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Review Article

# Effectiveness of filtering or decontaminating air to reduce or prevent respiratory infections: A systematic review

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ABSTRACT

Installation of technologies to remove or deactivate respiratory pathogens from indoor air is a plausible non-pharmaceutical infectious disease control strategy.

*Objective:* We undertook a systematic review of worldwide observational and experimental studies, published 1970–2022, to synthesise evidence about the effectiveness of suitable indoor air treatment technologies to prevent respiratory or gastrointestinal infections.

*Methods:* We searched for data about infection and symptom outcomes for persons who spent minimum 20 h/week in shared indoor spaces subjected to air treatment strategies hypothesised to change risk of respiratory or gastrointestinal infections or symptoms.

*Results:* Pooled data from 32 included studies suggested no net benefits of air treatment technologies for symptom severity or symptom presence, in absence of confirmed infection. Infection incidence was lower in three cohort studies for persons exposed to high efficiency particulate air filtration (RR 0.4, 95%CI 0.28–0.58, $p < 0.001$) and in one cohort study that combined ionisers with electrostatic nano filtration (RR 0.08, 95%CI 0.01–0.60, $p = 0.01$); other types of air treatment technologies and air treatment in other study designs were not strongly linked to fewer infections. The infection outcome data exhibited strong publication bias.

*Conclusions:* Although environmental and surface samples are reduced after air treatment by several air treatment strategies, especially germicidal lights and high efficiency particulate air filtration, robust evidence has yet to emerge that these technologies are effective at reducing respiratory or gastrointestinal infections in real world settings. Data from several randomised trials have yet to report and will be welcome to the evidence base.

## 1. Introduction

Some air treatment technologies (ATT) may prevent transmission of respiratory infections, while being safe to operate when people are present doing routine activities. For example, high efficiency particulate air (HEPA) filtration can remove microbes from air. The HEPA standard is to remove at least 99.97% of aerosols 0.3 μm (μm) in diameter (US Department of Energy, 2005). Alternatively, rather than remove microbes, an ATT might render microbes incapable of biological replication, and as such, incapable of causing infection. Germicidal ultraviolet light (GUVL) in bandwidths both safe for chronic human exposure and able to deactivate viruses, has been proposed as such a way to decontaminate air while people are present (Narita et al., 2020).

During the Covid-19 pandemic, ATT were promoted as a practical mitigation measure in environments where social distancing was difficult to maintain. Governments considered deploying ATT especially in schools (Camfil, 2021; Ulmair, 2021; Zimmer, 2021). These aspirations were hindered by the large cost involved and uncertainty about exactly which devices might be truly effective (Brandon, 2020; Akpan and Jeffrey-Wilensky, 2021; Wightwick, 2021). Some cluster randomised

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controlled trials to provide possible supporting evidence were subsequently initiated, using either HEPA or GUVL, in schools (ISRCTN46750688; NCT05016271) or long-term residential care homes (ACTRN12621000567820; NCT05084898; ISRCTN63437172). These trial results are not yet available.

Any proposed novel technology or treatment, such as vaccination or a new drug, must go through many stages of development, including rigorous safety testing and real-world experiments, before effectiveness is established and large population treatment is justified. Technologies that may purify/treat air are rapidly evolving and are concurrently at all stages of development. Using evidence published from 1970 to late 2022, we undertook a systematic review about the effectiveness of ATT in real world settings, examining respiratory and/or gastrointestinal infection outcomes in humans following exposure. We consider a broad range of potential technologies and both observational study designs (cohort or case control) as well as experimental trials. We consider ATT that are either portable devices or permanent installations.

## 2. Methods

We sought studies published in 1970 or later, using Google Scholar, OVID MEDLINE, Scopus, medRxiv, bioRxiv, preprints.org. Grey literature published by December 2022 was also searched; trial registries (NCT, ISRCTN and ACTRN) were searched in June 2022. Details of the search terms and parameters are in the Appendix. Eligible studies could be written in any language in which we had literacy (English, Spanish, Greek, French, Italian) or that we could fully translate into English using Google Translate.

