studies examine air flow patterns, dispersion of air particles within a space, or concentration of potentially infectious particles within air samples across time and space considerations; however, they may not consider the impacts in terms of transmission of infectious particles and occurrence of illness.

Suggested Tweet

- #ventilation #filters #hvac affect #coronavirus transmission. #iaq improves health and saves money.

Box 1: Context for synthesizing evidence about public health and social measures (PHSMs)

This series of living evidence syntheses was commissioned to understand the effects of PHSMs during a global pandemic to inform current and future use of PHSMs.

General considerations for identifying, appraising and synthesizing evidence about PHSMs

- PHSMs are population-level interventions and typically evaluated in observational studies.
  - Many PHSMs are interventions implemented at a population level, rather than at the level of individuals or clusters of individuals such as in clinical interventions.
  - Since it is typically not feasible and/or ethical to randomly allocate entire populations to different interventions, the effects of PHSMs are commonly evaluated using observational study designs that evaluate PHSMs in real-word settings.
  - As a result, a lack of evidence from RCTs does not necessarily mean the available evidence in this series of LESs is weak.
- Instruments for appraising the risk of bias in observational studies have been developed; however, rigorously tested and validated instruments are only available for clinical interventions.
  - Such instruments generally indicate that a study has less risk of bias when it was possible to directly assess outcomes and control for potential confounders for individual study participants.
  - Studies assessing PHSMs at the population level are not able to provide such assessments for all relevant individual-level variables that could affect outcomes, and therefore cannot be classified as low risk of bias.
- Given feasibility considerations related to synthesizing evidence in a timely manner to inform decision-making for PHSMs during a global pandemic, highly focused research questions and inclusion criteria for literature searches were required.
  - As a result, we acknowledge that this series of living evidence syntheses – about the effectiveness of specific PHSMs (i.e., quarantine and isolation; mask use, including unintended consequences; ventilation, reduction of contacts, physical distancing, hand hygiene and cleaning and disinfecting measures), interventions that promote adherence to PHSMs, and the effectiveness of combinations of PHSMs – does not incorporate all existing relevant evidence on PHSMs.
  - Ongoing work on this suite of products will allow us to broaden the scope of this review for a more comprehensive understanding of the effectiveness of PHSMs.
  - Decision-making with the best available evidence requires synthesizing findings from studies conducted in real-world settings (e.g., with people affected by misinformation, different levels of adherence to an intervention, different definitions and uses of the interventions, and in different stages of the pandemic, such as before and after availability of COVID-19 vaccines).

Our approach to presenting findings with an appraisal of risk of bias (ROB) of included studies

To ensure we used robust methods to identify, appraise and synthesize findings and to provide clear messages about the effects of different PHSMs, we:

- acknowledge that a lack of evidence from RCTs does not mean the evidence available is weak
- assessed included studies for ROB using the approach described in the methods box
- typically introduce the ROB assessments only once early in the document if they are consistent across sub-questions, sub-groups and outcomes, and provide insight about the reasons for the ROB assessment findings (e.g., confounding with other complementary PHSMs) and sources of additional insights (e.g., findings from LES 20 in this series that evaluates combinations of PHSMs)
- note where there are lower levels of ROB where appropriate
- note where it is likely that risk of bias (e.g., confounding variables) may reduce the strength of association with a PHSM and an outcome from the included studies

- identify when little evidence was found and when it was likely due to literature search criteria that prioritized RCTs over observational studies.

Implications for synthesizing evidence about PHSMs
Despite the ROB for studies conducted at the population level that are identified in studies in this LES and others in the series, they provide the best-available evidence about the effects of interventions in real life. Moreover, ROB (and GRADE, which was not used for this series of LESs) were designed for clinical programs, services and products, and there is an ongoing need to identify whether and how such assessments and the communication of such assessments, need to be adjusted for public-health programs, services and measures and for health-system arrangements.

Findings

- The search and reference check identified 1,441 studies. Three hundred and thirty-three studies were considered potentially relevant.
- Eight studies met the eligibility criteria for questions 1-3 on the effectiveness of ventilation or filtration (Table 1). We also identified five modelling studies that investigated COVID-19 outbreaks (Table 2). One study met the eligibility criteria for question 4 on the effectiveness of portable air cleaners (Table 3). No studies were identified for question 5 on negative impacts of ventilation, which may be due to the focus of the review on comparative studies and COVID-19. One study was identified for question 6 on negative impacts of portable air cleaners (Table 4).
- Figure 1 shows the flow of studies through the search and selection process.

Summary of findings about reducing transmission of COVID-19 or risk of infection

Questions 1-3, effectiveness of ventilation or filtration (Table 1)

Eight studies were included that reported on reducing transmission or incidence of COVID-19 as an outcome. The characteristics, findings and

Box 2: Our approach

We retrieved studies by searching: 1) PubMed via COVID-19+ Evidence Alerts; 2) pre-print servers through iCITE; 3) Compendex; and 4) Web of Science. Searches were conducted for studies reported in English, conducted with humans and published since 1 January 2020 (to coincide with the emergence of COVID-19 as a global pandemic). Detailed search strategy is included in **Appendix 2**, and eligibility criteria in **Appendix 3.**

Studies identified up to March 3, 2023 that reported on empirical data with a comparator were considered for inclusion. Modelling and simulation studies were identified but not included for review, unless they investigated an actual COVID-19 outbreak. Studies excluded based on full text review are provided in **Appendix 4**.

Population of interest: All population groups that report data related to all COVID-19 variants and sub-variants.

Intervention and control/comparator: Different rates and mechanisms (i.e., mechanical, natural, or infiltration) of air dilution; different filter ratings; and, different combinations of ventilation and filtration strategies. Portable air cleaners compared to other intervention or no intervention. Definitions provided in **Appendix 5**.

Effectiveness outcomes. Primary outcome: Reduction in transmission of COVID-19. **Secondary outcomes**: Reduction in transmission of other respiratory infections.

Study selection: One reviewer screened all titles and abstracts; a second reviewer screened those that were excluded by the first reviewer to ensure no potentially relevant records were missed. The full text of potentially relevant studies was reviewed by one reviewer. All team members discussed those that were unclear. The references of all included primary studies and relevant evidence syntheses (systematic reviews (SRs), meta-analysis, scoping reviews, etc.) were checked for inclusion.

Data extraction: Data extraction was conducted by one team member and checked for accuracy and consistency by another using the template provided in **Appendix 6**.

Critical appraisal: Risk of Bias (ROB) of individual studies was assessed using validated ROB tools. For cohort studies, we used a revised ROBINS-I tool and for cross-sectional and case-control studies we used JBI tools. Judgements for the domains within these tools were decided by consensus between at least two team members. Modelling studies were not assessed for ROB, as these are considered to provide indirect evidence of effects. Our detailed approach to critical appraisal is provided in **Appendix 7**.

Summaries: We synthesized the evidence by presenting a narrative summary of each study's findings. The next update to this document is to be determined.

Role of citizen partners: Researchers met with two citizen partners at the outset of the review to discuss the topic and focus. Citizen partners reviewed the draft report and provided feedback, including key take-away messages.

assessment of risk of bias for each study is presented in Table 1 (details for risk of bias available in Appendix 1). Community-based settings varied with 4 studies involving schools, 2 involving industrial workplaces, and 2 involving residential homes.

Schools (4 studies): A cross-sectional study examined the association between COVID-19 incidence and public health measures implemented at elementary schools in November and December 2020 in Georgia, United States.[14] Public health measures included "ventilation improvements" overall, and type of improvement (opening doors/windows, using fans to increase effectiveness of open windows, installation of HEPA filtration systems or installation of UVGI in high-risk areas). Among 169 schools, those that implemented ventilation improvements (n=87) showed reduced risk of COVID-19 incidence (risk ratio 0.61, 95% CI 0.43–0.87). Based on 123 schools with available data, the following associations were found for reduced risk of COVID-19 incidence compared to no ventilation improvements (n=37): dilution methods only (opening doors, opening windows, or using fans; n=39, 0.65, 95% CI 0.43–0.98); filtration +/- purification only (using HEPA filters with or without using UVGI and not opening doors, opening windows, or using fans; n=16, 0.69, 95% CI 0.40-1.21); and, dilution and filtration +/- purification (opening doors, opening windows, or using fans, and using HEPA filters with or without using UVGI; n=31, 0.52, 95% CI 0.32–0.83). A retrospective cohort study examined the impact of mechanical ventilation systems (MVS) installed in schools (total 10,441 classrooms, 1,419 schools) in Italy; the study period was September 2021 to January 2022.[13] The incidence of COVID-19 cases (per 1,000 students) was 4.9 and 15.3 for schools with and without MVS; the incidence proportion ratio over the entire period studied was 0.32. Based on most conservative estimates (and controlling for mechanical air changes per hour, compulsory schools, and number of students in the classroom), classrooms with MVS had a relative risk of 0.26 and relative risk reduction of 0.74; these estimates were statistically significant but no confidence intervals were reported. The authors found that higher ventilation rates resulted in greater relative risk reduction, and concluded that ACH >5 per hour ensures higher protection from respiratory infectious agents. A retrospective analysis following a school outbreak after reopening in September 2020 in Hamburg, Germany investigated teacher and students' condition/behaviour (e.g., time spent speaking, distance to students, mask use) as well as spatial conditions/ventilation across different classrooms where transmission occurred.[12] Authors concluded that factors contributing to spread of infection were "longtime exposure of pupils without mouth/ nose protection in crowded and poorly ventilated classrooms"; however, the individual and relative contribution of different parameters was not quantified. A cross-sectional survey of directors of state secondary/high schools in Pamplona, Spain was conducted in December 2020-January 2021 after re-opening schools.[15] The government had issued recommendations regarding public health measures in schools including protocols for natural ventilation with opening windows for specific amounts of time at various timepoints during the day. Directors from nine of eleven schools provided information and reported no cases of COVID-19 transmission in classrooms.

