COVID-19 Living Evidence Synthesis 15.2: Effectiveness of ventilation for reducing transmission of COVID-19 and other respiratory infections in non-health care community-based settings

Date of Literature Search: 3 Feb 2023

Suggested citation: Hartling L, Bialy L, Dandnayak D, Fleck B, COVID-END PHSM LES Working Group. COVID-19 living evidence synthesis 15.2: Effectiveness of ventilation for reducing transmission of COVID-19 and other respiratory infections in non-health care community-based settings. Alberta Research Centre for Health Evidence, University of Alberta, 10 February 2023.

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This living evidence synthesis (LES) 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. The LESs are updated every six weeks and include enhancements from the previous versions (e.g., inclusion of additional study designs and updated risk of bias assessments). The most up-to-date version of this and other LESs in the suite are available on the COVID-END website.

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 economic impacts of improving ventilation or introducing portable air cleaners?

6. What are the negative socio-economic impacts of improving ventilation or introducing portable air cleaners (e.g., 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. There are numerous features within HVAC systems that can be modified to potentially alter this risk. This review focused on: ventilation rates (often quantified as air changes per hour); 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.
- 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."
- 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]
- 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 in the air 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.
- There is a paucity of 'real world' evidence comparing ventilation or filtration strategies for reducing risk of COVID-19 infection.
- Two cross-sectional studies of elementary schools in the U.S. and meat packing plants in Germany found associations between ventilation and incidence of COVID-19 illness. Both studies were considered to have potential bias due to selection of participants, measurement of exposures and outcomes, and confounding.
- Three studies used modelling to investigate outbreaks of COVID-19 and demonstrated an association between ventilation rates and infection risk or attack rates.
- No studies were identified that examined the effectiveness of portable air cleaners in reducing transmission of COVID-19 or risk of infection.
- 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.).
- A number of principles regarding ventilation are well-established and supported by organizations that set standards for the HVAC industry such as 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. 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:*** Facilities should ensure that recommended standards 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. 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

- There is a paucity of 'real world' evidence comparing ventilation or filtration strategies for reducing transmission of COVID-19. We identified two studies that met the inclusion criteria.[12,13] Both studies were considered to be at risk of bias due to selection of participants, measurement of exposures and outcomes, and confounding. A cross-sectional study of elementary schools in Georgia, U.S. showed that COVID-19 incidence was 39% lower in schools that implemented some measures to improve ventilation.[12] Further, dilution methods alone (opening doors, opening windows, or using fans) resulted in 35% lower incidence, while a combined approach involving dilution and filtration (using HEPA filters [in air cleaners] with or without using UVGI) resulted in 48% lower incidence. A cross-sectional study of meat and chicken processing plants in Germany examined whether having a ventilation system reduced the chance of testing positive for COVID-19.[13] Results for the multivariable logistic regression showed a significant reduction among temporary and contract workers (aOR 0.541, 95% CI 0.368– 0.796). Assessment of "maximum outdoor air flow per employee" was also associated with reduced chance of COVID-19 infection (aOR 0.996, 95% CI 0.993-0.999).

- Another three studies used modelling and simulations to investigate outbreaks of COVID-19. Two studies used computational fluid dynamics and showed that increasing ventilation rates and fresh-air supply reduced risk of infection in the restaurant in Guangzhou, China where an outbreak occurred in January 2020. A third study investigated an outbreak caused by the same infected individual on two buses in Hunan Province, China in January 2020. 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.
- We did not identify any studies 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 in terms of reducing transmission of COVID-19 and other respiratory infections, and highlighted the urgent need for randomized controlled trials.[11] 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 bulk 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, they 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 saves lives and money.

Findings

- The search and reference check identified 1,105 studies. Two hundred and twenty-five studies were considered potentially relevant.
- Two studies met the eligibility criteria (Table 1). We also identified three modelling studies that investigated COVID-19 outbreaks (Table 2). Further, we identified 58 modelling and simulation studies that reported on risk or probability of transmission or infection.
- 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

Two studies were included that report on reducing transmission of COVID-19 as an outcome. The characteristics, findings and assessment of risk of bias for each study is presented in Table 1, with details about risk of bias available in Appendix 1.

A cross-sectional study examined the association between COVID-19 incidence and public health measures implemented at elementary schools in Georgia, United States.[12] 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 in high-risk areas, or installation of UVGI in high-risk areas). Among 169 schools, those that implemented ventilation improvements (n=87) showed reduced risk of COVID-19

Box 1: 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 February 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. Other study designs may be considered for future versions in the absence of other forms of evidence. A full list of included studies is provided in **Table 1**. **Table 2** lists modelling studies that investigated COVID-19 outbreaks. Studies excluded at the last stages of reviewing 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. 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.