Study design had to be controlled experiments, case-control or cohort studies with concurrent comparison groups. Pre-post comparisons were excluded because changes in other conditions are difficult to control (Thiese, 2014).

Study titles and abstracts were screened independently by two authors to decide which ones to take to full text review. A third researcher was consulted if disagreements could not be resolved by discussion. Full texts of studies not excluded from title/abstract screening were obtained where possible and reviewed for eligibility. A protocol was registered in association with this review (Prospero CRD42020208109); however, we had substantial protocol deviations due to resource constraints and improved understanding of the relevant literature. Further details on study selection are included in the Appendix.

### 2.1. Risk of bias (quality) assessment

Quality assessment approach depended on study design. Trials were assessed for risk of bias using the Cochrane risk of bias tool 1.0 (Higgins and Altman, 2008), with an additional domain for adherence (low risk of bias if reported to be $\geq$64%). One point was awarded for each domain with low risk of bias, and trials with least risk of bias were deemed to be those studies with scores $\geq$6. The quality checklist used for observational studies (cohort or case-control design) was based on the Newcastle Ottawa Scale (NOS; Wells et al., 2000) with a modification that the comparability domain was a single checklist item, whether the groups were balanced at baseline for age and sex. Synthesis using only studies with low risk of bias was also undertaken.

### 2.2. Outcomes

Eligible outcomes related to incidence of respiratory/gastrointestinal infection or compatible symptomatic illness in humans. Included studies had to report, at a minimum, the mean effect value for exposed/control cohorts; studies that collected relevant data but did not report raw outcome data or change from baseline, or that only reported between group differences after adjusting (in their own models) for possible confounders were ineligible. Ethics approval was not required to collect and process these anonymised data because they were already published.

Preferred outcome was incidence (dichotomous yes/no) of respiratory/gastrointestinal infection by a specific pathogen (such as influenza or norovirus) confirmed by a laboratory method. If laboratory-confirmed infection data were unavailable, we accepted respiratory symptoms such as: cough, acute breathing difficulty, anosmia, rhinitis, nasal congestion, scores for combined respiratory disease symptoms. Eligible gastrointestinal symptoms were nausea, abdominal cramping, vomiting, or diarrhoea that could not be attributed to non-infectious cause. Symptoms could be expressed as dichotomous or continuous (severity) data. Further descriptions of outcomes are in the Appendix.

### 2.3. Intervention(s), exposure(s)

ATT were eligible that treated indoor breathing air while humans were present doing routine activities (such as sleeping, working, eating, studying). Some chemical or radiation methods for removing pathogens could potentially cause harm to building occupants. These impacts include irritation to human eyes or skin (linked to some wavelengths of ultraviolet light; Reed, 2010) or lungs (by generating ozone; Nogrady and Furnass, 1983). In this review we focussed on ATT that could most facilitate usual patterns of human contact. Therefore, treatment methods that for safety reasons required humans to vacate the space during operation of the technology, chemical application to surfaces and/or air, and/or technology that required special protective equipment for humans to remain present, were ineligible.

Eligible technology could be radiation, chemical, or mechanical systems that aimed to safely purify the air freely circulating in the indoor environment without simply ventilating (putting old indoor out & bringing new air in). Exemplar technologies and treatment methods are HEPA filters, ionisers, GUVL in safe bandwidths for recurring exposure (Narita et al., 2020), and some types of chemical treatment. Studies that describe disinfection systems that move air to a private space where it may be exposed to chemicals/radiation/physical filter were eligible as long as these systems could operate while persons were present in the environment receiving the disinfected air *AND* the populated spaces that received the disinfected air normally received it within two hours of treatment. Two hours was not meant to be a definitive threshold, but rather a maximum reasonable period that still enabled the air processing to be relatively quick.

In absence of contrary information, we assumed that any air conditioning system was likely to include some amount of air filtration as part of routine operation, although we could not know how filtered the air was if not explicitly stated.