Industrial worksites (2 studies): A cross-sectional study of 22 meat and chicken processing plants in Germany in June to September 2020 assessed the association between infections and possible risk factors including ventilation, which was quantified as: outdoor air flow per employee in a working area = outdoor air flow / (number of employees in a working area / number of shifts in the working area).[18] Based on results of multivariable logistic regression analysis (for subsample of companies with many infected workers), having a ventilation system reduced chance of testing positive for COVID-19. The results overall (6,522 workers) were not statistically significant (adjusted OR 0.757, 95% CI 0.563-1.018). Results by type of worker showed no significant association for regular workers (aOR 1.076, 95% CI 0.619-1.869) but a significant reduction for temporary and contract workers (aOR 0.541, 95% CI 0.368-0.796). Overall results of multivariable logistic regression for maximum outdoor air flow (OAF) per employee found no significant difference (aOR 1.000 (95% CI 1.000-1.000). However, when the delivery, stunning/slinging/hanging, and slaughter areas were excluded from analysis (these areas have a process related high ventilation rate) (n=2,334) the association was significant (aOR 0.996, 95% CI 0.993–0.999; including interaction term for temperature and OAF, aOR 0.984, 95% CI 0.971– 0.996). A concurrent case-control study (296 cases, 536 controls) at an oilfield worksite in Kazakhstan in June to September 2020 investigated the association between 20 individual and 22 environmental factors (including ventilation at work, working indoors [office, kitchen, storeroom] and working outdoors) and occurrence of COVID-19.[16] Adjusted odds ratios for environmental factors showed no significant difference for ventilation at work (aOR 0.68 95% CI 0.36, 1.24), office work (aOR 0.93 95% CI 0.53-1.61), or outdoor work (aOR 0.75 95% CI 0.43-1.28). . Authors concluded that individual factors (e.g., rare hand sanitizer use, social interactions outside of work) were main drivers of transmission, with little contribution by environmental factors.

Private homes (2 studies): Wang et al conducted a retrospective cohort study examining accommodation and household hygiene practices in 124 homes (335 people) with at least one case of laboratory confirmed COVID-19 in Beijing, China in February and March 2020.[19] A large number of variables were examined for their association with secondary transmission within families. Ventilation was defined as the practice of opening the window to allow convection of indoor air and measured in hours per day. Though unadjusted analyses showed a significant association for ventilation (≤1 vs >1 hour/day, OR 2.55 95% CI 1.14 to 5.70), it was not significant in multivariable regression analyses. Authors concluded that highest risk of transmission occurred prior to symptom onset and that mask use, disinfection and social distancing were effective in preventing COVID-19. Oginawati et al conducted a field study in March-April 2021 examining environmental factors (temperature, humidity, brightness, ventilation size, and personal space area) in a convenience sample of 38 homes of recovered patients in Bandung City, Indonesia.[17] Homes were categorized as whether or not they met government guidelines for a "healthy house"; for ventilation, the healthy standard was defined as percentage of room area ≥10. Bivariate analyses showed that ventilation was significantly associated with transmission rate (i.e., number of family members having COVID-19 relative to number in house and categorized as low 0-50%, intermediate 50-99% and high 100%). Authors found a determination coefficient of 0.272 indicating the proportion of overall variation in transmission that is explained by the linear relationship with ventilation.

Modelling/simulation studies based on outbreaks (five studies): Five studies used modelling and simulations to investigate outbreaks of COVID-19 (Table 2). Two studies found that increasing ventilation rates and fresh-air supply could reduce risk of infection in the restaurant in Guangzhou, China where an outbreak occurred in January 2020.[20, 22] Ho et al showed that increasing the percentage of fresh-air in the supply air (by 10%, 50%, 100%) resulted in lower probability of infection (by 11%, 37%, and 51%, respectively). Liu et al simulated aerosol exposure index for individuals sitting at different tables in the restaurant and determined that infection risk for each individual was lower with increased ventilation. A third study investigated an outbreak caused by the same infected individual on two buses in Hunan Province, China in January 2020.[23] Through simulations, they estimated ventilation rates in each bus and found that attack rate (number of infected cases/number of persons) was higher on the bus with the lower ventilation rate (15.2% vs. 11.8%). A fourth study investigated an outbreak in a courtroom in Hamburg that occurred in October 2020.[24] Through simulations Vernez et al showed that probability of infection was lower with higher ventilation rates when the duration of the event was 1.5 and 3 hours but not at 0.5 hours. Authors concluded that ventilation is essential; however, other factors influence transmission, specifically duration of exposure and emission rate from the infected source (index case). A fifth study by Li et al conducted simulation experiments based on dormitory buildings in two provinces in China where outbreaks occurred in January to February 2020.[21] Results did not consistently show lower infection rates with higher ventilation rates. Authors attributed differences in infection rates to mask wearing habits.

Question 4, effectiveness of portable air filters

One descriptive epidemiological study examined the effectiveness of portable air cleaners on secondary attack rates based on outbreaks at two restaurants in Hong Kong in February and December 2021 (Table 3).[25] During the time, the government mandated enhancements of indoor air dilution in restaurants requiring at least 6 ACH or installation of air purifiers. The first outbreak occurred before the mandated enhancements in a restaurant with ACH 1.2; the second outbreak occurred after the mandate in a restaurant that had installed 14 UV-C air purifiers at ceiling level with ACH of 4.6. The secondary attack rate in the second restaurant was significantly lower (2.6% vs 33.7%, $p<0.001$). Authors concluded that the air purifiers significantly reduced the secondary attack rate; however, other public health measures (availability of vaccines) were not taken into account.

Summary of findings about negative outcomes

Question 5: No studies were identified that reported on negative outcomes (e.g., costs, inequities) of improving ventilation. This may have been due to the focus of the review on comparative studies with the search specific to COVID-19.

Question 6: One study involved cross-sectional surveys of students and teachers after installation of portable HEPA air purifiers in classrooms in a school in Germany.[26] The survey was completed twice: the first survey was completed in summer (July 2021) and in the months prior the sound pressure of the devices was ~55 decibels; the second survey was completed in winter (December 2021) and in the months prior the sound pressure was ~47 decibels. Authors noted that the "German Technical Rules for Work Environments (GMBl 2018) recommend that the additional noise level in school classrooms should be kept below 35 dB(A) and is not allowed to exceed 55 dB(A)." For the first survey (summer), approximately half of students and teachers found noise levels disturbing and a majority found communication in class difficult or impaired; however, a minority found their ability to concentrate to be bad. For the second survey (winter), approximately half of students and teachers found noise levels not disturbing or only marginally disturbing and a majority found communication was possible without problems or usually possible; a majority also found ability to concentrate was good or very good. More students supported using air purifiers in response to the second survey compared to the first; majority of teachers supported use of air purifiers in both surveys. Authors concluded that noise levels of air purifiers need to be considered and acceptance can be improved when noise level is reduced.

Discussion

Existing studies show some differences in results in terms of the role of ventilation in transmission of SARS-CoV-2 and incidence of COVID-19. Comparisons across studies are difficult due to: different research methods; definitions, measurements, and categorization of ventilation and other variables; and analytic approaches (in particular control for confounding). Further, many studies included in this review are of low quality (high risk of bias) due to issues with sample selection, measurement of exposure and outcomes, and/or confounding. Finally, comparisons within and across studies are complicated by different time periods during the pandemic when new variants appeared and diverse public health measures were available and enforced. Only one study was identified that examined the effectiveness of portable air cleaners; however, this study compared an outbreak at a restaurant before the local government mandated enhancements of indoor air dilution in restaurants with an outbreak at a different restaurant after the mandate. We found no research about the negative impacts of improving ventilation or filtration strategies to reduce COVID-19. Only one study of portable air cleaners examined negative impacts among students and teachers and found noise levels could be disturbing and affect communication in classrooms.

Recent SRs have investigated the impact of ventilation,[2] filtration,[3] humidity,[4] and ultraviolet irradiation[5] within mechanical HVAC systems and the impact of these features on aerosol transmission. A SR of ventilation included 32 studies (published between 2004 and 2021; majority modelling studies) examining the impact of ventilation rates and airflow patterns on coronavirus transmission. The findings confirmed a number of well-understood principles: "increased ventilation rate was associated with decreased transmission…; increased ventilation rate decreased risk at longer exposure times; some ventilation was better than no ventilation; airflow patterns affected transmission; ventilation feature (e.g., supply/exhaust, fans) placement influenced particle distribution." However, the review found few studies that offered specific quantitative ventilation parameters. While the review authors offered some implications for practice, they highlighted that there is "not a one-solution-fits-all approach" as multiple "factors such as ventilation rate, airflow patterns, air balancing, occupancy, and feature placement" influence aerosol transmission and risk.

A SR of filtration included 23 studies (published between 1966 and 2021) examining seven viruses and three bacteriophages and included animal studies (n=17), aerosolized virus studies (n=7) and modelling studies (n=9). This review also confirmed several well-understood principles: "filtration was associated with decreased transmission; filters removed viruses from the air; increasing filter efficiency (efficiency of particle removal) was associated with decreased transmission, decreased infection risk, and increased viral filtration efficiency (efficiency of virus removal); increasing filter efficiency above MERV 13 was associated with limited benefit in further reduction of virus concentration and infection risk; and filters with the same efficiency rating from different companies showed variable performance." The review authors concluded that "adapting HVAC systems to mitigate virus transmission requires a multi-factorial approach and filtration is one factor offering demonstrated potential for decreased transmission." Review authors noted that the costs associated with increasing filter efficiency may be "lower than the cost of ventilation options with the equivalent reduction in transmission."