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 assessment and for cross-sectional studies we used the JBI checklist. 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. This document will be updated every six weeks up to the end of March 2023.

incidence (risk ratio 0.61, 95% CI 0.43–0.87). Based on 123 schools with available data, the following were associated with 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). The study was at risk of bias due to selection of participants (including low response, 11.6% of 1,461 schools), measurement of exposures and outcomes, and lack of control for confounding (including other public health measures).

A cross-sectional study of 22 meat and chicken processing plants in Germany 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). 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. This study was considered at risk of bias due to selection of participants, measurement of exposures and outcomes, and lack of control for all possible sources of confounding.

Three studies used modelling and simulations to investigate outbreaks of COVID-19 (Table 2). Two studies used computational fluid dynamics and found that increasing ventilation rates and fresh-air supply reduced risk of infection in the restaurant in Guangzhou, China where an outbreak occurred in January 2020.[14,15] Ho et al 2021 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 2020 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.[16] 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%).

No studies were identified that reported on the effectiveness of portable air cleaners in terms of reducing transmission of COVID-19 or risk of infection in community-based settings.

Summary of findings about negative outcomes

No studies were identified that reported on negative outcomes (e.g., costs, inequities) of improving ventilation or introducing portable air cleaners.

Discussion

Several epidemiologic investigations of COVID-19 outbreaks in different community-based settings (e.g., restaurant, meat processing plant, sports facility, etc.) have determined that airborne transmission was a likely cause and that ventilation in the space was a contributing factor, either due to low ventilation rates, high occupancy, and/or air flow patterns created by air conditioning.[17-19] Recent systematic reviews (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.[20]

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, and airflow patterns. 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 may be 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.[21] 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.[22]" 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).[22] Costs to install and maintain HVAC systems, retrofit systems in older buildings, 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, 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)