### 2.4. Settings

The technology must have operated in a non-laboratory setting and must have been designed to potentially be applied to an air space shared by five or more persons. This stipulation about size of population exposed was applied because we wanted to exclude cases of specialist negative pressure rooms, small spaces under laminar flow tents, or other resource-intensive, typically clinical/laboratory environments that are typically intended to create very sterile conditions for a single patient or experimental participant. Outcomes had to be in people. Virions or other pathogens in air had to be removed directly from the air, not observed to be reduced after pathogen removal from surfaces or from standing water in the shared environment. Incidence of microbes on surfaces or in air samples were ineligible outcomes. The setting could be anywhere in the world.

We excluded observational studies about workers in a small number ($\langle$12) of different buildings, in the context of 'sick building syndrome.' Often these studies considered correlation between respiratory symptoms and presence of air conditioner filters, which were theorised to be clogged with harmful dust or pathogens, and otherwise hindering ventilation. However, other factors that affect air quality, both

unobserved and observed, were reported to be highly heterogenous, such as concentration of volatile organic compounds, temperature, humidity, density of staff, types of office equipment and ventilation rates. Our own study was not designed to adequately address this diversity of confounding in clustered cohort studies.

### 2.5. Intervention: minimum exposure

Most members of the intervention group had to be present in the setting where air was disinfected for a mean duration of at least 20 h a week during the monitoring period (about 12.5% of a person's lived hours per week). The persons could be present for any reason (such as residence, education, work, receiving inpatient treatment, etc).

### 2.6. Comparator(s)/control

The comparator group had to simultaneously experience usual ventilation regimes in same or similar settings, so exposed to systems that manage air flow but did not attempt to disinfect air or remove microbes from the air. Simple mechanical ventilation (i.e., expelling indoor air and replacing it with outdoor air) was the ideal comparator.

### 2.7. Synthesis

We summarise the data narratively and quantitatively. All trials (randomised or not) are grouped for synthesis; all observational study designs are grouped. Where suitable data were supplied (participant count in each exposure group, event count or mean effect and standard deviation/error for ratio outcomes) in at least 2 studies of the same design assessing a specific type of air treatment method and outcome, we carried out random-effects meta-analysis with Review Manager version 5 (RevMan, 2014). Studies with results that were too incompletely described to synthesise with other evidence are described narratively.

The diversity of reported respiratory symptoms meant that pooled analysis was often only possible by grouping similar measures. To enable synthesis, outcomes were grouped by: laboratory or clinical diagnosis of infection; symptomatic status (dichotomous data); symptom severity (continuous data). The direction of scales in synthesis forest plots was standardised so that a lower value signified less illness/fewer symptoms. Where one study reported multiple eligible outcomes, we did not count the same participants twice in synthesis. We extracted both continuous and dichotomous outcome from the eligible studies. Further description of the synthesis methods are included in the Appendix. Subgroup

