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¹COVID-19 Rapid Evidence Service, UK Health Security Agency, London, UK

²MRC Integrative Epidemiology Unit, University of Bristol, Bristol, UK

³Population Health Science, Bristol Medical School. University of Bristol, Bristol, UK

4COVID-19 Advice and Guidance, UK Health Security Agency, London, UK

⁵Biosafety, Air, and Water Microbiology Group, Research and Evaluation, UK Health Security Agency, Porton, UK

Correspondence to: D Duval covid19evidence@phe.gov.uk (ORCID 0000-0002-1042-2114)

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Long distance airborne transmission of SARS-CoV-2: rapid systematic review

Daphne Duval, ¹ Jennifer C Palmer, ^{1,2,3} Isobel Tudge, ¹ Nicola Pearce-Smith, ¹ Emer O'Connell, ⁴ Allan Bennett. 5 Rachel Clark 1

Abstract

OBIECTIVES

To evaluate the potential for long distance airborne transmission of SARS-CoV-2 in indoor community settings and to investigate factors that might influence transmission.

DESIGN

Rapid systematic review and narrative synthesis.

DATA SOURCES

Medline, Embase, medRxiv, Arxiv, and WHO COVID-19 Research Database for studies published from 27 July 2020 to 19 January 2022; existing relevant rapid systematic review for studies published from 1 January 2020 to 27 July 2020; and citation analysis in Web of Science and Cocites.

ELIGIBILITY CRITERIA FOR STUDY SELECTION

Observational studies reporting on transmission events in indoor community (non-healthcare) settings in which long distance airborne transmission of SARS-CoV-2 was the most likely route. Studies such as those of household transmission where the main transmission route was likely to be close contact or fomite transmission were excluded.

DATA EXTRACTION AND SYNTHESIS

Data extraction was done by one reviewer and independently checked by a second reviewer. Primary outcomes were SARS-CoV-2 infections through long distance airborne transmission (>2 m) and any modifying factors. Methodological quality of included

studies was rated using the quality criteria checklist. and certainty of primary outcomes was determined using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) framework. Narrative synthesis was themed by setting.

RESULTS

22 reports relating to 18 studies were identified (methodological quality was high in three, medium in five, and low in 10); all the studies were outbreak investigations. Long distance airborne transmission was likely to have occurred for some or all transmission events in 16 studies and was unclear in two studies (GRADE: very low certainty). In the 16 studies, one or more factors plausibly increased the likelihood of long distance airborne transmission, particularly insufficient air replacement (very low certainty), directional air flow (very low certainty), and activities associated with increased emission of aerosols, such as singing or speaking loudly (very low certainty). In 13 studies, the primary cases were reported as being asymptomatic, presymptomatic, or around symptom onset at the time of transmission. Although some of the included studies were well conducted outbreak investigations, they remain at risk of bias owing to study design and do not always provide the level of detail needed to fully assess transmission routes.

CONCLUSION

This rapid systematic review found evidence suggesting that long distance airborne transmission of SARS-CoV-2 might occur in indoor settings such as restaurants, workplaces, and venues for choirs, and identified factors such as insufficient air replacement that probably contributed to transmission. These results strengthen the need for mitigation measures in indoor settings, particularly the use of adequate ventilation.

SYSTEMATIC REVIEW REGISTRATION

PROSPERO CRD42021236762.

Introduction

Since the early stages of the covid-19 pandemic and the first reports of superspreader events, 1 2 the body of evidence suggesting airborne transmission of SARS-CoV-2 in the absence of aerosol generating procedures has grown. However, despite the publication of numerous opinion pieces and narrative reviews in support of airborne transmission of SARS-CoV-2,3-9 scientific consensus on the relative importance of this route of transmission is lacking. Part of the controversy arises from differences in terminology, definitions, and size thresholds for respiratory particles. 10

Traditionally, close contact transmission was assumed to occur through droplets with ballistic trajectory that directly deposit on mucous membranes,

WHAT IS ALREADY KNOWN ON THIS TOPIC

The risk of SARS-CoV-2 transmission is likely to be greatest when in close proximity (<2 m) to someone who is infected

The potential for long distance airborne transmission (>2 m) is unclear, although widespread reporting of superspreader events suggests it may occur Emission rates of respiratory particles released vary considerably between individuals but are generally higher for singing and speaking compared with breathing and tend to increase with loudness of vocalisation

WHAT THIS STUDY ADDS

The findings from this rapid systematic review suggest that long distance airborne transmission of SARS-CoV-2 might happen in indoor settings such as restaurants, public transport, workplaces, or choir venues

These results show that factors such as insufficient air replacement, directional air flow, and activities associated with increased emissions of respiratory particles (eg, singing or speaking loudly) might contribute to long distance airborne transmission

Well conducted epidemiological investigations can provide critical insight into transmission routes, especially when other types of studies are not feasible; the question of what level of public health evidence is sufficient to support decision making for a novel infection warrants further consideration

whereas airborne transmission was assumed to occur over longer distances via smaller particles (aerosols) that remained suspended in the air and were subsequently inhaled. ¹⁰ ¹¹ Limitations of this dichotomy are well illustrated by the challenge in defining a size range to characterise particles that are droplets or aerosols. ⁶ ⁷ ¹⁰ ¹² For example, the World Health Organization threshold is set at 5-10 microns ¹³ whereas in the UK the threshold is based on the work by Milton ¹⁴ and set to 100 microns. ¹⁵ This is also complicated by the role of evaporation, as a particle will get smaller as it moves from human sources.

Regardless of terminology and definitions, it is now understood that short range transmission can occur through both droplets and aerosols and that the concentration of respiratory particles is higher at short range than over longer distances.⁷ 11 16 17 Consensus is, however, still lacking on the risk for long distance airborne transmission in indoor settings in the community such as hospitality venues, leisure facilities, workplaces, or apartment blocks. This lack of consensus also reflects the challenging nature of the evidence base, and high quality review level evidence is still needed; some systematic reviews have relied on environmental sampling studies, which only provide indirect evidence of the potential risk of airborne transmission. 18-20 whereas systematic reviews that have included a wider range of study designs (epidemiological, environmental, and modelling) and settings (healthcare and community) remain inconclusive. 21-24

This gap needs to be addressed from a public health perspective, focusing on long distance transmission (>2 m) in indoor community settings. As evidence on the biological plausibility of long distance airborne transmission is available from environmental and experimental studies, ¹⁸ ²¹ ²² we focused on epidemiological observational studies to assess where and when human-to-human transmission are likely to occur. In this rapid review we systematically identified and examined such studies to evaluate the potential for long distance airborne transmission of SARS-CoV-2 in indoor community settings and to assess the impact of potential modifying factors.