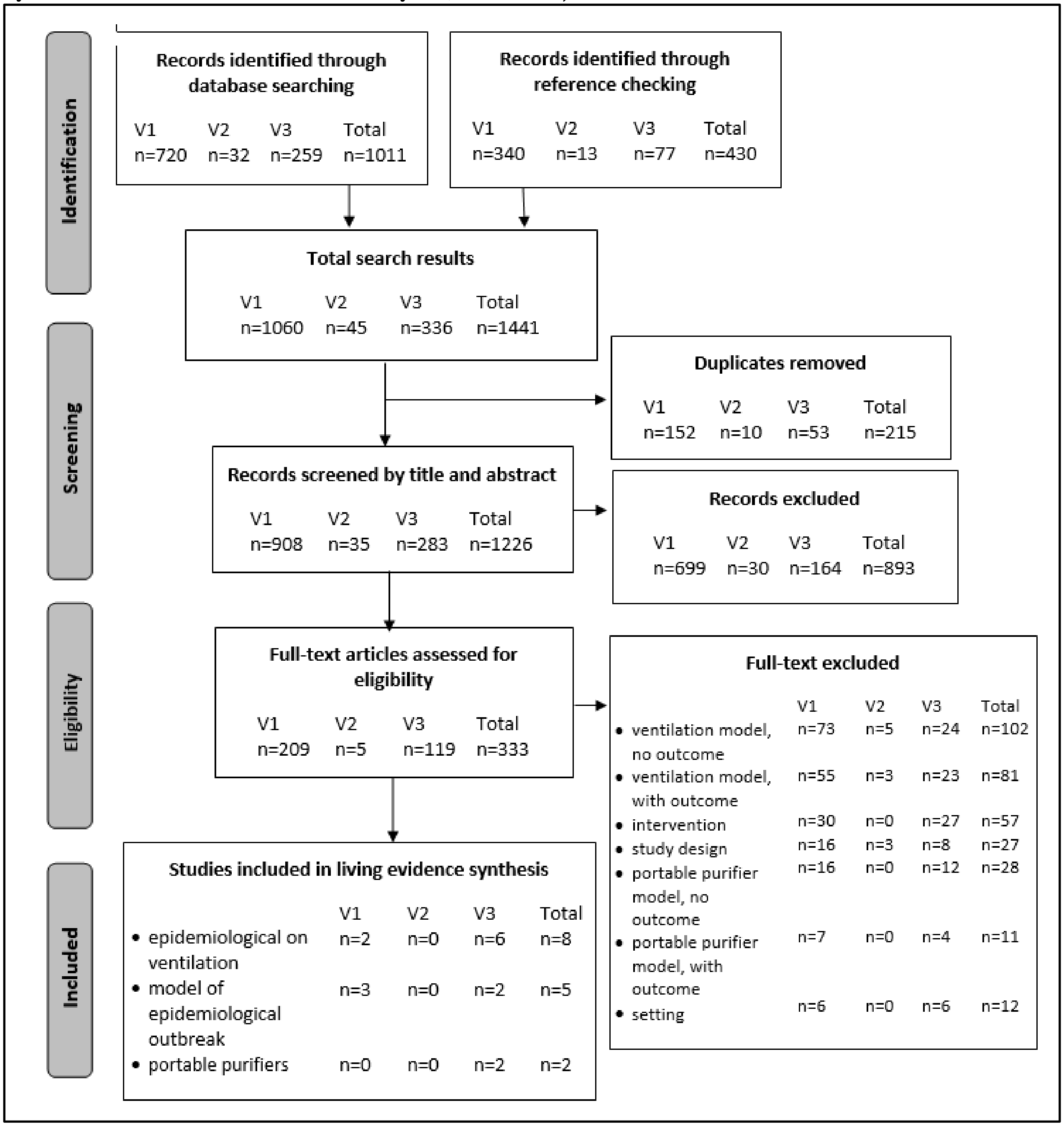
Two SRs have recently examined the effectiveness of portable air cleaners in indoor settings in the context of SARS-CoV-2. One SR focused on portable HEPA (high efficiency particulate air) purifiers.[10, 11] Authors searched from inception of databases to January 2021 and included 11 experimental studies. While studies varied greatly in their experimental protocols, all showed that portable HEPA purifiers could significantly decrease the concentration of particles in the air similar in size to SARS-CoV-2. A second SR focused on the effectiveness of portable, commercially available air cleaners (including HEPA filters) in reducing the incidence of respiratory infections and/or removing bacteria and viruses from indoor air. Authors searched databases from January 2000 to March 2021; they found no studies examining the effect of air filters on incidence of respiratory infections, but identified two studies showing that filters can capture airborne bacteria.[11] Neither study tested for effect of filters on capturing airborne viruses. The authors noted that there is a "complete absence of evidence" as to whether portable air cleaners reduce the spread of SARS-CoV-2 or other respiratory infections. They discussed several urgent research needs including randomized controlled trials to demonstrate effectiveness, understanding effects within different indoor environments (e.g., large open-plan offices, care homes, private homes), and cost-benefit analyses.

The American Society of Heating, Refrigerating and Air Conditioning Engineers (ASHRAE) sets standards for testing and application of HVAC features that guide practices in North America. A statement from ASHRAE in April 2021 acknowledged that airborne transmission of SARS-CoV-2 is significant and provided guidance on changes to building operations including HVAC systems.[6] A summary of their recommendations can be found at https://www.ashrae.org/file%20library/technical%20resources/covid-19/core-recommendations-for-reducing-airborne-infectious-aerosol-exposure.pdf, while guidance for specific settings (e.g., industrial settings, residential buildings, schools, dining structures, etc.) is available at https://www.ashrae.org/technical-resources/covid-19-one-page-guidance-documents. The Heating, Refrigeration and Air Conditioning Institute (HRAI) of Canada represents the HVAC industry in Canada and follows ASHRAE standards. HRAI has produced HVAC guidance for schools in the context of COVID-19.[27]

ASHRAE and the United States Environmental Protection Agency (EPA) have released guidance documents concerning portable air cleaners.[6-9] Both organizations advise that portable air cleaners are not to be relied upon as the only strategy for protecting individuals from COVID-19, and should be used to supplement existing HVAC systems. The EPA cautions that "the use of air cleaners alone cannot ensure adequate indoor air quality, particularly where significant pollutant sources are present and ventilation is insufficient."[8] There are a number of factors to consider when using a portable air cleaner such as specifications of a given unit, size of the space, placement with respect to existing HVAC system or other ventilation source or potential source of infection, airflow patterns, and maintenance (e.g., cleaning / changing filter). For portable air cleaners that intake and outlet into the same space, the parameter that best assesses effectiveness is the clean air delivery rate which is the product of volume flow times the filter efficiency; given there are minimal differences across filters in efficiencies, the device air flow rate becomes the more important feature. Portable air cleaners may not be appropriate for all indoor settings.[28] Further, ASHRAE advises that portable air cleaners using some technologies such as ionisers and photocatalytic oxidation (UV-PCO) are considered emerging without proven efficacy, and may convert known contaminants to other potentially harmful compounds.[9]

We did not identify any studies meeting our eligibility criteria that examined negative outcomes of increased ventilation and improved filtration. One of the key negative outcomes is costs, including those associated with installation, operations, and changes to the design of HVAC systems. Increasing ventilation results in a change to "the heating or cooling load necessary to maintain indoor air temperature, which thus results in a change in energy consumption."[29] Increasing filter efficiency creates higher pressure requirements to maintain the same air flow rate resulting in higher energy consumption. Costs will vary based on age and design of HVAC systems, weather conditions (if increasing outdoor air fraction in supply air stream), and interaction of different air cleaning mechanisms (e.g., ventilation, filtration, ultraviolet).[29] Costs to retrofit HVAC systems in older buildings, maintenance costs, and differential costs based on weather conditions could lead to inequities across population groups. Changes to ventilation can also impact occupant comfort (e.g., through air velocity and currents, ambient temperature, noise) which may affect occupant behaviour (e.g., attention, productivity). The costs of improving indoor air quality need to be considered in light of cost savings in terms of reduced illness and occupant well-being; investments in improving indoor air quality yield benefits in terms of reducing other respiratory illnesses, negative health effects, and potential future outbreaks. We expect that there is a body of literature on the benefits, harms (i.e., negative outcomes), and cost-effectiveness of improving indoor air quality; however, our search was limited to the time period and context of the COVID-19 pandemic.

Figure 1: Flow diagram for study identification (from Preferred Reporting Items for Systematic Reviews and Meta-Analyses, PRISMA)



V1 = version 1 search (January 1, 2020 – December 23, 2022); V2 = version 2 (December 24, 2022 – February 19, 2023); V3 = version 3 (February 10, 2023 – March 3, 2023)

Table 1: Summary of studies reporting on effectiveness of ventilation in reducing COVID-19 infections (n=8)

<table>
<tr><th>Author
Year/Date
Country</th><th>Setting and time covered</th><th>Study characteristics</th><th>Summary of key findings in relation to the outcome(s)</th></tr>
<tr><td rowspan="2">Baumgarte[12]
January 4, 2022
Germany</td><td>School outbreak in Hamburg, Germany after reopening in 2020

September 2020</td><td>Design: retrospective analysis of epidemiological data, using and validating the data of the health department and the school management and interviews
Intervention: regional public health service guidelines including recommendation to ventilate several times a day through fully opened windows via intermittent or cross ventilation, usually during breaks and only occasionally during class
Sample: 368 students; 117 staff
Key outcomes: COVID-19 attack and infection rate
Agents assessed: SARS-CoV-2</td><td>• Total PCR positive: 33 (9%) students; 3 (1.7%) staff
<table>
<tr><th>Classroom (day after index case was infected)</th><th>2 (day 3)</th><th>1 (day 3)</th><th>3, like 2 (day 4)</th><th>4, like 2 (day 4)</th></tr>
<tr><td># people infected / # people present</td><td>8/25</td><td>16/29</td><td>3/25</td><td>1/28</td></tr>
<tr><td># normal windows always open at breaks</td><td>2/3 lg</td><td>2/6 sm</td><td>2/3 lg</td><td>2/3 lg</td></tr>
<tr><td># always open window flaps</td><td>3/3 lg</td><td>4/6 sm</td><td>3/3 lg</td><td>3/3 lg</td></tr>
<tr><td>Open door</td><td>+/-</td><td>-</td><td>+/-</td><td>+/-</td></tr>
<tr><td>Attack rate (%)</td><td>33.33</td><td>57.14</td><td>12.5</td><td>3.7</td></tr>
<tr><td>Infection rate (1/h)</td><td>0.22</td><td>0.19</td><td>0.08</td><td>0.05</td></tr>
</table>
• Authors concluded that a number of factors contributed to spread of infection: condition/behavior of teacher and students (e.g., amount of time speaking, distance to students, mask use) and classroom conditions (crowding, ventilation). Individual and relative effects of different variables were not quantified.</td></tr>
<tr><td colspan="3">Critical; considered at risk of bias for confounding and classification/measurement of intervention/exposure</td></tr>
</table>