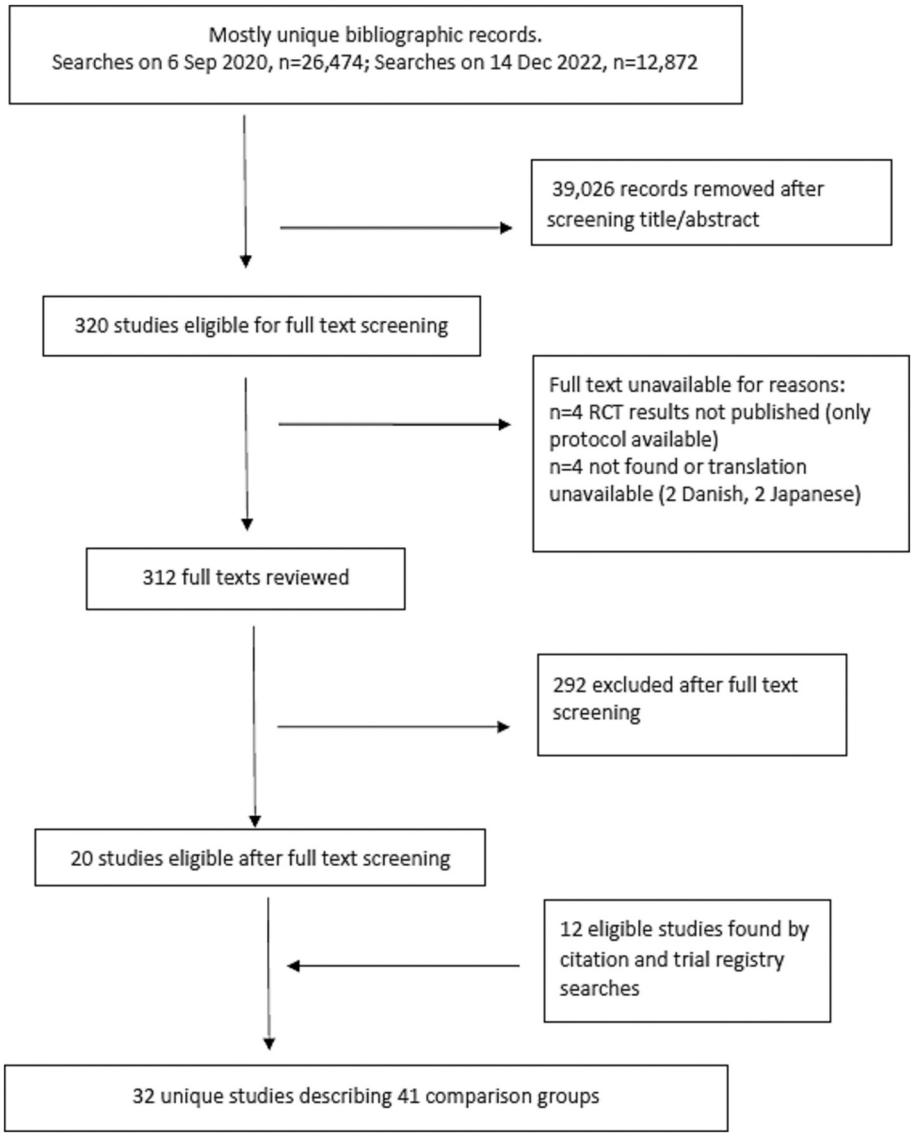


**Fig. 1.** Selection procedure for eligible studies.

synthesis using only studies with low risk of bias was also undertaken.

## 3. Results

Study selection is in Fig. 1. From 39,346 initial bibliographic and grey literature hits, we found 32 eligible studies within which 41 outcomes were compared between groups. All included studies were either trials or cohort design (no case-control studies). All outcomes related to respiratory infections or symptoms, except for one study in care homes, which looked for norovirus outbreaks related to air conditioning status. Studies are described in Table 1 by type of outcome, technology, and study design (which is how they were grouped in synthesis). Median year of publication was 2008, with seven studies published after 2013 (in most recent ten years). Six studies were about research undertaken after 2013. Eleven studies took place in the USA, 9 in Europe, 12 elsewhere (Canada, Singapore, China, South Korea, Hong Kong, Israel, Australia). Exposure settings were private homes ($n = 16$), offices ($n = 6$), clinical ($n = 5$), childcare providers or schools ($n = 3$) and shared residences (care homes or military barracks, $n = 2$). Technologies were HEPA standard air filtration ($n = 14$), filters as part of air conditioning (not specified as HEPA standard, $n = 8$), GUVL (n = 3), Ionisers ($n = 4$), laminar air flow filter and air flow system with or without HEPA standard (n = 2), electrostatic cleaner (n = 2) and chemical (mugwort leaf smoke, n = 1); sometimes multiple ATT were applied simultaneously. One article was in Chinese; all other articles were written in English. Study designs were controlled trials ($n = 25$) and cohort ($n = 7$). 26 studies provided data suitable for pooling (with participant counts, unadjusted mean effect size, variance indicator such as standard error or