Methods

We used a rapid systematic review approach, following streamlined systematic methodologies to accelerate the review process, ²⁵ and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. ²⁶ The protocol for this review was registered on PROSPERO before screening took place. ²⁷

Data sources and searches

We identified primary studies through two sources. Firstly, we screened studies included in the rapid systematic review by Comber et al for those published from 1 January 2020 to 27 July 2020.²¹ This systematic review, assessed to be of moderate quality using the AMSTAR 2 (A MeaSurement Tool to Assess systematic

Reviews, revised) critical appraisal tool,²⁸ contains a comprehensive search strategy and wider inclusion criteria than the current rapid review (studies related to all airborne transmission of SARS-CoV-2) and was the only relevant review available at the time we wrote our protocol.

Secondly, we conducted electronic searches in Ovid Medline, Ovid Embase, medRxiv, Arxiv, and WHO COVID-19 Research Database for studies published from 27 July 2020 to 19 January 2022. The initial search was conducted on 8 February 2021 and last updated on 19 January 2022. The search strategy was drafted by an information scientist and peer reviewed by a second information scientist. Supplementary material 1 (section 1) shows the full search strategy.

Using the studies that met our inclusion criteria, we performed a citation analysis on 1 February 2022 on Web of Science and Cocites (co-citation analysis, forward and backwards snowballing). Although this was not part of the search strategy outlined in the protocol, it was agreed a posteriori by the review team to increase the chance of additional relevant studies being retrieved.

Eligibility criteria for study selection

Our eligibility criteria for study selection were published articles, accepted manuscripts, and preprints reporting on the potential for airborne transmission of SARS-CoV-2 in indoor community (non-healthcare) settings at a distance >2 m (the 2 m threshold is based on UK regulations; we also considered for inclusion non-UK studies that used thresholds based on their respective national recommendations, such as 1.5 m or 6 feet/1.8 m). The aim was to include all observational studies (outbreak investigations and epidemiological case series, cohort, case-control, and cross sectional studies) of any human population in non-healthcare settings. We excluded systematic or narrative reviews, guidelines, opinion pieces, intervention studies, modelling studies, environmental sampling studies without epidemiological investigation, laboratory or virology studies, and animal studies. We also excluded observational studies in which close contact or fomite were the most likely transmission routes (eg. studies reporting on transmission in households).

Screening was performed using Rayyan Systems, a freely available online screening tool. ²⁹ Two reviewers independently screened the first 10% of records retrieved from the initial search on title and abstract, with substantial agreement (97.7%; Cohen's κ =0.61). A single reviewer screened the remainder, and two reviewers independently screened a further 10% (of the total number of records), with almost perfect agreement (99.6%; Cohen's κ =0.92). All records selected were screened at full text by one reviewer and checked by a second reviewer, with any discrepancies resolved by discussion with a third reviewer.

Outcomes

The primary outcomes were SARS-CoV-2 infections through long distance airborne transmission (at

a distance >2 m), and any factors that might have modified the risk of transmission under these conditions. Included measures for SARS-CoV-2 infections were number of covid-19 cases; secondary attack rates; risk, rate, or odds of transmission over the stipulated distances; or any other reported measure related to transmission rate. For the modifying factors, we considered narrative on the type of effect and any potentially relevant information to be acceptable.

Additional outcomes extracted, when available, were time spent in the setting and distance over which airborne transmission was thought to have occurred

Data extraction and synthesis

We developed a data extraction table to gather information on methods, participants, settings, outcomes, key findings, and any additional relevant information (eg, whether participants wore face coverings). Data extraction was completed for each included study by one reviewer and independently checked by a second reviewer, with discrepancies resolved by discussion. Only evidence directly relevant to the review question was extracted. For example, if studies reported on different outbreaks or on onward transmission that might have happened in different settings, we only extracted the results of outbreaks or settings when distance and transmission routes could be assessed.

A narrative summary of results according to indoor setting was produced.

Quality assessment and certainty of evidence

We used a quality criteria checklist for primary research to assess the methodological quality of each included study. This checklist tool is composed of 10 questions, four of which are considered critical (questions on selection bias, group comparability, description of exposure/assessment of transmission routes, and validity of outcome measurements). Strict criteria were used to assess the two critical questions related to exposure and outcome assessment. In particular, a cluster of covid-19 cases in the setting of interest had to be confirmed with viral genomic sequencing to be considered as low risk of bias for validity of outcome measurements. Supplementary material 1 (section 2) lists the 10 questions of the quality criteria checklist.

A study was rated as high methodological quality if the answers were yes to the four critical questions plus at least one of the remaining questions. A study was rated as low methodological quality if answers were no to $\geq 50\%$ of the critical questions. Otherwise, the study was rated as medium methodological quality. Each study was assessed independently in duplicate, with disagreements resolved by consensus.

Certainty of the evidence was assessed using a variation of the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) framework for systematic reviews without meta-analysis.³¹ We assessed each of the five GRADE domains (methodological limitations of the studies,

indirectness, imprecision, inconsistency, and likelihood of publication bias) and classified them as no limitation or not serious (not important enough to warrant downgrading), serious (downgrading the certainty rating by one level), or very serious (downgrading the certainty rating by two levels). We then classified the body of evidence for a specific outcome as high certainty, moderate certainty, low certainty, or very low certainty.

Patient and public involvement

Patients and members of the public were not involved in this rapid systematic review mainly because of time restrictions. The review question was, however, developed with the input of several public health experts and stakeholders.

Results

Study selection

After removal of duplicates, 7439 records were screened for relevance on title and abstract, with 90 reports assessed for eligibility (fig 1). Fifty six additional reports identified from the Comber et al rapid review²¹ and by citation analysis were also assessed. From these 146 reports, 124 were excluded (see supplementary material 1 (section 3) for list of reasons for exclusion), and 22 reports^{1 32-52} relating to 18 studies were included. When two or more reports related to the same study, we considered the most comprehensive report as the main publication.