Author Year/Date Country	Setting and time covered	Study characteristics	Summary of key findings in relation to the outcome(s)
Buonanno[13] December 9, 2022 Italy	Pre-, primary, middle and high **schools** in Italy's Marche region 13 September 2021 - 31 January 2022	**Design**: retrospective cohort **Intervention**: MVS installed in schools in March 2021; consisting of single room units, most equipped with heat recovery and filters; switched on manually before class start and run constantly throughout school day; maximum air flow rates ranged from 100 to 1000 m3 h−1; with a ventilation rate between 1.4 and 14 L s−1 student−1 **Sample**: Total = 10,441 classrooms in 1,419 schools; MVS = 316 classrooms in 56 schools; Natural (leakage of building and manual opening of windows) = 1,363 classrooms in 10,125 schools; classrooms had an average occupancy of 20 students (total student population 205,347) **Key outcomes**: incidence cases and incidence proportions (number of positive students per 1,000); both presented as number of positive students counted only within clusters for classrooms with and without MVSs and for 12 different sub-periods **Agents assessed**: SARS-CoV-2	• Incidence proportion (per 1,000 students) was 4.9 (31 cases) with MVS and 15.3 (3,090 cases) without MVS. Incidence proportion ratio for the entire period was 0.32. • Based on most conservative estimate (classrooms with vs. without MVS), RR = 0.26, RRR = 0.74 (statistically significant, no confidence intervals reported) [analyses controlled for ACH, compulsory schools, number of students in classroom] • Analysis by time period showed effectiveness of MVS greater during month with high incidence of infection at regional level • Analyses showed increased effectiveness with higher ACH
	Critical; considered at risk of bias for confounding and measurement of outcomes		
Gettings[14] May 28, 2021 USA	Georgia state elementary **schools** (kindergarten through grade 5) November 16 – December 11, 2020	**Design**: cross-sectional study (self-reported cases to state public health department; online survey completed by school representatives) **Intervention**: ventilation improvements: "steps being taken to improve air quality and increase the ventilation in the school"; those who responded "yes" were asked to select one or more of the following: opening doors/windows, using fans to increase effectiveness of open windows, installation of HEPA filtration systems in high-risk areas, or installation of UVGI in high-risk areas **Sample**: 169 (11.6% of 1,461) schools including 91,893 students with available case data (number of cases = 566) **Key outcomes**: COVID-19 cases and incidence **Agents assessed**: SARS-CoV-2	• COVID-19 incidence 39% lower in schools that improved ventilation, compared with schools that did not (RR 0.61, 95% CI 0.43–0.87) • Ventilation strategies associated with lower school incidence included methods to dilute airborne particles alone by opening windows, opening doors, or using fans (35% lower incidence, RR=0.65, 95% CI: 0.43–0.98), or in combination with methods to filter airborne particles using HEPA filtration with or without purification with UVGI (48% lower incidence, RR=0.52, 95% CI: 0.32–0.83)
	Critical; considered at risk of bias for confounding, selection of participants, measurement of exposures and outcomes		

Author Year/Date Country	Setting and time covered	Study characteristics	Summary of key findings in relation to the outcome(s)
Monge-Barrio[15] October 9, 2021 Spain	High **schools** in Pamplona, Northern Spain with temperate climate, before and during the pandemic Indoor environmental conditions studied during March 2020 and January 2021	**Design**: cross-sectional survey of students and teachers, and monitoring of various indoor environmental conditions **Intervention**: increased natural ventilation during post-pandemic data collection in January 2021; all schools opened all windows and doors during the break (30 minutes), at the end of each class, and at the end of the day; one school opened windows at beginning of day and not at the end of each class; during class natural ventilation determined by teacher (windows mainly closed or slightly opened depending on outdoor temperatures and type of openings) **Sample**: 9 high schools **Key outcomes**: "evidence of COVID-19 infections" in classrooms reported by school directors **Agents assessed**: SARS-CoV-2	• 6/9 (67%) schools were naturally ventilated and did not have any MV or air conditioning • 3/9 (33%) schools had MV with heating recovery ventilation; when surveyed they did not use these systems due to the noise and in one case, additional energy consumption (2 also had air conditioning but did not use) • None of the schools self-reported COVID-19 transmission
	Critical; considered at risk of bias for measurement of outcomes and confounding was not examined		

Nabirova[16] 10 March 2022 Kazakhstan	Tengizchevroil (TCO) **oilfield** in Kazakhstan
	
	June 1 – September 15 2020
		Design: concurrent case-control study among TCO oilfield workers who worked on-site (standardized, structured CDC questionnaire consisting of 123 questions and study participant interviews)
		Intervention: 20 individual and 22 environmental factors examined, including ventilation at work, air conditioner at work, working indoors (office, kitchen, and storeroom) and working outdoors
		Sample: eight shift camps with the highest COVID-19 incidence were selected to participate in June and July 2020; intended to recruit 296 cases and 590 controls
		<u>Cases</u>: employees identified as COVID-19 positive by PCR test, regardless of symptoms
		<u>Controls</u>: two per one case patient randomly selected among COVID-19 negative employees working or living in the same shift camps during same rotation period
		Key Outcomes: COVID-19 cases
		Agents assessed: SARS-CoV-2
			• Adjusted odds ratios (95% CI) for environmental factors related to ventilation and COVID-19 among employees (cases n=296, controls n=536):
			  ○ Ventilation at work = 0.68 (0.36, 1.24)
			  ○ Air conditioner at work = 3.95 (1.30, 13.12) significant difference
			  ○ Office work = 0.93 (0.53, 1.61)
			  ○ Outdoor work = 0.75 (0.43, 1.28)
			• Based on multivariate analysis only air-conditioning on premises was associated with SARS-CoV-2 transmission (aOR = 4.0, 95% CI = 1.3–13.1)
			• Authors conclude that individual factors (e.g., rare hand sanitizer use, social interactions outside of work) were main drivers of transmission, with little contribution by environmental factors.

	Moderate; considered at unclear risk of bias for measurement of exposure		

Author Year/Date Country	Setting and time covered	Study characteristics	Summary of key findings in relation to the outcome(s)

Pokora[18]
June 10, 2021
Germany
	Meat and poultry processing plants in Germany
	
	June to September 2020
		Design: cross-sectional study (self-administered questionnaire)
		Intervention: multiple possible risk factors including ventilation, quantified as outdoor air flow per employee in a working area = outdoor air flow / (number of employees in a working area / number of shifts in the working area)
		Sample: 22 companies for 19,027 employees, including 880 COVID-19 infected workers divided into the following groups:
		• 7 = many infected workers prevalence between 2.94 to 35.10 infections per 100 employees
		• 5 = with fewer than 10 infected workers
		• 10 = with no infected workers
		Key outcomes: COVID-19 infection
		Agents assessed: SARS-CoV-2
			• Based on results of multivariable logistic regression analysis (for subsample of companies with many infected workers), having a ventilation system reduced chance of testing positive for COVID-19:
			  • overall (6,522 workers): aOR 0.757 (95% CI 0.563– 1.018)
			  • results also presented by type of worker: regular workers (aOR 1.076, 95% CI 0.619– 1.869) vs. temporary and contract (aOR 0.541, 95% CI 0.368– 0.796)
			• results of multivariable logistic regression for maximum outdoor air flow (OAF) per employee:
			  • when delivery, stunning/slinging/hanging, and slaughter areas were excluded from analysis (these areas have a process related high ventilation rate) (n=2,334), aOR 0.996 95% (CI 0.993–0.999); including interaction term for temperature and OAF, aOR 0.984 (0.971– 0.996)

	Critical; considered at risk of bias for confounding, selection of participants, measurement of exposures and outcomes		
Oginawati[17] 2022 Indonesia	**Homes** of recovered patients in Coblong District, Bandung City, Indonesia (subdistricts: Dago and Sekeloa) March to April 2021	**Design:** field study regarding the relation of residential environmental factors against COVID-19 (including temperature, humidity, brightness, ventilation size, and personal space area); using a convenient sampling method to select households that survived COVID-19 infections (questionnaires and interviews with recovered patients, and physical observations in residences) **Intervention**: ventilation size – comparing size of vent hole (assessed using measuring tape) and home's total area (bigger vent hole size = better ACH in house) **Sample**: 38 houses of survivor/recovered patients **Key Outcomes**: transmission rate in households meeting healthy ventilation standards, i.e., number having COVID-19 relative to number in house and categorized as low (0-50%), intermediate (50-99%) and high (100%) **Agents assessed**: SARS-CoV-2	• Number of households meeting healthy ventilation standard of ≥10% of room area = 31/38 (82%) • requirements for the ventilation parameters for a standard healthy house independently associated with transmission of COVID-19 (p-value = 0.021) • based on the correlation values the size of ventilation in the house is, inversely, significantly related to the transmission of COVID-19 in the house (correlation coefficient -0.522; determination coefficient 0.272 (i.e., proportion of overall variation in transmission explained by linear relationship with ventilation); p=0.002) • ventilation was the only environmental parameter examined that had significant association with transmission
	Critical; considered at risk of bias for confounding and potential selection and measurement bias		

Author Year/Date Country	Setting and time covered	Study characteristics	Summary of key findings in relation to the outcome(s)
Wang[19] May 11, 2020 China	**Homes** of families with at least one case of laboratory confirmed COVID-19 in Beijing, China February 28 to March 27, 2020	**Design**: retrospective cohort of families; structured questionnaire including demographics, clinical information, primary case's knowledge and attitude toward COVID-19; self-reported practices of primary case and family members; accommodation and household hygiene practices **Intervention**: multiple characteristics and practices, including ventilation duration per day (the practice of opening the window to allow convection of indoor air) **Sample**: 83 families without secondary transmission; 41 families with secondary transmission **Key outcomes**: families with and without secondary transmission, attack rate **Agents assessed**: SARS-CoV-2	• Overall secondary attack rate in families was 23% (77/335) • Ventilation duration per day (Median, IQR in hours): overall = 2 (1-6); without transmission = 3 (1.5-8); with transmission = 1.8 (1-4) • Household ventilation duration was protective against infection in univariate analysis: unadjusted OR 2.55 (95% CI 1.14, 5.70) for ≤1 hour per day vs >1 hour per day • Ventilation not significant in multivariable analysis • Authors conclude that highest risk of transmission occurs prior to symptom onset and that mask use, disinfection and social distancing are effective in preventing COVID-19
	Serious; considered at risk of bias for measurement of exposure, and unclear for measurement of outcome		