**Table 1**
Included studies, technologies, outcomes and participant counts.

| Umbrella outcome | Technology | Design | Primary results article | Setting | Specific outcome | #pts |
|---|---|---|---|---|---|---|
| Respiratory infections | HEPA | Trial | Walker et al. (2022) | Private residence | Lower RTI | 307 |
| | | Cohorts | Oren et al. (2001) | Hospital wards | Invasive pulmonary aspergillosis | 71 |
| | | | Salam et al. (2010) | Hospital wards | *Aspergillus* sp. from histology | 18,089 |
| | | | Vokurka et al. (2014) | Hospital rooms | Pneumonia | 289 |
| | GUVL | Trial | Li and Jiang (2011) | Hospital wards | Influenza | 104 |
| | | | | | Upper RTI | 104 |
| | Ioniser + electrostatic nano filtration | Cohort | Fernandez-Gerlinger et al. (2016) | Hospital rooms | Invasive aspergillosis | 156 |
| | Air conditioning | Cohorts | Zuraimi et al. (2007) | Preschool/ nursery | Pneumonia, bronchitis | 3752 |
| | | | White et al. (2011) | Military barracks | Febrile acute RTI | 12,220 |
| | | | | | Afrebrile acute RTI | 12,220 |
| | Mugwort leaf smoke | Trial | Li and Jiang (2011) | Hospital wards | Influenza | 111 |
| | | | | Hospital wards | Upper RTI | 111 |
| Norovirus | Air conditioning | Cohort | Lin et al. (2011) | Care homes | Norovirus outbreaks | 748 |
| Respiratory symptoms (event counts) | HEPA | Trials | Hedge et al. (1993) | Office building | Respiratory symptoms | 112 |
| | | | Lanphear et al. (2011) | Private residence | Asthma symptoms | 225 |
| | | | Jhun et al. (2017) | Schools | Asthma-like symptoms | 25 |
| | GUVL | Trials | Menzies et al. (1999) | Office buildings | Cough or difficulty breathing | 399 |
| | | | Menzies et al. (2003) | Office buildings | Respiratory symptoms | 1542 |
| | Air conditioning | Cohorts | Preziosi et al. (2004) | Office buildings | Otorhinolaryngologist attendance | 920 |
| | | | Zuraimi et al. (2007) | Preschool/ nursery | Coughs with cold/flu | 3752 |
| Respiratory symptoms (continuous outcomes) | HEPA | Trials | Villaveces et al. (1977) | Private residence | Change in asthma, rhinitis | 13 |
| | | | Antonicelli et al. (1991) | Private residence | Symptom score | 18 |
| | | | Warburton et al. (1994) | Private residence | Cough scores | 24 |
| | | | Thiam et al. (1999) | Private residence | Symptom scores | 18 |
| | | | Butz et al. (2011) | Private residence | Change in symptom free days | 77 |
| | | | | | Change in symptom free nights | 77 |
| | | | Park et al. (2017) | Private residence | Allergic rhinitis | 17 |
| | | | Li et al. (2020) | Private residence | Allergy induced nasal symptoms | 90 |
| | | | Park et al. (2020) | Private residence | Symptom score | 44 |
| | | | Phipatanakul et al. (2021) | Schools | Frequency days with asthma | 202 |
| | HEPA + Charcoal filter | Trial | Hansel et al. (2022) | Private residence | Breathlessness, coughing, sputum scale | 94 |
| | GUVL + filters | Trial | Bernstein et al. (2006) | Private residence | Average #days with cough | 38 |
| | Filtered & cooled air | Trial | Boyle et al. (2012) | Private residence | Symptom domain quality of life scale | 282 |
| | Electrostatic cleaner | Trial | Skulberg et al. (2005) | Offices | Dry/irritated throat symptom | 72 |
| | Ionisers | Trials | Nogrady and Furnass (1983) | Private residence | Symptom score | 19 |
| | | | Daniell et al. (1991) | Office building | Average symptom count | 54 |
| | | | Warner et al. (1993) | Private residence | Night time cough severity | 28 |
| | | | Johnsen et al. (1997) | Private residence | Symptom grade | 30 |

Notes: RTI = respiratory tract infection, #pts. = count of participants monitored. **Cyan font** = all participants were asthmatic or living with chronic allergies.

deviation on effect size).

### 3.1. Quality assessment

Outcomes were grouped as shown in Table 1. Risk of bias assessment is in Table 2 (trials) and Table 3 (cohort studies). Figs. 2a-2c show funnel plots for the meta-analyses in Figs. 3–5. Fig. 2a (pertaining to data shown in Fig. 3) suggests strong publication bias (from visually imbalanced distribution of effect sizes; Malički and Marušić, 2014) for infection outcomes, but publication bias is not obvious for symptomatic outcomes (funnel plots 2b and 2c, pertaining to data used to construct syntheses in Figs. 4–5).