All the studies investigated outbreaks of clusters of SARS-CoV-2 infections, and one study had an analytical component. Eight studies were conducted in Asia, 44.40 to five in Europe, 41.43 44.47 48 three in Oceania, 32.33 46 and two in the United States. At Three studies reported on transmission between flats in apartment blocks, 88.40 two in quarantine hotels, 32.33 two in restaurants, 43.55 two in buses, 36.37 one in a food processing factory, and one in a courtroom, and one in an office, 44 one in a fitness facility, and one in a department store, 54 and four during singing events. All the outbreaks occurred in 2020, except for one in January 2021 in South Korea (before vaccine rollout started in this country) and one in July 2021 in a quarantine hotel in New Zealand.

Table 1 and table 2 summarise the studies by setting. Supplementary material 2 provides detailed information on each study.

Quality assessment

Figure 2 provides details of the methodological quality ratings: three studies were rated as high quality, ^{33 35 46} five as medium quality, ^{32 34 36 41 47} and 10 as low quality. ^{1 37-40 42-45 48} These ratings represent the methodological quality of descriptive studies.

Transmission settings

Quarantine hotels

Two outbreaks of covid-19 in quarantine hotels were identified, both in New Zealand and involving cases part of the same genomic cluster who had quarantined

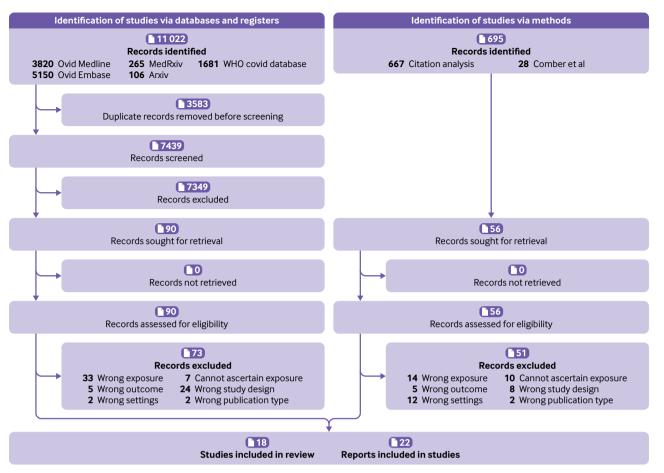


Fig 1 | Flow of articles through the review

in separate rooms. The first outbreak, reported by Eichler et al³² (rated as medium methodological quality) occurred in September 2020, and although primary and secondary cases had travelled on the same flight, transmission is believed to have happened in the hotel on day 12 of quarantine, after the primary case had developed symptoms on day 10. No information was provided on the measures in place at this quarantine hotel (eg, use of face coverings). The second outbreak, reported by Fox-Lewis et al³³ (rated as high methodological quality) occurred in July 2021. The primary case (asymptomatic) and secondary cases had travelled on different flights and arrived at the hotel on different days. Staff members, all vaccinated, wore full personal protective equipment and were regularly tested. Participants were asked to wear surgical masks when opening doors, but this could not be validated in the investigation. None of the cases (primary or secondary) were vaccinated; the only person who was vaccinated tested negative despite being part of the same travel group as the secondary cases.

Close contact and fomite transmission were ruled out by video analysis in both studies, although in the outbreak reported by Eichler et al³² fomite transmission through a communal bin—although unlikely, cannot be ruled out. Video analysis showed that in both outbreaks the doors of the rooms had

been opened simultaneously for a short period during which infected respiratory particles could have moved between rooms. Both investigations included a review of the ventilation systems and found that pressure differences between rooms and corridors could support this hypothesis. Long distance airborne transmission between a primary case and at least one secondary case was therefore considered to be the most likely route in both outbreaks.

Restaurants

Two separate outbreaks of covid-19 in restaurants were identified. The first outbreak, in China in January 2020, was mainly reported by Li et al34 (rated as medium methodological quality), with additional evidence provided in two other reports. 49 50 This outbreak involved a primary case (with symptom onset later that day) and at least two secondary cases who were seated on tables between 1.4 and 4.6 m away from the primary case. The second outbreak, reported by Kwon et al³⁵ (rated as high methodological quality), occurred in June 2020 in South Korea and involved three people with confirmed covid-19 who belonged to the same genomic cluster. The primary case, which was presymptomatic at the time, sat 6.5 m from one secondary case for five minutes, and 4.8 m from the other secondary cases for 21 minutes, all at different

Table 1 Summa	ary of included st	udies, in chrono	ological order by setting: c	uarantine hotels, restaura	ints, buses, and apartmen	t blocks
Reference (quality rating)	Transmission event, setting, date	No of cases	Outcome and exposure assessment	Potential for other trans- mission routes	Potential for airborne transmission >2 m*	Modifying factors
Li et al, ³⁴ Lu et al, ⁴⁹ Zhang et al ⁵⁰ (medium)	Restaurant, China, January 2020	Ten confirmed cases from three tables	No genomic sequencing. Epidemiological data, video recording, on-site visit, design of air conditioning and ventilation system, experiments to assess airflow and ventilation rates	Close contact or fomite transmission unlikely (except for cases in same household). Transmission from outside event possible for some cases	Possible airborne transmission between primary case and at least two secondary cases; up to 1.4 m (53 min) and 4.6 m (75 min) from primary case	Insufficient air replacement. Directional air flow through air circulation units
Shen et al ³⁶ (medium)	Buses, China, January 2020	Twenty four confirmed cases	No genomic sequencing. Questionnaires and interviews, contact tracing data, bus design, and ventilation system	Close contact, fomite transmission, or transmission from outside event possible for some cases	Possible airborne transmission >2 m from primary case (50 min)	Insufficient air replacement. Directional air flow from central heating system
Luo et al, ³⁷ Ou et al ⁵¹ (low)	Buses, China, January 2020	Nine confirmed cases	No genomic sequencing. Epidemiological data, information on loading and unloading stops of all passengers, and seating positions, ventilation systems, tracer gas experiments	Close contact unlikely. Fomite transmission or transmission from outside event possible for some cases	Possible airborne transmission >2 m for some cases (1 hour to 2.5 hours)	Insufficient air replacement. Directional air flow due to exhaust system
Lin et al ³⁸ (low)	Apartment block, China, January 2020	Nine confirmed cases from three households	No whole genome sequencing (partial S gene only). Interviews with cases, CCTV of lift, tracer gas and wind speed experiments	Close contact or fomite transmission unlikely (except for cases in same household); transmission from outside event possible for some cases	Possible airborne transmission between cases in one flat to two different flats (up to 10 floors from flat of primary case)	Insufficient air replacement. Directional air flow through drainage and exhaust system
Kwon et al ³⁵ (high)	Restaurant, South Korea, June 2020		Genomic sequencing. Contact tracing, interviews, credit card records, video recording, mobile phone location data, on-site visits, air flow measurement, environmental sampling	Close contact, fomite transmission, or transmission from outside event unlikely	Possible airborne transmission between cases seated 4.8 m (21 min) and 6.5 m (5 min) from the primary case	Insufficient air replacement. Directional air flow through air circulation units
Hwang et al ³⁹ (low)	Apartment block, South Korea, August 2020	Ten confirmed cases from seven households	No genomic sequencing. Epidemiological data, surface sampling, building assessment	Close contact or fomite transmission unlikely (except for cases in same household). Transmission from outside event possible	Possible airborne transmission through ventilation ducts across floors for some secondary cases	Directional air flow through vertical air duct or floor drain. Insufficient air replacement (unclear)
Eichler et al ³² (medium)	Quarantine hotel, New Zealand, August- September 2020		Genomic sequencing. Epidemiological data, surveillance video, review of ventilation system in hotel	Close contact or fomite transmission unclear. Transmission from outside event unlikely	Possible airborne transmission from hotel room of the primary case to doorway or corridor for one secondary case	Insufficient air replacement. Directional air flow
Han et al ⁴⁰ (low)	Apartment block, South Korea, January 2021		Genomic sequencing. Epidemiological data, interviews, mobile phone location tracking, surface sampling	Close contact or fomite transmission unlikely (except for cases in same household). Transmission from outside event unlikely	Possible airborne transmission through floor drains across three floors for two secondary cases	Insufficient air replacement. Directional air flow through vertical floor drain
Fox-Lewis et al ³³ (high)	Quarantine hotel, New Zealand, July 2021		Genomic sequencing. Epidemiological data, surveillance video, review of ventilation system in hotel	Close contact, fomite transmission, or transmission from outside of event unlikely	Possible airborne transmission from hotel room of primary case to hotel room for at least one secondary case (2.1 m)	Insufficient air replacement. Directional air flow