Abbreviations: ACH = air changes per hour; aOR = adjusted odds ratio; CDC = Centres for Disease Control; CI = confidence interval; HEPA = high-efficiency particulate absorbing; IQR = interquartile range; lg = large; MVS = mechanical ventilation system; OR = odds ratio; PCR = polymerase chain reaction; RR = rate ratio; RRR = relative risk reduction; sm = small; UVGI = ultraviolet germicidal irradiation

Table 2: Summary of modelling studies investigating COVID-19 outbreaks and reporting on effect of ventilation in reducing COVID-19 infection risk or probability

Reference Year/Date Country	Objective / Summary	Methods / Experiments	Transmission / Infection Outcomes	Summary of Findings
Ho[20] 2021 China	To develop CFD simulations and methods to model the airflow, exposure, and probability of infection for the reported conditions at the Guangzhou restaurant (where an outbreak of COVID-19 occurred in January 2020). Different configurations of the air conditioning (direction and magnitude of air flow, percentage of fresh air supplied) and boundary conditions (e.g., temperature, pressure, humidity) were investigated to determine the sensitivity of the results to these parameters and processes.	CFD models were used to simulate expelled aerosol plume transport and dispersion and to perform comparative studies of exposure risks under various scenarios. Spatial and temporal simulations of the relative concentrations of the expelled pathogen (assumed to be uniformly distributed in the vapour plume) are compared and used to determine risks of exposure and probability of infection.	Probability of infection	Simulations confirmed that poor ventilation and recirculation increased pathogen concentrations and probability of infection. Increasing the fresh-air supply to the ventilation decreased the pathogen concentrations and probability of infection. Increasing the fresh-air percentage to 10%, 50%, and 100% of the supply air reduced the accumulated pathogen mass in the room by an average of ~30%, ~70%, and ~80%, respectively, over 73 min. The probability of infection was reduced by 11%, 37%, and 51%, respectively.

Reference Year/Date Country	Objective / Summary	Methods / Experiments	Transmission / Infection Outcomes	Summary of Findings
Li[21] 2020 China	Simulation experiments in dormitory buildings according to original conditions when two COVID-19 outbreaks occurred. Epidemiological data were collected and ventilation conditions (doors/windows open and operation of ventilation equipment) were investigated at time of occurrence. Data was collected about date of symptom onset, mask wearing, number infected and their distributions. Ventilation rate was measured by CO_2 tracer concentration decay method.	The *Shandong Province* dormitory was mainly mechanically ventilated with 30 rooms averaging 9 residents/room. Transmission period Jan 21 to Feb 12, 2020. Calculated infection was between 29–100%, of which 7 rooms had a 100% rate of infection. During outbreak interior doors were open and exterior windows closed, no masks. The dormitory in *Hubei province* had no mechanical ventilation, with 90 rooms averaging 21 residents/room. Outbreak between January 21 to February 11, 2020. Zone M had older residents with door and windows closed and wore masks day and night. Zone N had young and middle-aged residents, did not wear masks at night and opened windows all day. Calculated infection rate was between 0% and 56%, of which 14 rooms had a 0% rate of infection.	Infection rate	**Hubei M Zone:** ventilation rate = 236 m3/h, average per person was 7.7 m3/h**;** infection rate = 8% **Hubei N Zone:** ventilation rate = 601 m3/h, average per person was 28 m3/h; Infection rate = 16% -Zone M had lower infection rate with worse ventilation levels, which was attributed to mask wearing. **Shandong:** ventilation rate = 178 m3/h, average per person was 21 m3/h**;** infection rate = 74% -Difference in infection rates between Shandong and Hubei attributed to mask wearing habits. -Data from Zone N in Hubei showed a threshold of ventilation rate. When the room ventilation rate was > 800 m3/h or 40 m3/h per person, rate of infection was <25%. When room ventilation rate was < 800 m3/h or 40 m3/h per person, the highest infection rate reached 56%.
Liu[22] 2020 USA	CFD-based investigation of indoor air flow and the associated aerosol transport in a restaurant setting (Guangzhou, China; January 2020), where likely cases of airborne infection of COVID-19 caused by asymptomatic individuals were widely reported by the media. To demonstrate direct linkage between the simulation results (under different ventilation and thermal settings) and reported infection patterns as well as the corresponding detailed physical mechanisms that lead to airborne disease transmission.	We employed an advanced in-house large eddy simulation solver and other cutting-edge numerical methods to resolve complex indoor processes simultaneously, including turbulence, flow–aerosol interplay, thermal effect, and the filtration effect by air conditioners. Using the aerosol exposure index derived from the simulation, we are able to provide a spatial map of the airborne infection risk under different settings.	Infection risk	In simulation with increased ventilation, the risk of infection is decreased (Fig 13 and 14, values presented graphically for each individual based on position at tables relative to infected source). The infection risk evaluation from our current CFD is only derived from the aerosol exposure index. To yield a more substantiated metric of infection risk, a relevant infection-dose model, currently not available for SARS-CoV-2, is needed.

Reference Year/Date Country	Objective / Summary	Methods / Experiments	Transmission / Infection Outcomes	Summary of Findings
Ou[23] 2022 China	CFD was utilized to model airflows and investigate ventilation requirements of airborne transmission in a COVID-19 outbreak initiating with a 24-year old man. Two buses (B1 and B2) were involved, with 10 non-associated infected passengers. We collected epidemiological data, bus itineraries, the seating plans of passengers, and the details of the ventilation systems and operation, and we performed detailed ventilation and dispersion measurements on the two buses with the original drivers on the original route.	Dates of symptom onset and the seating arrangements on the two buses were obtained, as well as interviews with drivers and passengers. Various combinations of air conditioning/heating and windows open/ closed were considered to simulate the airflow at the time of infection. The ventilation rates on the buses were measured using a tracer-concentration decay method with the original driver on the original route. We measured and calculated the spread of the exhaled virus-laden droplet tracer from the suspected index case.	Infection risk / attack rate	On both buses, the distribution of the exhaled tracer gas was rather uniform due to the airflow patterns. **Bus 1 (B1)** - Attack rate = 7/46, 15.2% - Ventilation rate = 1.72 L/s per person 1.72 L/s per person - Exposure time = 200 minutes **Bus 2 (B2)** - Attack rate = 2/17, 11.8% - Ventilation rate = 3.22 L/s per person - Exposure time = 60 minutes The ventilation rate of a bus depended on the driving speed and extent of window opening. The difference in ventilation rates and exposure time could explain why B1 had a higher attack rate than B2. Airborne transmission due to poor ventilation below 3.2 L/s played a role in this two-bus outbreak of COVID-19.
Vernez[24] May 23, 2021 Switzerland	Investigation of an outbreak in a courtroom in Vaud state of Switzerland, October 30, 2020. Ten people participated in hearing in the same courtroom. Without considering the index case, 4 of the 9 people present became infected within days of the hearing. For one of the cases, it was deemed that infection most likely came from another source.	Field investigation of outbreak with ventilation system not working and single window and all doors closed, with the exception of window being open during breaks (masking and social distancing requirements were in effect). Estimated air renewal rate of 0.23 h^{-1} Modelling to estimate probability of infection under different conditions including ventilation rate, emission rate, and duration of exposure. Simulation with variable air exchange rates, ranging from 0 to 5 h^{-1}. Assumed secondary attack rate of 33-44% (3-4/9).	Probability of infection	• Results presented graphically; probability of infection lower with higher ventilation rates when duration of event was 1.5 and 3 hours; little difference in probability of infection across different ventilation rates when event duration was 0.5 hours • Authors concluded that while room ventilation is essential, it is difficult to control risk of contamination with this parameter alone because of the residual probability of infection at high ventilation rates, brought by the variability of the other parameters (e.g., duration of exposure and emission rate)

Abbreviations: CFD = computational fluid dynamics; CO_2 = carbon dioxide

Table 3: Summary of studies reporting on effectiveness of air filters/purifiers in reducing COVID-19 infections

Author Year/Date Country	Setting and time covered	Study characteristics	Summary of key findings in relation to the outcome(s)
Cheng[25] February 13, 2022 China	Restaurants in Hong Kong with COVID-19 outbreaks before (R1) and after enhancement of indoor air dilution (R2) February 19, 2021 and December 27, 2021	**Design**: descriptive epidemiological study to evaluate the effect of mandatory enhancement of indoor air dilution in restaurants (requirement for ACH of ≥6 in seating areas of restaurants or, if not feasible, installation of air purifiers as alternate measure) **Intervention**: indoor air dilution enhancement by ultraviolet-C air purifying system (R2); 14 air purifiers mounted at ceiling level near return air grilles (post-adjustment ACH was 4.6 in seating area of R2 compared with ACH 1.2 in R1) **Sample**: customers and staff at different restaurants before and after mandatory air dilution enhancement; for R1 outbreak none of the customers or staff were vaccinated, all cases in R2 were fully vaccinated **Key Outcomes**: secondary attack rate **Agents assessed**: SARS-CoV-2 (Omicron variant)	• secondary attack rate among customers in R2 was significantly lower than that in R1 (3.4%, 7/207 vs 28.9%, 22/76, $p<0.001$) • secondary attack rate among restaurant staff in R2 was significantly lower than that in R1 (0%, 0/22 vs 52.6%, 10.19, $p<0.001$) • secondary attack rate overall was lower in R2 compared with R1 (2.6% vs 33.7%, $p<0.001$) • authors concluded that improvement in air dilution with installation of air purifiers and upper-room UVGI significantly decreased secondary attack rate
	Critical; considered at risk of bias for confounding and selection of participants/samples		

Abbreviations: ACH = air changes per hour; UVGI = ultraviolet germicidal irradiation

Table 4: Summary of studies reporting on negative outcomes of portable air purifiers for reducing COVID-19 infections