### 3.2. Synthesis and outcomes

Fig. 3 shows pooled risk ratios for infections as outcomes, with subgroups by umbrella outcome, study design (trial or cohort) and technology. Treatment groups tended to have fewer infections. This finding was more consistent for observational studies, especially HEPA cohorts. Confidence in the HEPA cohort comparisons can be boosted because of their low heterogeneity ($I^2 = 0\%$); in contrast to the high heterogeneity (95%) in the air conditioning cohort comparison for respiratory infections. Ionisers with electrostatic technology also appeared to have a strong protective effect, however this finding is from only one moderate size study for a specific group (care home residents, unbalanced for sex/age at baseline). No trials had effects that were in favour of ATT to reduce infection at $p < 0.05$. There is strong evidence of publication bias (Fig. 2a). The only gastrointestinal study was for norovirus outbreaks. Comparison 3.1.7 found fewer norovirus outbreaks in care homes with air conditioning; however, this result may be interpreted with caution given that only a small percentage of participants lived without air conditioning.

Fig. 4 shows pooled data for dichotomous respiratory symptom outcomes. There was no overall trend towards favouring controls or treatment. Heterogeneity was especially high ($I^2 = 88\%$) for air conditioning treatment method, similar to the high heterogeneity for air conditioning treatment in Fig. 3.

Fig. 5 shows respiratory symptomatic severity outcomes, where higher scores are worse outcomes for patients, using standardised mean differences (SMD). Between group effects could not be estimated for some studies because variance data were unavailable in Skulberg et al. (2005), Villaveces et al. (1977), Warburton et al. (1994), Johnsen et al. (1997) and Thiam et al. (1999). Most studies did not find statistically significant evidence to support treatment effect in reducing symptom severity. Combined air treatment (such as cooled and filtered, or HEPA with additional charcoal filtration) seemed to perform better than single technology approaches (e.g., just HEPA or ionisers). Filtered (non HEPA) and cooled air had the best results in terms of reducing symptom severity. The mean effect in Boyle et al., 2012 was −0.31 (95%CI -0.56 to −0.06). One study gave especially strong support in favour of HEPA treatment for asthmatics (Park et al., 2017). Evidence was especially heterogenous for ionisers ($I^2 = 83\%$), with the untreated groups tending to have fewer symptoms (pooled SMD 0.40, 95%CI -0.43 to 1.24).

The syntheses shown in Figs. 3–5 were repeated using only studies with relatively lower risk of bias scores (quality score ≥ 6, as reported in Tables 2–3). The forest plots for the lower risk-of-bias studies are in the Appendix. For infection incidence (Fig. S1), pooled data from 2 cohort studies that used HEPA filters (Oren et al., 2001; Salam et al., 2010) were associated with lower incidence at $p = 0.18$ (above our predesignated significance threshold). Air conditioning was not associated with lower infection incidence ($p = 0.29$). Lin et al. (2011) found fewer norovirus infections where air conditioning was used. Neither the control nor the intervention group studies with low risk of bias (Fig. S2) had strong ($p > 0.05$) associations between symptom incidence and HEPA or air conditioning. For symptom severity (Fig. S3), two trials reported significantly ($p < 0.05$) lower severity in the active trial arm. One of these trials tested HEPA (Hansel et al., 2022), the other trial (Boyle et al., 2012) tested filtered and cooled air. Two trials (Park et al., 2020; Phipatanakul et al., 2021) did not find reduced symptom severity for asthma symptoms was associated with HEPA filters ($p = 0.68$). The