After extensive epidemiological and environmental investigations, both studies suggested that the most plausible route was long distance airborne transmission, which could have been facilitated by air circulation units generating a directional air flow from the primary to secondary cases combined with lack of air replacement. In both outbreaks close contact and fomite transmission were ruled out based on video

This review's assessment of likelihood of airborne transmission of SARS-CoV-2 over distances >2 m is based on likelihood of it occurring in some, but not necessarily all, transmission events.

Buses and coaches

surveillance analysis.

*Exposure distance and time are stated when known; if not stated they are categorised as not clear or not specified.

Two separate outbreaks of covid-19 on buses in China in January 2020 were identified, one on a journey to

and from a worship event among lay Buddhists 36 and one on a long distance journey using a public coach and minibus. $^{37\,51}$

The outbreak at a worship event was reported by Shen et al³⁶ who conducted a retrospective epidemiological investigation with an analytical component (rated as medium methodological quality). Thirty one of the 300 participants tested positive for SARS-CoV-2 of whom seven were likely to have been infected by close contact transmission during the religious event. The other 23 cases had travelled to the event in the same bus as the primary case and were thought to have been mainly infected during the bus journey, throughout

Table 2 Summary of included studies, in chronological order by setting: department store, singing events, meat processing plant, fitness facility,
courtroom, and office

courtroom, and	l office					
Reference (quality rating)	Transmission event, setting, date	No of cases	Outcome and exposure assessment	Potential for other trans- mission routes	Potential for airborne transmission >2 m*	Modifying factors
Jiang et al ⁴⁵ (low)	Department store, China, January 2020	Twenty four cases, with 12 secondary cases considered for long distance transmission	No genomic sequencing. Epidemiological data, surveillance video, assessment of ventilation conditions	Close contact, fomite transmission, or transmission from outside event all possible	Unclear airborne transmission across different sections of the store	Not applicable
Hamner et al, ¹ Miller et al ⁵² (low)	Singing event, USA, March 2020	Fifty two: 32 confirmed cases, 20 probable cases	No genomic sequencing. Telephone interviews	Close contact or transmission from outside event possible for some cases. Fomite transmission unlikely	Possible airborne transmission >2 m for some cases, owing to high secondary attack rate (2.5 hours)	
Charlotte et al ⁴⁸ (low)	Singing event, France, March 2020	Nineteen: seven confirmed cases, 12 probable cases	No genomic sequencing. Questionnaire and telephone interviews	Close contact possible for some cases. Fomite transmission unlikely. Transmission from outside event possible for at least two cases	Possible airborne transmission >2 m for some cases, owing to high secondary attack rate (2 hours)	Insufficient air replacement. Increased aerosol emission—singing
Gunther et al ⁴¹ (medium)	Meat processing plant, Germany, May-June 2020	Thirty one confirmed cases	Genomic sequencing. On- site visit (work condition and ventilation system) and information provided by employer on housing, commuting, and workplaces of employees	Close contact and fomite transmission possible for some cases. Transmission from outside event unlikely	Possible airborne transmission for some cases on the production line, up to 12 m from the primary case	Insufficient air replacement. Directional air flow from air circulation system. Increased aerosol emission— physical work (unclea
Groves et al ⁴² (low)	Fitness facility, USA, June 2020	Twenty one confirmed cases, with10 secondary cases considered for long distance transmission	No genomic sequencing. Questionnaire and on-site assessment	Close contact possible for some cases. Fomite transmission unclear. Transmission from outside event unlikely	Possible airborne transmission >2 m for some cases, owing to high secondary attack rate (1 hour)	Insufficient air replacement. Directional air flow from air fan. Increased aerosol emission— shouting
Katelaris et al ⁴⁶ (high)	Singing event, Australia, July 2020	Thirteen confirmed cases	Genomic sequencing. Interviews with cases, video recording, on-site visit (ventilation system)	Close contact or fomite transmission unlikely (except for five cases in same household). Transmission from outside event unlikely	Possible airborne transmission with secondary cases seated 1-15 m from the primary case (1 hour)	Insufficient air replacement. Increased aerosol emission—singing
Vernez et ⁴³ (low)	Courtroom, Switzerland, September 2020	Five confirmed cases	No genomic sequencing. Court records, contact tracing data, and field measurements	Close contact cannot be ruled out, especially for the two secondary cases at 1.5 m from the primary case. Fomite transmission unlikely. Transmission from outside event likely for one secondary case	Possible long distance airborne transmission for three secondary cases (1.5-3 m; 3 hours)	Insufficient air replacement
Shah et al ⁴⁷ (medium)	Five singing events, Netherlands, September-October 2020	Fifty: 48 confirmed cases and two probable cases	Genomic sequencing for seven cases. Phone and email correspondence, questionnaires, epidemiological data, aerosol transmission model	Close contact possible for some cases. Fomite transmission unlikely (except for one event). Transmission from outside event possible for some cases, but unlikely in others	Possible airborne transmission >1.5 m for some cases (1 hour to 2.5 hours)	Increased aerosol emission—singing. Directional air flow (unclear). Insufficient air replacement (unclear)
Sarti et al ⁴⁴ (low)	Office, Italy, November 2020	Five confirmed cases	No genomic sequencing. Telephone interviews	Close contact, fomite transmission, or transmission from outside event possible	Unclear airborne transmission between coworkers	Not applicable