Author Year/Date Country	Setting and time covered	Study characteristics	Summary of key findings in relation to the outcome(s)
Granzin[26] November 5, 2022 Germany	Two schools in Bad Homburg vor der Hohe, Germany November 2020 – June 2021 (monthly measurements) Surveys completed in July and December 2021	**Design**: epidemiological study measuring efficiency of mobile air purifiers (no transmission outcome); followed by two (summer and winter) anonymous cross-sectional surveys on the acceptance of air purifiers in classrooms **Intervention**: four different models of air purifiers with HEPA filters (all rated >99.97% efficiency); all with mesh + activated charcoal + electret HEPA (regular household appliance), except the Trotec TAC V+ with F9 + H14 HEPA (commercial device) **Sample**: two schools ranging in classroom size of 8-28 students plus one teacher; survey involved staff and students (grades 5-12, ages 10-19) at one school **Key Outcomes**: acceptance (e.g., noise level, communication, concentration) **Agents assessed**: SARS-CoV-2	<u>Survey #1</u> (summer, in months prior sound pressure of devices was ~55dB; 1070 students, 22 teachers responded) • 48% of students and 54% of teachers found noise levels “rather disturbing” or “very disturbing”; 22% of students and 27% of teachers found noise levels “not disturbing” or “marginally disturbing” • Majority found communication in class “difficult but possible” (42% students, 63% teachers) or “strongly impaired” (10% students, 5% teachers) • Majority found ability to concentrate was “good” or “very good” (55% students, 71% teachers); minority found ability to concentrate was “rather bad” or “very bad” (16% students, 10% teachers) <u>Survey #2</u> (winter, in months prior sound pressure of devices was ~47 dB; 1060 students, 74 teachers responded) • 24% of students and 20% of teachers found noise levels “rather disturbing” or “very disturbing”; 49% of students and 59% of teachers found noise levels “not disturbing” or “marginally disturbing” • Majority found communication in class “possible without problems” (26% students, 25% teachers) or “usually possible” (44% students, 50% teachers) • Fraction of students supporting use of air purifiers increased by 17% from summer to winter survey; difference for teachers was marginal • Majority found ability to concentrate was “good” or “very good” (62% students, 83% teachers); minority found ability to concentrate was “rather bad” or “very bad” (11% students, 9% teachers)
	Critical; considered at risk of bias for confounding and potential selection and measurement bias		

<u>Abbreviations</u>: HEPA = high-efficiency particulate absorbing

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Appendices

Appendix 1: Risk of Bias for Epidemiological Studies

Risk of Bias assessments for included cross-sectional studies*

	Baumgarte Germany	Gettings USA	Granzin Germany	Monge-Barrio Spain	Oginawati Indonsia	Pokora Germany
1. Were the criteria for inclusion in the sample clearly defined?	NA	Y	N	U	Y	N
2. Were the study subjects and the setting described in detail?	PY	PY	N	PY	N	PY
3. Was the exposure measured in a valid and reliable way?	N	N	U	PY	U	N
4. Were objective, standard criteria used for measurement of the condition?	NA	NA	NA	N	N	NA
5. Were confounding factors identified?	Y	N	U	N	N	PY
6. Were strategies to deal with confounding factors stated?	PY	N	N	N	N	Y
7. Were the outcomes measured in a valid and reliable way?	N	N	N	N	N	N
8. Was appropriate statistical analysis used?	N	N	N	N	PY	Y

NA = not applicable; Y = yes; PY = partial yes; PN = partial no; N = no; U = unclear

* Moola S, Munn Z, Tufanaru C, Aromataris E, Sears K, Sfetcu R, Currie M, Qureshi R, Mattis P, Lisy K, Mu P-F. Chapter 7: Systematic reviews of etiology and risk . In: Aromataris E, Munn Z (Editors). *JBI Manual for Evidence Synthesis*. JBI, 2020. Available from https://synthesismanual.jbi.global

Risk of Bias assessments for included cohort studies*

	Buonanno Italy	Cheng China	Wang China
Bias due to confounding			
Did the study adjust for other COVID protective interventions (including vaccination)?**	N	N	Y
Did the study adjust for calendar time (implications for circulating variant, season), demographics, and other relevant factors?**	N	N	Y
Were participants free of confirmed COVID infection at the start of the study?**	U	U	U
Bias in selection of participants			
Were both study groups recruited from the same population during the same time period?	Y	N	Y
Were the COVID protective interventions implemented prior to period of data collection? (prevalent users)	Y	N	Y

Were the study groups balanced with respect to participant adherence (based on internal and external factors unrelated to COVID)?	U	U	U
Bias in classification of interventions			
Was the method for confirming the intervention clearly defined and applied consistently across study samples (e.g., districts within a country)?	Y	Y	N
In periods of co-occurring interventions, do the authors clearly classify each individual intervention?	N	NA	Y
Does classification into intervention/control group depend on self-report in a way that might introduce bias?	N	N	Y
For household transmission studies, was it clear that exposure to the index case was the most likely the only exposure to COVID for household or close contacts?	NA	NA	N
Bias due to deviations from intended intervention			
Did the authors assess adherence to the protective behaviours/interventions after intervention implementation?**	NA	N	N
Risk of bias due to missing data			
Was outcome data at the end of the study period available for all or nearly all participants?	U	Y	Y
Were participants excluded due to missing data?	N	N	U
Risk of bias in measurement of outcomes			
Was the outcome of COVID confirmed by laboratory testing?**	U	Y	U
If the outcomes were derived from databases, were the databases constructed specifically for the collection of COVID data?**	Y	U	NA
Were appropriate tools/methods with validated/justified cut-points used to determine outcomes of interest (other than COVID infection/transmission which is covered under laboratory testing)? **	NA	NA	NA
If the outcome was self-reported, did the authors attempt to control for social desirability?**	U	NA	U
Was the frequency of testing for the outcome different between the study groups?	N	U	U
If outcome was observed, was there more than one assessor and if so, was interrater agreement reported?	NA	NA	U

NA = not applicable; Y = yes; PY = partial yes; PN = partial no; N = no; U = unclear

* Linkins LA. Critical appraisal process for assessment of public health measures for COVID-19 cohort studies. Hamilton, Canada: Health Information Research Unit, 22 March 2023. https://www.mcmasterforum.org/docs/default-source/product-documents/living-evidence-syntheses/rob-assessment-methods.pdf?sfvrsn=1b41c595_5

** relevant to single arm cohort studies

Risk of Bias assessments for included case-control studies*

	Nabirova Kazakhstan
1. Were the groups comparable other than the presence of disease in cases or the absence of disease in controls?	PY
2. Were cases and controls matched appropriately?	Y
3. Were the same criteria used for identification of cases and controls?	Y
4. Was exposure measured in a standard, valid and reliable way?	U
5. Was exposure measured in the same way for cases and controls?	Y
6. Were confounding factors identified?	Y
7. Were strategies to deal with confounding factors stated?	Y
8. Were outcomes assessed in a standard, valid and reliable way for cases and controls?	Y
9. Was the exposure period of interest long enough to be meaningful?	Y
10. Was appropriate statistical analysis used?	Y

NA = not applicable; Y = yes; PY = partial yes; PN = partial no; N = no; U = unclear

* Moola S, Munn Z, Tufanaru C, Aromataris E, Sears K, Sfetcu R, Currie M, Qureshi R, Mattis P, Lisy K, Mu P-F. Chapter 7: Systematic reviews of etiology and risk . In: Aromataris E, Munn Z (Editors). JBI Manual for Evidence Synthesis. JBI, 2020. Available from https://synthesismanual.jbi.global

Appendix 2: Detailed search strategy (PubMed)

#1 ("COVID 19"[MeSH] OR "COVID 19"[All Fields] OR "sars cov 2"[All Fields] OR "sars cov 2"[MeSH] OR "severe acute respiratory syndrome coronavirus 2"[All Fields] OR ncov[All Fields] OR "2019 ncov"[All Fields] OR "coronavirus infections"[MeSH] OR coronavirus[MeSH] OR coronavirus[All Fields] OR coronaviruses[All Fields] OR betacoronavirus[MeSH] OR betacoronavirus[All Fields] OR betacoronaviruses[All Fields] OR "wuhan coronavirus"[All Fields] OR 2019nCoV[All Fields] OR Betacoronavirus*[All Fields] OR "Corona Virus*"[All Fields] OR Coronavirus*[All Fields] OR Coronovirus*[All Fields] OR CoV[All Fields] OR CoV2[All Fields] OR COVID[All Fields] OR COVID19[All Fields] OR COVID-19[All Fields] OR HCoV-19[All Fields] OR nCoV[All Fields] OR "SARS CoV 2"[All Fields] OR SARS2[All Fields] OR SARSCoV[All Fields] OR SARS-CoV[All Fields] OR SARS-CoV2[All Fields]) AND English[la]

#2 (environment, controlled[MeSH] OR air conditioning[MeSH] OR ventilation[MeSH] OR sanitary engineering[MeSH] OR filtration[MeSH] OR filtration[All fields] OR "air condition*"[All fields] OR "air-condition*"[All fields] OR "building ventilation"[All fields] OR "ventilation system"[All fields] OR "indoor ventilation"[All Fields] OR HVAC[TIAB] OR air samples[TIAB] OR ventilation rate[TIAB] OR ventilation[TIAB]) AND (Disease Transmission, Infectious*[Mesh] OR Air Pollution, Indoor[MeSH] OR transmission[Subheading] OR Infections[Mesh:NoExp] OR transmi*[All fields] OR infect*[TIAB] OR contagi*[TIAB] OR outbreak*[TIAB] OR spread*[TIAB] OR decontamination[TIAB]) AND (Aerosols[MeSH] OR Air Microbiology[MeSH] OR Aerosol*[All Fields] OR bioaerosol*[TIAB] OR airborne[TIAB] OR droplet*[TIAB] OR "air exchange"[TIAB] OR "air change"[TIAB] OR "air flow"[TIAB] OR airflow[TIAB] OR "fluid dynamics"[TIAB] OR air dilution[All Fields])

#1 and #2

#4 search*[Title/Abstract] OR meta-analysis[Publication Type] OR meta analysis[Title/Abstract] OR meta analysis[MeSH Terms] OR review[Publication Type] OR diagnosis[MeSH Subheading] OR associated[Title/Abstract]

#5 (clinical[TIAB] AND trial[TIAB]) OR clinical trials as topic[MeSH] OR clinical trial[Publication Type] OR random*[TIAB] OR random allocation[MeSH] OR therapeutic use[MeSH Subheading]