**Table 2**
Risk of Bias for controlled trials, Cochane RoB 1.0.

| *Trials* | RSG | Alloc | SelRep | PerfBias | DetBias | Attrn | Adherence | Summary |
|---|---|---|---|---|---|---|---|---|
| Villaveces 1977 | Low | Low | High | Low | Unclear | Unclear | Unclear | 3 |
| Nogrady 1983 | Low | Low | High | Low | Low | Unclear | Low | 5 |
| Antonicelli 1991 | Low | High | High | High | High | High | Unclear | 1 |
| Daniell 1991 | High | Low | High | Low | Low | Low | Low | **5** |
| Hedge 1993 | High | Unclear | High | High | Unclear | Unclear | Low | 1 |
| Warner 1993 | Low | Low | High | Low | Low | Unclear | Unclear | 4 |
| Warburton 1994 | Unclear | Unclear | High | Low | Unclear | Unclear | Unclear | 1 |
| Johnsen 1997 | Low | Low | High | Low | Low | Unclear | Unclear | 4 |
| Menzies 1999 | High | Low | High | Low | High | Unclear | Low | 3 |
| Thiam 1999 | Unclear | High | High | High | High | Unclear | Unclear | 0 |
| Menzies 2003 | High | Low | High | Low | Low | Low | Low | 4 |
| Skulberg 2005 | Low | Low | High | Low | Low | Low | Unclear | 5 |
| Bernstein 2006 | Low | Low | High | Low | Low | Low | Unclear | 5 |
| Li & Jiang 2011 | High | High | High | High | High | Unclear | Low | 1 |
| Butz 2011 | Low | Low | Low | High | Low | Low | High | 5 |
| Lanphear 2011 | Low | Low | Low | Low | Low | Low | High | **6** |
| Boyle 2012 | Low | Low | Low | Low | Low | Low | Unclear | **6** |
| Jhun 2017 | Low | Low | High | Low | High | Low | Unclear | 4 |
| Park 2017 | High | Unclear | High | High | High | Unclear | Unclear | 0 |
| Li & Chen 2020 | Unclear | Unclear | Low | Unclear | Unclear | Unclear | Unclear | 2 |
| Park 2020 | Low | Low | Low | Low | Low | Low | Low | **7** |
| Phipatanakul 2021 | Low | Low | Low | Low | Low | Low | Low | **7** |
| Hansel 2022 | Low | Low | Low | Low | Low | Low | High | **6** |
| Walker 2022 | Low | Unclear | Low | Unclear | Unclear | Low | Low | 4 |

Cochrane RoB key

| | |
|---|---|
| RSG | Random sequence generation |
| Alloc | Allocation concealment |
| SelRep | Selective outcome reporting |
| Perf | Performance bias |
| Det | Detection bias |
| Attrn | Attrition bias |
| Adh | Mean adherence, ≥ or < 64% |

Key, risk of bias: High, Low, Unclear

Note: Green font for total score indicates lowest risk of bias for these studies, as described in text, ≤ 6 for trials.

**Table 3**
Risk of Bias for observational studies, Newcastle Ottawa Scale.

| | Selection | | | | Comparability | Outcome | | Total | Score |
|---|---|---|---|---|---|---|---|---|---|
| *Cohort Studies* | Rep | Sel | Asc | Dem | Comp | Ass | Dur | Foll | |
| Oren 2001 | | | | | | | | | 7 |
| Preziosi 2004 | | | | | | | | | 8 |
| Zuraimi 2007 | | | | | | | | | 7 |
| Salam 2010 | | | | | | | | | 7 |
| Lin 2011 | | | | | | | | | 7 |
| White 2011 | | | | | | | | | 8 |
| Vokurka 2013 | | | | | | | | | 6 |
| Fernandez-Gerlinger 2016 | | | | | | | | | 6 |

*NOS Key:*

| | |
|---|---|
| | ideal answers, (a) answers in NOS |
| | adequate, (b) answers in NOS |
| | not known, information missing |
| | other answers, inadequate |

*NOS fields, bias with respect to ….*

| | |
|---|---|
| Rep | Representativeness (generalisability of) cohort |
| Sel | Controls from same community as exposed |
| Asc | How exposure was verified |
| Dem | Outcome not present or was balanced at baseline |
| Comp | Groups are balanced for age & sex |
| Ass | Assessment of outcome is objective |
| Dur | Duration of monitoring, long enough? |
| Foll | Adequacy of follow up, < 20% loss |

Note: Green font for total score indicates lowest risk of bias for these studies, as described in text, ≤ 7 for cohort studies.

subgroup analysis for studies with lower risk of bias are more encouraging than the all-data analysis, however the subgroup analyses are usually based on findings of only a single study. Benefits for the same outcome using the same technology at a $p < 0.05$ threshold were not found in multiple studies with low risk-of-bias.