The review's assessment of likelihood of airborne transmission of SARS-CoV-2 over distances >2 m is based on likelihood of it occurring in some, but not necessarily all, transmission events. *Exposure distance and time are stated when known; if not stated they are categorised as not clear or not specified.

which no one wore face coverings. Those travelling on the bus with the primary case were 11 times more likely to develop covid-19 compared with the other participants (relative risk 11.4, 95% confidence interval 5.1 to 25.4; P<0.01) and 42 times more likely compared with those travelling in the other bus (42.2, 2.6 to 679.3; P<0.01). Close contact transmission, fomite transmission, and transmission from outside the event cannot be ruled out for some of the cases but are unlikely to have accounted for all 23 secondary cases.

The second outbreak, reported by Luo et al³⁷ (rated as low methodological quality) with additional environmental investigations conducted by Ou et al,⁵¹ involved one primary case (symptom onset occurred on the day of the event) who had travelled without wearing a face covering on a coach for 2.5 hours with 48 other individuals and then on a minibus for one hour with 12 other individuals. Nine secondary cases were identified, resulting in a secondary attack rate of 15% (95% confidence interval 6% to 24%), with most seated >2 m from the primary case: up to 4.5 m based

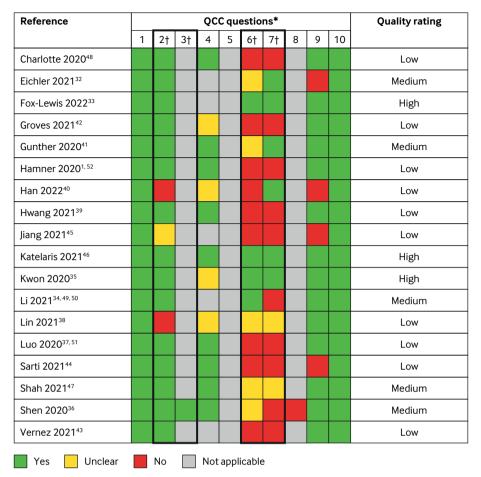


Fig 2 | Quality assessment. *Assessments using quality criteria checklist (QCC) for primary research (see supplementary material 1). †Critical questions: 2 on selection bias, 3 on group comparability, 6 on description of exposure/assessment of transmission routes, and 7 on validity of outcome measurements

on one report³⁷ and up to 9.5 m based on the other report.⁵¹ Genomic sequencing was not performed and, based on symptom onset dates, it is plausible that more than one primary case was present, reducing our confidence in the distances reported. However, even taking into account all potential primary cases, it is possible that airborne transmission occurred for some secondary cases seated >2 m from a primary case. Some passengers wore face coverings, but none of the secondary cases did.

In both outbreaks, insufficient air replacement and directional airflow from the heating system were hypothesised as promoting long distance airborne transmission, supported by tracer gas experiments in the buses involved in one of the outbreaks.⁵¹

Apartment blocks

Three outbreaks of covid-19 in three separate residential apartment blocks were identified. The study by Lin et al³⁸ (rated as low methodological quality) investigated an outbreak involving nine people who tested positive for SARS-CoV-2 in three flats of a 29 storey apartment block in China. The nine cases, identified between 27 January and 13 February 2020, lived in flats that shared drain and sewer pipes connected via an exhaust pipe to the roof. Except for

cases in the same household, close contact and fomite transmission were ruled out based on interviews with the cases and partial video analysis (lift only). Some but not all of the cases reported wearing face coverings in the communal areas of the building.

The two other outbreaks were in South Korea. The first, reported by Hwang et al³⁹ (rated as low methodological quality), occurred in August 2020 in an apartment block of 267 flats and involved 10 cases from seven households located around two ventilation ducts (eight cases around one, two around another). The second outbreak, reported by Han et al⁴⁰ (rated as low methodological quality), occurred in January 2021 in a complex of 260 flats, in which cases located in three flats along the same drainpipe and ventilation duct could not be explained by close contact or fomite transmission. For both outbreaks, transmission routes were mainly investigated through interviews with cases, and therefore recall bias (no video analysis) was possible. All cases reported wearing face coverings in the communal areas of the buildings.

For all three outbreaks, long distance airborne transmission between flats through vertical air ducts or floor drains was deemed possible for at least some of the secondary cases, although environmental investigation (tracer gas experiment) to support this

hypothesis was conducted in only one³⁸ of the three studies. In two of the three studies,^{38 40} the ventilation ducts were found to be malfunctioning, which could have contributed to transmission risk. However, only one of these studies³⁹ tested all residents and only one conducted whole genome sequencing,⁴⁰ which reduces confidence in the results.

Other indoor settings

The other outbreaks identified in this review occurred in a food processing factory, ⁴¹ fitness facility, ⁴² courtroom, ⁴³ office, ⁴⁴ and department store. ⁴⁵

Gunther et al⁴¹ (rated as medium methodological quality) reported on an outbreak in a meat processing plant in Germany in May and June 2020 in which 31 out of the 140 workers on the same shift had tested positive for SARS-CoV-2 and were part of the same genomic cluster. Although close contact or fomite transmission in other areas of the processing plant and outside the factory (some workers shared accommodation and carpools) was possible for some cases, the spatial distribution of the cases suggested that transmission was likely to have occurred on the processing line at distances up to 12 m from the primary case who was asymptomatic. The authors hypothesised that factors such as increased respiratory rates (from physically demanding work), lack of air replacement, and continuous recirculation of cooled unfiltered air might have promoted long distance airborne transmission, but these were not investigated further. Some covid-19 measures were in place, including increased distance between workers and use of single layer face coverings, but adherence was not assessed as part of the study.