#6 comparative study[pt] OR Controlled Clinical Trial[pt] OR quasiexperiment*[TIAB] OR "quasi experiment"[TIAB] OR quasiexperimental[TIAB] OR "quasi experimental"[TIAB] OR quasi-randomized[TIAB] OR "natural experiment"[TIAB] OR "natural control"[TIAB] OR "Matched control"[TIAB] OR (unobserved[TI] AND heterogeneity[TI]) OR "interrupted time series"[TIAB] OR "difference studies"[TIAB] OR "two stage residual inclusion"[TIAB] OR "regression discontinuity"[TIAB] OR non-randomized[TIAB] OR pretest-posttest[TIAB] OR "outbreak study"[TIAB] OR "outbreak investigation"[TIAB] OR ecological study[TIAB] OR ecological investigation[TIAB] OR Cross-Sectional Studies[MH] OR Risk Assessment[MH] OR epidemiology[SH] OR Prevalence[MH] OR etiology[SH] OR Risk Factors[MH] OR incidence[TIAB] OR prevalence[TIAB] OR epidemiology[TIAB] OR "relative risk"[TIAB] OR "risk factor"[TIAB] OR "risk factors"[TIAB] OR "association between"[TIAB] OR "associated risk"[TIAB]

#7 cohort studies[mesh:noexp] OR longitudinal studies[mesh:noexp] OR follow-up studies[mesh:noexp] OR prospective studies[mesh:noexp] OR retrospective studies[mesh:noexp] OR cohort[TIAB] OR longitudinal[TIAB] OR prospective[TIAB] OR retrospective[TIAB]

#8 Case-Control Studies[Mesh:noexp] OR retrospective studies[mesh:noexp] OR Control Groups[Mesh:noexp] OR (case[TIAB] AND control[TIAB]) OR (cases[TIAB] AND controls[TIAB]) OR (cases[TIAB] AND controlled[TIAB]) OR (case[TIAB] AND comparison*[TIAB]) OR (cases[TIAB] AND comparison*[TIAB]) OR "control group"[TIAB] OR "control groups"[TIAB]

#9 #4 or #5 or #6 or #7 or #8

#10 #3 an #9

#11 #10 NOT (Animals[Mesh] NOT (Animals[Mesh] AND Humans[Mesh]))

Appendix 3: Detailed study eligibility criteria

Characteristic	**Inclusion Criteria**	**Exclusion Criteria**
Publication date	January 01, 2020	Prior to 2020
Language	English	Languages other than English
Study design	Epidemiological / Ecological: experimental studies at the population or group level with a comparator Primary / Experimental: quantitative with comparator Primary / Observational: cohort, case-control, cross-sectional	Opinions pieces: commentaries or editorials published in peer-reviewed journals Qualitative studies Reviews: narrative and literature reviews; check references of systematic/rapid reviews or meta-analysis with relevant to any of the public health measures
Population	All ages	Involving animals
Setting	Indoor built environments such as: office buildings, public buildings (schools, day cares), residential buildings, retail buildings (malls, restaurants), athletic facilities (gyms), transport vehicles (aircraft) or hubs (airports)	Healthcare or clinical settings
Intervention	Ventilation systems in the built environment Filters or filtration features within mechanical ventilation systems Portable ventilators or air filtration devices that are not part of mechanical ventilation systems	Open air / outdoor environments
Comparison	Different rates and mechanisms (i.e., mechanical, natural, or filtration) of air dilution (including flow rates, air flow patterns, ratio of outdoor air to re-used air) Different filter ratings Different combinations of ventilation and filtration strategies	No comparison of ventilation parameters
Outcome	Primary: quantitative data evaluating virus transmission in reducing transmission of COVID-19 (i.e., attack rates, reproduction number, etc.) Secondary: probability or risk of transmission or infection Negative effects, e.g., costs, inequities	Qualitative data

Abbreviations: TBD=to be determined

Appendix 4: Studies excluded at the last stages of reviewing

Excluded – ventilation modelling studies without infection outcome (n = 102)

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Appendix 5: Definitions

Ventilation refers to dilution of indoor air with outdoor air. Air dilution can occur through natural means (e.g., opening windows or doors) or mechanical means (e.g., Heating, Ventilation and Air Condition [HVAC] systems). Improving ventilation helps to limit the number of infectious particles indoors by diluting indoor air with outdoor air that has fewer infectious particles.

Air filtration refers to removing unwanted matter (e.g., particles, droplets) from the air stream by passing the airflow through fine mesh obstructions. In principle, some fraction of the unwanted matter will stay upstream of the filter and relatively cleaner air will flow downstream of the filter.

Portable air cleaners also known as air purifiers or air sanitizers, are designed to filter the air in a single room or area.

Filter ratings or Minimum Efficiency Reporting Values (MERV) report a filter's ability to capture larger particles between 0.3 and 10 microns.

Appendix 6: Data extraction form

Data extraction for studies reporting outcomes on effectiveness of ventilation in reducing COVID-19 infections (Table 1)

Data extraction category	Data extraction element
Reference details	First author Date of publication Country of publication
Study characteristics	Design Intervention Key outcomes Agents assessed
Population characteristics	Sample description
Results	Summary of key findings in relation to infection/transmission outcome

Data extraction for studies modelling COVID-19 outbreaks reporting on effectiveness of ventilation in reducing COVID-19 infections (Table 2)

Data extraction category	Data extraction element
Reference details	First author Date of publication Country of publication
Study characteristics	Objective/summary of study Description of methods/model Key outcomes
Results	Summary of key findings in relation to infection/transmission outcome

Data extraction for studies reporting or modelling COVID-19 outbreaks and the effectiveness of stand-along/portable air purifiers reducing COVID-19 infections (Table 3)

Data extraction category	Data extraction element
Reference details	First author Date of publication Country of publication
Study characteristics	Objective/summary of study Description of methods/model Key outcomes
Results	Summary of key findings in relation to infection/transmission outcome

Data extraction for studies reporting on negative outcomes of portable air purifiers for reducing COVID-19 infections (Table 4)

Data extraction category	Data extraction element
Reference details	First author Date of publication Country of publication
Study characteristics	Objective/summary of study Description of methods/model Key outcomes
Results	Summary of key findings in relation to infection/transmission outcome

Appendix 7: Critical Appraisal Process for Assessment of Public Health Measures for COVID-19

For all epidemiological studies reporting on effectiveness of ventilation in reducing COVID-19 infections RoB will be assessed.

Critical appraisal tool for cohort studies

Questions	Possible responses
1. Bias due to confounding **Did the study adjust for other COVID protective interventions (including vaccination)?**** (critical = multiple co-interventions with no controlling or adjustment; serious = one co-intervention not controlled for; moderate = all known important interventions controlled for) **Did the study adjust for calendar time (implications for circulating variant, season), demographics, and other relevant factors?**** (critical = no adjustment; serious = at least one known important domain not measured or controlled for; moderate = all known important confounding domains measured) **Were participants free of confirmed COVID infection at the start of the study?**** (critical = unclear or high likelihood pts had COVID at start of study; serious = COVID status of intervention group known but unclear for control group OR COVID status of both groups known by self-report only; low = negative COVID status of both groups known at study start (lab confirmed))	NA = not applicable; Y = yes; PY = partial yes; PN = partial no; N = no; U = unclear

<table>
<tr><td>2. Bias in selection of participants

Were both study groups recruited from the same population during the same time period?
(critical = same or diff country/province/state measured at a diff time <u>prior</u> to pandemic)
(serious = same or diff country/province/state measured at a diff time <u>during</u> pandemic)
(moderate = same country/province/state measured at same time)
Were the COVID protective interventions implemented prior to period of data collection? (prevalent users)
(critical = not addressed and highly likelihood of prevalent users; moderate = prevalent users likely but appropriately controlled for; low = start of data collection at same time as implementation with no prevalent users)
Were the study groups balanced with respect to participant adherence (based on internal and external factors unrelated to COVID)?
(For example, people who are less likely to adhere to PHSMs anyway may be more likely to be exposed to COVID and require quarantine & isolation but then are less likely to adhere. Similar for e.g. people who work are essential workers without paid time off.)
(critical = not addressed and highly likelihood of difference in adherence; moderate = difference in adherence likely but appropriately controlled for; low = adherence confirmed to be same in both groups at start of study)</td><td rowspan="2">NA = not applicable;
Y = yes;
PY = partial yes;
PN = partial no;
N = no;
U = unclear</td></tr>
<tr><td>3. Bias in classification of interventions

Was the method for confirming the intervention clearly defined and applied consistently across study samples (e.g., districts within a country)?
(critical = not addressed; serious = intervention status not well defined or applied inconsistently; moderate = well defined but some aspects of assignment of intervention status determined retrospectively; low = well defined and solely based on information collected at time of intervention)
In periods of co-occurring interventions, do the authors clearly classify each individual intervention?
(critical = not addressed and co-interventions present; serious = co-intervention classification not well defined or applied inconsistently; moderate = co-intervention classification well defined but some aspects of assignment of status determined retrospectively; low = all co-interventions well defined and solely based on information collected at time of intervention)
Does classification into intervention/control group depend on self-report in a way that might introduce bias?
(For example, where negative consequences of providing truthful responses may lead to negative consequences e.g. self-reporting COVID symptoms would trigger 14 day quarantine and loss of income)
(critical = not addressed and reliant on self-report; moderate = reliant on self-report but appropriately controlled for/analyzed separately; low = not reliant on self-report)
For household transmission studies, was it clear that exposure to the index case was the most likely the only exposure to COVID for household or close contacts?
(critical = not addressed; serious = high risk occupational and social exposures likely and not accounted for; moderate = all participants isolated to same house or hospital from time of index case identification; low = all participants isolated to same house or hospital prior to index case identification)</td></tr>
</table>