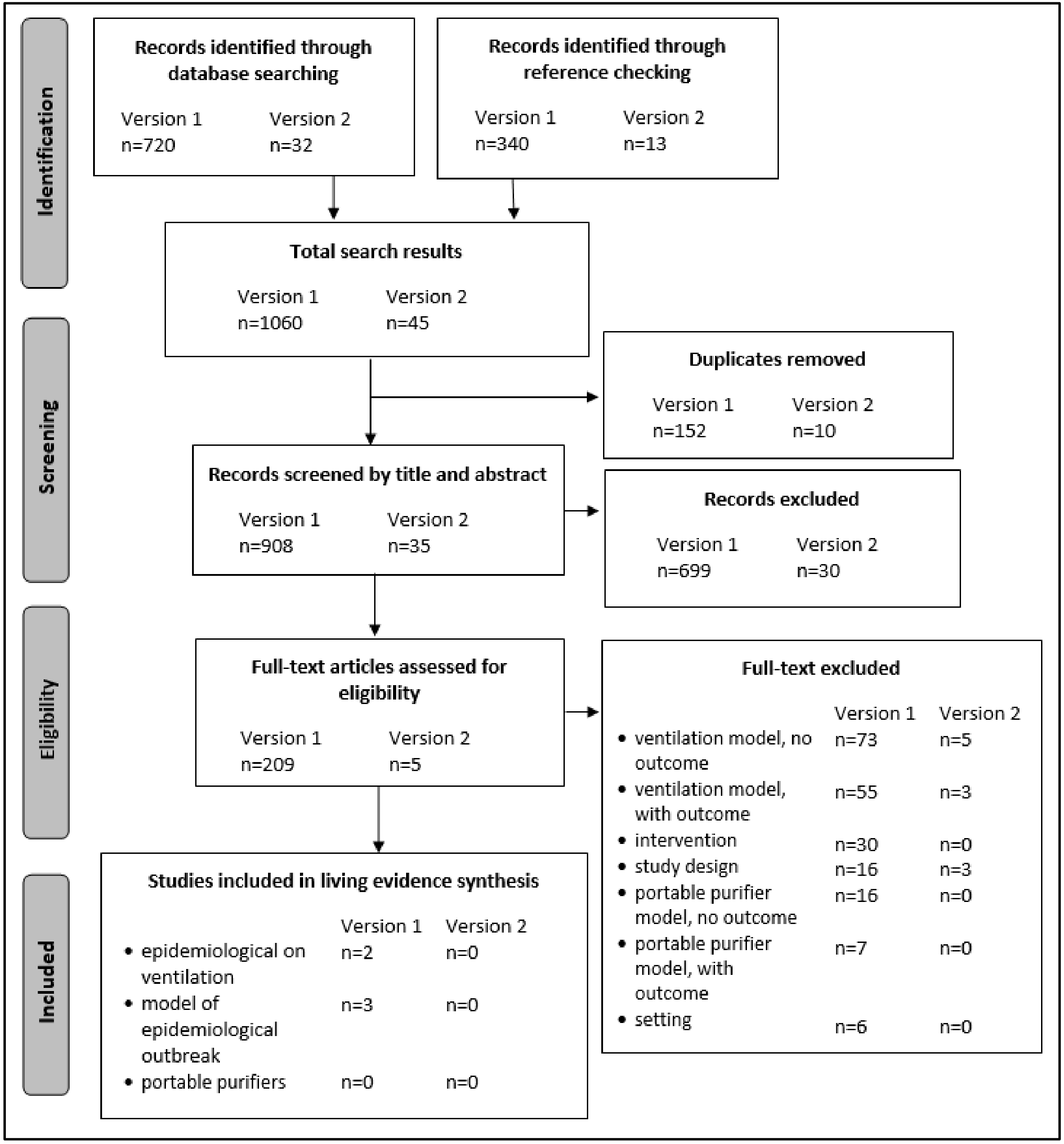

Table 1: Summary of studies reporting on effectiveness of ventilation in reducing COVID-19 infections

Author Year/Date Country	Setting and time covered	Study characteristics	Summary of key findings in relation to the outcome(s)
Gettings[12] 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)
	Considered at risk of bias for selection of participants, measurement of exposures and outcomes, and lack of control for confounding		

Pokora[13]
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)

	Considered at risk of bias for selection of participants, measurement of exposures and outcomes, and lack of control for all possible sources of confounding		

Abbreviations: aOR=adjusted odds ratio; HEPA=high-efficiency particulate absorbing; OR=odds ratio; RR=rate ratio; 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[14] 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.
Liu[15] 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[16] 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. **Bus1** - Attack rate = 7/46, 15.2% - Ventilation rate = 1.72 L/s per person 1.72 L/s per person - Exposure time = 200 minutes **Bus2** - 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.

Abbreviations: CFD=computational fluid dynamics

Acknowledgements

To help Canadian decision-makers as they respond to unprecedented challenges related to the COVID-19 pandemic, COVID-END in Canada is preparing evidence syntheses like this one. This living evidence synthesis was commissioned by the Office of the Chief Science Officer, Public Health Agency of Canada. The development and continued updating of this living evidence synthesis has been funded by the Canadian Institutes of Health Research (CIHR) and the Public Health Agency of Canada. The opinions, results, and conclusions are those of the team that prepared the evidence synthesis, and independent of the Government of Canada, CIHR, and the Public Health Agency of Canada. No endorsement by the Government of Canada, Public Health Agency of Canada or CIHR is intended or should be inferred.

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Appendices

Appendix 1: Risk of Bias assessments for included epidemiological studies*

	Gettings[12] USA	Pokora[13] Germany
1. Were the criteria for inclusion in the sample clearly defined?	Y	N
2. Were the study subjects and the setting described in detail?	PY	PY
3. Was the exposure measured in a valid and reliable way?	N	N
4. Were objective, standard criteria used for measurement of the condition?	NA	NA
5. Were confounding factors identified?	N	PY
6. Were strategies to deal with confounding factors stated?	N	Y
7. Were the outcomes measured in a valid and reliable way?	N	N
8. Was appropriate statistical analysis used?	N	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[TIAB] OR "air condition*"[TIAB] OR "building ventilation"[TIAB] OR "ventilation system"[TIAB] OR "indoor ventilation"[TIAB] OR HVAC[TIAB] OR air samples[TIAB]) AND (Disease Transmission, Infectious*[Mesh] OR Air Pollution, Indoor[MeSH] OR transmission[Subheading] OR Infections[Mesh:NoExp] OR transmi*[TIAB] OR infect*[TIAB] OR contagi*[TIAB] OR outbreak*[TIAB] OR spread*[TIAB] OR decontamination[TIAB]) AND (Aerosols[MeSH] OR Air Microbiology[MeSH] OR Aerosol*[TIAB] 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])

#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]

#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 #3 and #4 (will retrieve Reviews)

#10 #3 and #5 (will retrieve RCTs)

#11 #3 and #6 (will retrieve Quasi-experimental studies)

#12 #3 and #7 (will retrieve Cohort studies)

#13 #3 and #8

#14 #9 or #10 or #11 or #12 or #13

#15 #14 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 data Reviews: narrative and literature reviews; check references of systematic/rapid reviews or meta-analysis with relevant to any of the public health measures
Population	Involving animals or humans	None
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 air cleaners 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 = 78)

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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.

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

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.

RoB in cohort studies

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 <u>OR</u> COVID status of both groups known by self-report only; low = negative COVID status of both groups known at study start (lab confirmed))

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)

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)

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)

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 / Y / PY / PN / N
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.	NA / Y / PY / PN / N
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.	NA / Y / PY / PN / N
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	NA / Y / PY / PN / N
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.	NA / Y / PY / PN / N
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.	NA / Y / PY / PN / N

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 / Y / PY / PN / N
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.	NA / Y / PY / PN / N

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