Groves et al⁴² (rated as low methodological quality) reported on an outbreak involving two fitness instructors at classes taught in three different facilities in June and July 2020, although the investigation suggested that close contact and fomite transmission were likely to have occurred in all classes but one. The class in which long distance airborne transmission might have happened was a one hour static cycling class in which bikes were placed at least 1.8 m apart, with doors and windows closed and three large fans directed towards the class participants. The instructor, who had shouted instructions while facing the participants, was identified as being the primary case (with symptom onset the next day) and all 10 class participants had tested positive for SARS-CoV-2 three to six days after the class. Face coverings had not been used during the class.

In an outbreak in a courtroom in Switzerland reported by Vernez et al⁴³ (study rated as low methodological quality), five out of the 10 participants at a three hour hearing held on the 30 September 2020 tested positive for SARS-CoV-2. The use of face coverings was mandatory in the building, but not when seated, and social distancing measures were in place, with a minimum of 1.5 m between each seat. Long distance airborne transmission (1.5-3 m) was likely to have happened between a primary case (with symptom onset on that day) and three secondary cases, although

close contact or fomite transmission after the hearing or in the bathroom cannot be ruled out. The hypothesis that a lack of air replacement (doors and windows were closed and there was no mechanical ventilation) might have promoted long distance airborne transmission was supported by field measurements and modelling.

Sarti et al⁴⁴ (rated as low methodological quality) reported on an outbreak in an office in Italy in which five of six coworkers were identified as cases. One of the five coworkers was identified as the primary case, and transmission happened before symptom onset. The sixth coworker, who was not infected, was not present in the office for the two days before symptom onset of the primary case. This transmission event happened in November and December 2020 when mitigation measures were in place, including social distancing, acrylic panels between desks, hand hygiene, and use of a face covering except when seated at a desk. The office was not well ventilated (no air conditioning and windows were closed), which could have promoted long distance airborne transmission. On the basis of the investigation, however, close contact, fomite transmission, and transmission from outside the event cannot be ruled out, so it is unclear as to whether long distance airborne transmission was the most likely

Jiang et al⁴⁵ (rated as low methodological quality) reported on an outbreak linked to a department store that occurred in January 2020 in Tianjin, China, involving 24 cases (six staff and 18 customers). Airborne transmission was considered as the most likely route of transmission between a primary case and 12 secondary cases, which might have been promoted by a lack of air replacement (doors were closed) and high density of people in the store. As genomic sequencing of SARS-CoV-2 was not performed, however, transmission from outside this event cannot be ruled out and, based on symptom onset dates, it is possible that several primary cases were present. On the basis of this investigation, it is unclear whether long distance airborne transmission had occurred in the store.

Singing events

In addition to transmission events associated with specific settings, four epidemiological investigations reporting on outbreaks linked to singing events were identified.

Katelaris et al⁴⁶ (rated as high methodological quality) reported on an outbreak in Sydney, Australia, linked to a series of four church services held between 15 and 17 July 2020. The probable primary case, a choir member, had sung at each of these one hour services, and 12 secondary cases were identified (2.4% secondary attack rate across the four services), who had sat in the same section of the church, between 1 m and 15 m from the primary case. Viral genomic sequencing of the primary case and 10 secondary cases showed a single genomic cluster, suggesting that transmission had occurred during the church services.

The second epidemiological investigation⁴⁷ (rated as medium methodological quality; preprint) reported on five singing events held between September and October 2020 in the Netherlands. At the time, national recommendations were in place to reduce covid-19 transmission, and although singing in groups was allowed, physical distancing (>1.5 m) and ventilation were recommended. Each singing event had between nine and 21 attendees, and attack rates of between 53% and 74% were observed. Fomite transmission was deemed unlikely in all but one event, but close contact transmission was considered possible for some of the secondary cases in three of the five events. However, owing to the high secondary attack rates, it is possible that at least some of the secondary cases had been infected via long distance airborne transmission and, even though ventilation through open doors or windows was reported for all events, air exchange rates were likely to have been low in at least three of the five events

The two other outbreaks occurred in March 2020 that is, during the early stage of the pandemic when no mitigation measures were in place. One of them (70% attack rate, including probable cases) happened in France during a two hour choral rehearsal in a narrow, indoor, non-ventilated space⁴⁸ (study rated as low methodological quality). The second outbreak (87% secondary attack rate, including probable cases) after a 2.5 hour choral rehearsal on 10 March 2020 in Washington (USA) was initially reported by Hamner et al¹ (rated as low methodological quality) and further discussed by Miller et al.⁵² For both outbreaks, close contact and fomite transmission were only assessed through interviews and cannot be fully ruled out. The high secondary attack rate, however, suggests that long distance airborne transmission might have occurred for at least some of the cases.

The results from the four studies suggest that long distance airborne transmission was likely to have occurred for at least some of the transmission events, and that singing may have increased the amount of aerosol generated by the primary cases, which is consistent with modelling results reported by some of these authors.^{52 53}

Summary and critical analysis of results

Seven of the outbreaks identified 13436-384548 occurred in the early stage of the pandemic (January-March 2020) when knowledge of covid-19 was limited, especially the incubation period and the extent of asymptomatic or presymptomatic transmission. As a result, most of these studies only conducted symptomatic testing and considered potential secondary cases to be participants with symptom onset soon after the potential exposure event, including the next day. In addition, for the studies conducted in January 2020 in China and in March 2020 in Europe or the US, it is possible that community transmission was higher than perceived at the time.