4. Bias due to deviations from intended intervention? **Did the authors assess adherence to the protective behaviours/interventions after intervention implementation?**** (critical = not addressed; serious = reliant on self-report of adherence without verification or adjustment; moderate = adherence verified in at least a subset of each study group or appropriately adjusted for; low = adherence verified in all study participants)	NA = not applicable; Y = yes; PY = partial yes; PN = partial no; N = no; U = unclear
5. Risk of bias due to missing data **Was outcome data at the end of the study period available for all or nearly all participants?** (critical = critical differences in missing data between groups; moderate: missing data did not differ between groups or was accounted for by appropriate statistical methods; low = no missing data) **Were participants excluded due to missing data?** (critical = participants excluded based on data missing unevenly across groups; moderate = participants excluded due to missing data, but rationale was appropriate and applied the same across all groups; low = no exclusions due to missing data)	
6. Risk of bias in measurement of outcomes? **Was the outcome of COVID confirmed by laboratory testing?**** (critical = not reported; serious = only sample or subset of population had PCR; moderate = most participants had PCR; low = all participants had PCR) **If the outcomes were derived from databases, were the databases constructed specifically for the collection of COVID data?**** (critical = no or unclear; serious = database for non-COVID purpose without individual level data; moderate = database for non-COVID purpose with individual level data (e.g. health records, employee records); low = national/state/province level surveillance database or specifically for COVID) **Were appropriate tools/methods with validated/justified cut-points used to determine outcomes of interest (other than COVID infection/transmission which is covered under laboratory testing)? **** (critical = not reported; serious = outcomes solely dependent on self-report without a validated measure; moderate = objective measure applied but validation uncertain; low = objective validated measure used consistently across all groups) **If the outcome was self-reported, did the authors attempt to control for social desirability?**** (critical = not reported and outcome likely to be influenced by social desirability; moderate = attempt made to control for social desirability; low = outcome not influenced by social desirability) **Was the frequency of testing for the outcome different between the study groups?** (critical = routinely done more frequently in one group more than the other; moderate = some differences but rationale appropriate; low = no difference in frequency of testing between groups) **If outcome was observed, was there more than one assessor and if so, was interrater agreement reported?** (critical = not reported; serious = reported with low agreement; moderate = reported with moderate agreement; low = reported with excellent agreement)	

**relevant to single arm cohort studies

Critical appraisal checklist for cross-sectional studies

Questions	**Possible responses**
1. Were the criteria for inclusion in the sample clearly defined? The authors should provide clear inclusion and exclusion criteria that they developed prior to recruitment of the study participants. The inclusion/exclusion criteria should be specified (e.g., risk, stage of disease progression) with sufficient detail and all the necessary information critical to the study.	NA = not applicable; Y = yes; PY = partial yes; PN = partial no; N = no; U = unclear
2. Were the study subjects and the setting described in detail? The study sample should be described in sufficient detail so that other researchers can determine if it is comparable to the population of interest to them. The authors should provide a clear description of the population from which the study participants were selected or recruited, including demographics, location, and time period.	
3. Was the exposure measured in a valid and reliable way? The study should clearly describe the method of measurement of exposure. Assessing validity requires that a 'gold standard' is available to which the measure can be compared. The validity of exposure measurement usually relates to whether a current measure is appropriate or whether a measure of past exposure is needed. Reliability refers to the processes included in an epidemiological study to check repeatability of measurements of the exposures. These usually include intra-observer reliability and inter-observer reliability.	
4. Were objective, standard criteria used for measurement of the condition? It is useful to determine if patients were included in the study based on either a specified diagnosis or definition. This is more likely to decrease the risk of bias. Characteristics are another useful approach to matching groups, and studies that did not use specified diagnostic methods or definitions should provide evidence on matching by key characteristics	
5. Were confounding factors identified? Confounding has occurred where the estimated intervention exposure effect is biased by the presence of some difference between the comparison groups (apart from the exposure investigated/of interest). Typical confounders include baseline characteristics, prognostic factors, or concomitant exposures (e.g. smoking). A confounder is a difference between the comparison groups and it influences the direction of the study results. A high quality study at the level of cohort design will identify the potential confounders and measure them (where possible). This is difficult for studies where behavioral, attitudinal or lifestyle factors may impact on the results.	
6. Were strategies to deal with confounding factors stated? Strategies to deal with effects of confounding factors may be dealt within the study design or in data analysis. By matching or stratifying sampling of participants, effects of confounding factors can be adjusted for. When dealing with adjustment in data analysis, assess the statistics used in the study. Most will be some form of multivariate regression analysis to account for the confounding factors measured.	

7. Were the outcomes measured in a valid and reliable way? Read the methods section of the paper. If for e.g. lung cancer is assessed based on existing definitions or diagnostic criteria, then the answer to this question is likely to be yes. If lung cancer is assessed using observer reported, or self-reported scales, the risk of over- or under-reporting is increased, and objectivity is compromised. Importantly, determine if the measurement tools used were validated instruments as this has a significant impact on outcome assessment validity. Having established the objectivity of the outcome measurement (e.g. lung cancer) instrument, it's important to establish how the measurement was conducted. Were those involved in collecting data trained or educated in the use of the instrument/s? (e.g. radiographers). If there was more than one data collector, were they similar in terms of level of education, clinical or research experience, or level of responsibility in the piece of research being appraised?	NA = not applicable; Y = yes; PY = partial yes; PN = partial no; N = no; U = unclear
8. Was appropriate statistical analysis used? As with any consideration of statistical analysis, consideration should be given to whether there was a more appropriate alternate statistical method that could have been used. The methods section should be detailed enough for reviewers to identify which analytical techniques were used (in particular, regression or stratification) and how specific confounders were measured. For studies utilizing regression analysis, it is useful to identify if the study identified which variables were included and how they related to the outcome. If stratification was the analytical approach used, were the strata of analysis defined by the specified variables? Additionally, it is also important to assess the appropriateness of the analytical strategy in terms of the assumptions associated with the approach as differing methods of analysis are based on differing assumptions about the data and how it will respond.	

Critical appraisal tool for case-control studies

Questions	Possible responses
1. Were the groups comparable other than presence of disease in cases or absence of disease in controls? The control group should be representative of the source population that produced the cases. This is usually done by individual matching; wherein controls are selected for each case on the basis of similarity with respect to certain characteristics other than the exposure of interest. Frequency or group matching is an alternative method. Selection bias may result if the groups are not comparable.	NA = not applicable; Y = yes; PY = partial yes; PN = partial no; N = no; U = unclear
2. Were cases and controls matched appropriately? As in item 1, the study should include clear definitions of the source population. Sources from which cases and controls were recruited should be carefully looked at. For example, cancer registries may be used to recruit participants in a study examining risk factors for lung cancer, which typify population-based case control studies. Study participants may be selected from the target population, the source population, or from a pool of eligible participants (such as in hospital-based case control studies).	

3. Were the same criteria used for identification of cases and controls? It is useful to determine if patients were included in the study based on either a specified diagnosis or definition. This is more likely to decrease the risk of bias. Characteristics are another useful approach to matching groups, and studies that did not use specified diagnostic methods or definitions should provide evidence on matching by key characteristics. A case should be defined clearly. It is also important that controls must fulfil all the eligibility criteria defined for the cases except for those relating to diagnosis of the disease.	NA = not applicable; Y = yes; PY = partial yes; PN = partial no; N = no; U = unclear
4. Was exposure measured in a standard, valid and reliable way? The study should clearly describe the method of measurement of exposure. Assessing validity requires that a 'gold standard' is available to which the measure can be compared. The validity of exposure measurement usually relates to whether a current measure is appropriate or whether a measure of past exposure is needed. Case control studies may investigate many different 'exposures' that may or may not be associated with the condition. In these cases, reviewers should use the main exposure of interest for their review to answer this question when using this tool at the study level. Reliability refers to the processes included in an epidemiological study to check repeatability of measurements of the exposures. These usually include intra-observer reliability and inter-observer reliability.	
5. Was exposure measured in the same way for cases and controls? As in item 4, the study should clearly describe the method of measurement of exposure. The exposure measures should be clearly defined and described in detail. Assessment of exposure or risk factors should have been carried out according to same procedures or protocols for both cases and controls.	
6. Were confounding factors identified? Confounding has occurred where the estimated intervention exposure effect is biased by the presence of some difference between the comparison groups (apart from the exposure investigated/of interest). Typical confounders include baseline characteristics, prognostic factors, or concomitant exposures (e.g. smoking). A confounder is a difference between the comparison groups and it influences the direction of the study results. A high quality study at the level of case control design will identify the potential confounders and measure them (where possible). This is difficult for studies where behavioral, attitudinal or lifestyle factors may impact on the results.	
7. Were strategies to deal with confounding factors stated? Strategies to deal with effects of confounding factors may be dealt within the study design or in data analysis. By matching or stratifying sampling of participants, effects of confounding factors can be adjusted for. When dealing with adjustment in data analysis, assess the statistics used in the study. Most will be some form of multivariate regression analysis to account for the confounding factors measured. Look out for a description of statistical methods as regression methods such as logistic regression are usually employed to deal with confounding factors/ variables of interest.	

8. Were outcomes assessed in a standard, valid and reliable way for cases and controls? Read the methods section of the paper. If for e.g. lung cancer is assessed based on existing definitions or diagnostic criteria, then the answer to this question is likely to be yes. If lung cancer is assessed using observer reported, or self-reported scales, the risk of over- or under-reporting is increased, and objectivity is compromised. Importantly, determine if the measurement tools used were validated instruments as this has a significant impact on outcome assessment validity. Having established the objectivity of the outcome measurement (e.g. lung cancer) instrument, it's important to establish how the measurement was conducted. Were those involved in collecting data trained or educated in the use of the instrument/s? (e.g. radiographers). If there was more than one data collector, were they similar in terms of level of education, clinical or research experience, or level of responsibility in the piece of research being appraised?	NA = not applicable; Y = yes; PY = partial yes; PN = partial no; N = no; U = unclear
9. Was the exposure period of interest long enough to be meaningful? It is particularly important in a case control study that the exposure time was sufficient enough to show an association between the exposure and the outcome. It may be that the exposure period may be too short or too long to influence the outcome.	
10. Was appropriate statistical analysis used? As with any consideration of statistical analysis, consideration should be given to whether there was a more appropriate alternate statistical method that could have been used. The methods section should be detailed enough for reviewers to identify which analytical techniques were used (in particular, regression or stratification) and how specific confounders were measured. For studies utilizing regression analysis, it is useful to identify if the study identified which variables were included and how they related to the outcome. If stratification was the analytical approach used, were the strata of analysis defined by the specified variables? Additionally, it is also important to assess the appropriateness of the analytical strategy in terms of the assumptions associated with the approach as differing methods of analysis are based on differing assumptions about the data and how it will respond.	