Therefore, in an outbreak such as the one reported by Luo et al³⁷ where no genomic sequencing was conducted and three of the nine secondary cases developed symptoms or tested positive for SARS-CoV-2 one or two days after exposure, it is plausible that more than one primary case was present and that transmission occurred through means other than long distance airborne transmission. In two of the studies reporting on singing events,1 48 genomic sequencing and asymptomatic testing were not carried out and some of the secondary cases developed symptoms in the days after exposure but because of the high attack rates reported for these outbreaks, it is possible that long distance airborne transmission had happened for at least some of the transmission events. Long distance airborne transmission was also considered possible for two other early studies as a result of detailed epidemiological investigations.^{34 36} However, the plausibility of long distance airborne transmission for the outbreak in the department store was unclear as other transmission routes could not be ruled out. 45

Among the other studies, four^{33 35 41 46} provided convincing evidence for long distance airborne transmission as a result of detailed epidemiological investigations combined with genomic sequencing. Eichler et al³² also conducted genomic sequencing but their reporting of the epidemiological investigation was not sufficiently exhaustive to exclude other transmission routes (close contact or fomite) for the only secondary cases who could have been infected by long distance airborne transmission. The investigations by Shah et al,⁴⁷ Hwang et al,³⁹ Groves et al,⁴² Han et al,40 and Vernez et al43 suggested that long distance airborne transmission was possible for at least some of the transmission events (close contact or fomite could not be fully ruled out), but stronger conclusions could not be drawn owing to methodological limitations (including the absence of genomic sequencing and risk of selection bias). Finally, the likelihood of long distance airborne transmission was unclear in the outbreak in the office reported by Sarti et al⁴⁴ despite the covid-19 measures in place, close contact and fomite transmission could not be completely ruled out on the basis of the investigation.

Eleven of the 18 studies reported on the use of face coverings.³³ ³⁵⁻⁴⁴ Overall, the information provided was limited, and two of these studies only mentioned that face coverings were compulsory in the settings of interest (quarantine hotel³³ and food processing factory⁴¹) without reporting on adherence or behaviour (eg, whether workers wore face coverings correctly for the duration of their shift). Based on this limited information, we found no evidence of long distance airborne transmission where participants were known to have worn face coverings for the duration of exposure.

Only one of the outbreaks³³ identified occurred at a time when covid-19 vaccines were available, although in this outbreak the primary and secondary cases were not vaccinated.

Grading of the evidence

Table 3 provides the grading of the evidence for each of the primary outcomes: SARS-CoV-2 infection via

airborne transmission at a distance >2 m, insufficient air replacement (modifying factor), directional air flow (modifying factor), and increased aerosol emission when singing, speaking loudly, or doing intense physical work (modifying factor). Assessment of modifying factors was considered not applicable for the two outbreaks where the likelihood of long distance airborne transmission had been judged as unclear.

For all four outcomes, the evidence was judged as having methodological limitations owing to study design and to be at serious risk of imprecision owing to small numbers of participants as well as some risk of bias in exposure or outcome assessment, or both, However, the risks of inconsistency and indirectness were judged as not serious as the results were consistent across studies conducted in a range of settings and with different populations and provide evidence of direct relevance to the public health question of interest. The risk of publication bias was judged to be serious for the outcome of SARS-CoV-2 infection through airborne transmission at a distance >2 m and for the modifying factor of activities associated with increased emission of aerosols, but not serious for the modifying factors of insufficient air replacement and directional air flow. As a result, the certainty of evidence was judged as very low for all outcomes.

Because of high heterogeneity between studies, the additional outcomes of time spent in the transmission setting and distance over which airborne transmission was thought to have occurred could not be summarised or graded using the GRADE framework. Exposure timings ranged from five minutes to three hours, and distances were up to 15 m.

Discussion

Evidence from the outbreak investigations discussed in this review suggests that airborne transmission of SARS-CoV-2 from an infectious individual to others located >2 m away can occur in different indoor nonhealthcare settings. The results of this review show that when long distance transmission occurred, one or more factors were thought to have contributed. Modifying factors such as insufficient air replacement and singing are likely to result in an increased concentration of infectious respiratory particles within the indoor space, whereas factors such as directional air flow are likely to allow viable virus to travel further in a certain direction, which could potentially infect someone downstream of a primary case. The results of this review therefore confirm the importance of the role of ventilation to mitigate the risk of long distance aerosol transmission.⁵⁴⁻⁵⁷

A total of eight events (from four studies) in which singing may have contributed to long distance airborne transmission were identified. These results are in line with experimental and modelling studies that have reported on singing and aerosol generation, suggesting that more virus-containing respiratory particles tend to be emitted when singing compared with speaking or breathing. More generally, the quantity of respiratory particles emitted increases with

loudness of vocalisation, ⁵⁹ 60 which was thought to have contributed to long distance aerosol transmission in a fitness facility. ⁴²

In 13 out of 18 studies identified, ^{33-37 41-48} suspected primary cases were asymptomatic, presymptomatic, or near the time of symptom onset when transmission occurred. This finding is consistent with wider evidence that people with asymptomatic or presymptomatic SARS-CoV-2 infection can contribute to the community spread of covid-19, ⁶¹⁻⁶³ including from long distance airborne transmission.

Although the evidence on face coverings was limited, no outbreaks in which participants had been wearing face coverings for the duration of the exposure were identified. Evidence suggests that face coverings can reduce the number of respiratory particles emitted from the nose and mouth.⁶⁴ However, it is not possible to deduce from the evidence assessed in this review if wearing a face covering can prevent or reduce the risk of long distance transmission of SARS-CoV-2.

Most of the outbreaks we identified occurred at a time when population immunity was limited, either naturally acquired or vaccine mediated. This limits the applicability of our findings to the current context, although there is evidence that transmission of SARS-CoV-2 after vaccination does occur.⁶⁵ While the lack of evidence identified in vaccinated populations may to some extent reflect the successes of vaccine rollout, there may also be a time lag in publication of outbreak reports since vaccine programmes were initiated. There may also be less interest in publishing reports on SARS-CoV-2 associated outbreaks over time.

The evidence from our rapid systematic review was deemed to be of very low certainty based on 18 studies. The relatively small number of studies identified could suggest that outbreaks related to long distance airborne transmission are rare, although also likely to result from difficulties in identifying such events or to underreporting-for example, in countries without sufficient contact tracing. It can also be partly explained by the level of detail needed to assess transmission routes. Indeed, even outbreak investigations that follow reporting guidelines such as the Outbreak Reports and Intervention studies Of Nosocomial infection (ORION) statement published by the Canada Communicable Disease Report⁶⁶ are not necessarily thorough enough to be able to fully rule out other transmission routes. As a result, several outbreaks in which long distance airborne transmission may have happened were excluded on full text, including a few reports on clusters in aeroplanes that did not properly consider transmission routes during boarding and disembarking.67-70 Finally, the wider challenges of the pandemic should be acknowledged, including the limited resources in public health teams to conduct detailed epidemiological investigations.

The outcomes were rated as being of very low certainty using the GRADE framework, although this reflects the principles of GRADE rather than a lack of quality of the included studies because in traditional evidence hierarchies, outbreak investigations are

Table 3 Summary of findings using Grading of Recommendations, Assessment, Development, and Evaluation approach						
Outcome	Effect	No of studies	Certainty in the evidence			
SARS-CoV-2 infection through airborne transmission over a distance >2 m	Sixteen studies suggested that long distance airborne transmission was the main transmission route for at least some of the transmission events in the reported outbreaks. Unclear in two studies	18	Very low owing to methodological limitations of the studies and serious risk of imprecision and publication bias			
Modifying factor: insufficient air replacement	Fourteen studies suggested that insufficient air replacement had increased the likelihood of long distance airborne transmission. Unclear in two studies	16	Very low owing to methodological limitations of the studies and serious risk of imprecision			
Modifying factor: directional air flow	Eleven studies suggested that directional air flow might have increased the likelihood of long distance airborne transmission. Unclear in one study	12	Very low owing to methodological limitations of the studies and serious risk of imprecision			
Modifying factor: activities associated with increased emission of aerosols	Five studies (reporting on nine events) suggested that singing and speaking loudly might have increased the likelihood of long distance airborne transmission. Unclear in one study (intense physical work)	6	Very low owing to methodological limitations of the studies and serious risk of imprecision and publication bias			

classed as a low level of evidence. However, some of the included studies were well conducted investigations of covid-19 outbreaks and their contribution to this particular research question should not be underestimated—they provide critical insight where other types of study are just not feasible. The GRADE framework was developed to inform clinical practice where randomised controlled trials are feasible, and linear causal pathways are more often the norm. Public health research does not always fit easily within this framework and the question of what level of public health evidence is sufficient to support decision making for a novel infection warrants further consideration.

Comparison with other studies

These findings are an important addition to the wider body of evidence that supports the biological plausibility of airborne transmission as a potentially important route of transmission in certain scenarios. The wider evidence includes experimental evidence from animal studies⁷² as well as experimental studies that have shown that SARS-CoV-2 can remain viable in artificially generated aerosols for up to 16 hours, and that the stability and viability depends on environmental factors such as temperature, humidity, and exposure to sunlight.²² Similarly, biological monitoring studies have shown that SARS-CoV-2 RNA can be detected in exhaled breath and environmental air samples, but the evidence on viable virus remains limited to a few studies that mostly detected infectious virus in air samples collected at <2 m from the infectious individual.²²⁻²⁴ These experimental and biological studies provide evidence that SARS-CoV-2 can be viable in aerosols and therefore support the epidemiological evidence from this rapid review, and from others^{22 23} that suggest that airborne transmission can happen in some settings.

Strengths and limitations of this review

This rapid systematic review critically assessed the likelihood of long distance airborne transmission of SARS-CoV-2 using only direct real world evidence from observational studies from indoor non-healthcare settings. The application of inclusion criteria that focused the critical appraisal on those studies, which involved comprehensive investigations, is a key

strength of our approach: some of these studies not only included epidemiological data, but also genomic analysis, video surveillance, analysis of seating arrangements, and environmental hypothesis testing.

The main limitation of selecting studies of only real world human-to-human transmission events is that scenarios where transmission has not occurred were not included, and likewise where transmission events have not been detected by contact tracing systems. which could be seen as a form of publication bias. All the evidence is from retrospective epidemiological investigations of outbreaks and therefore this review cannot make inferences on the extent to which long distance airborne transmission occurs or the contribution it may have on community rates of transmission: these remain critical questions for policy and practice. In addition, most of the outbreaks occurred before vaccine rollouts and it is unclear how these results apply to populations with a high level of immunity to infection. Finally, and as with all reviews assessing evidence related to covid-19, this rapid review is limited by the fact that the evidence assessed is from an emerging specialty.

Future work and policy implications

Well conducted outbreak investigations continue to be needed to assess the potential for long distance airborne transmission in vaccinated populations, and with more transmissible SARS-CoV-2 variants such as omicron. To assess transmission routes, such outbreak investigations should deploy robust and mixed methods, ranging from genomic analysis to environmental assessment, and they should be conducted as early as possible to reduce recall bias.

The results from this rapid systematic review highlight the need to ensure measures to mitigate SARS-CoV-2 long distance transmission in indoor settings, especially in poorly ventilated spaces. Identification of poorly ventilated public spaces should be undertaken and improvements made. Other factors such as directional air flow or singing that could increase the risk for long distance airborne transmission should also be considered in risk mitigation.

A need also exists to develop a new framework, or to adapt the existing GRADE framework, to support a pragmatic and consistent approach to the collation, interpretation, and synthesis of epidemiological investigations, especially when other types of studies are not feasible. The question of what level of public health evidence is sufficient to support decision making for a novel infection warrants further consideration.

Conclusion

This rapid review found evidence suggesting that long distance (>2 m) airborne transmission of SARS-CoV-2 might happen in indoor non-healthcare settings, and that it can occur from people who are asymptomatic or presymptomatic. All transmission events identified occurred alongside factors believed to have contributed to this type of transmission, including lack of air replacement (absence or little ventilation with fresh air), directional air flow (mainly through air circulation systems), and activities such as singing that increased aerosol emission. In the review, we found no evidence of long distance airborne transmission occurring without one or more of these factors present.

Based on the results from this review, indoor non-healthcare settings that might be at risk of long distance airborne transmission include hospitality settings such as restaurants, public transport, and workplaces with inadequate ventilation, as well as settings where activities resulting in increased aerosol emission, such as singing or speaking loudly are carried out.

These results highlight the importance of assessing ventilation, especially in indoor spaces where people meet others from outside their household. Particular attention should be given to ventilation in settings with activities that might increase the number of respiratory particles, for example, singing. Where ventilation is assessed to be inadequate, improvements should be made.

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The manuscript's guarantor (RC) affirms that the manuscript is an honest, accurate, and transparent account of the study being

reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Dissemination to participants and related patient and public communities: This paper will be shared widely within the UK Health Security Agency and used to inform relevant guidance. It will also be shared with relevant stakeholders, policy makers, and other public health agencies within the United Kingdom and internationally. Further dissemination will include our website https://ukhsalibrary.koha-ptfs.co.uk/covid19rapidreviews/ and through colleagues working in covid-19 evidence synthesis.

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Supplementary information: supplementary material 1: search strategy, quality criteria checklist, and list of excluded studies

Supplementary information: supplementary material 2: data extraction of included studies