### 3.3. Costs and maintenance

Most studies ($n = 28$) made no statement about costs of the technology. Menzies et al. (1999) said that GUVL was a "relatively low cost intervention". Menzies et al. (2003) were more specific, saying that to install GUVL in an office building with 1000 staff would cost circa (USD) $52,000 to install and about $14,000 in annual running costs (electricity and replacement bulbs), resulting in an investment cost of $52 and annual running costs of $14 per employee. With respect to HEPA filtration, Salam et al. (2010; device used in private homes) said that two portable HEPA filtration units cost about $900 each with annual running costs circa $500, while Butz et al. (2011; devices used in hospital rooms) said that likely costs were $200–$400 per installed unit. Authors relied on citation of other documents to address sustainability or maintenance issues related to device, operation, although Jhun et al. (2017) said that the HEPA device filters only needed to be changed once a year, while Park et al. (2017) said that HEPA filters had been changed during the intervention period after 12 weeks.

### 3.4. Adverse effects

Most studies ($n = 18$) did not comment on whether adverse effects were looked for or analysed. Four of the ioniser studies (Nogrady and Furnass, 1983; Daniell et al., 1991; Warner et al., 1993; Johnsen et al., 1997) monitored for potential air contaminants. Nogrady and Furnass (1983) and Warner et al. (1993) both monitored for only ozone, and reported that any ozone generated was below levels that their equipment could detect (thresholds for detection were not stated). These last two studies implied that since the levels were below levels of detection, then the ambient levels must be safe. Johnsen et al. (1997) also only monitored for ozone, finding that detected ozone levels were 0.013 mg/m$^3$ which compared to a concurrent suggested safety standard of 0.2 mg/m$^3$. Daniell et al. (1991) looked for four potential indoor air contaminants, finding that they were all below thresholds of detection, which thresholds were: ozone (< 0.05 ppm), hydrocarbons (< 1 ppm), formaldehyde (< 0.02 ppm) and carbon monoxide (< 2 ppm). Noise was the most common participant complaint, otherwise ($n = 4$). Li et al. (2020) undertook especially systematic data collection for device tolerability, with weekly Likert scale questions about whether the device operation was tolerable. Eye irritation from mugwort smoke was mentioned in Li and Jiang (2011). Five studies looked for other adverse effects (such as headaches) but did not conclude that any were related to the ATT.

## 4. Discussion

A previous systematic review (Hammond et al., 2021) concluded that no existing studies had yet investigated incidence of respiratory infections using portable HEPA filter devices. Our literature search is both updated and applies much wider inclusion search criteria because we included both portable and installed ATT, and a greater variety of ATT. Our review also considered more outcomes: respiratory symptoms (severity scales or incidence) as well as incidence of respiratory infections.

ATT that successfully inactivated SARS-CoV-2 in air samples and on surfaces has been widely described (Rodríguez et al., 2021; Myers et al., 2022; Zhang et al., 2022). Those studies suggest that ATT can be very effective at reducing microbe presence in the environment. However, while those environmental sampling results are promising, our synthesis of symptom and infection outcomes could not confirm that ATT is likely to reduce respiratory or gastrointestinal infections. Where symptoms or infections seemed to most reduce was in association with combined technology, such as ionisers with electrostatic cleaners, or HEPA standard filters with additional charcoal-based filtration.

Controlled swine farms studies found reduced clinical signs of enzootic pneumonia, atrophic rhinitis and other viral indicators among animals subject to air filtration (HEPA or MERV rating 14 / 16) and resident in the facilities at all times (Lau et al., 1996; Dee et al., 2012). A key difference between a livestock farm and human activities is that most humans are not confined to a single indoor space for weeks or months, with large groups of similarly confined co-residents. Exceptions are prisoners and in general, many care home residents. One Portuguese

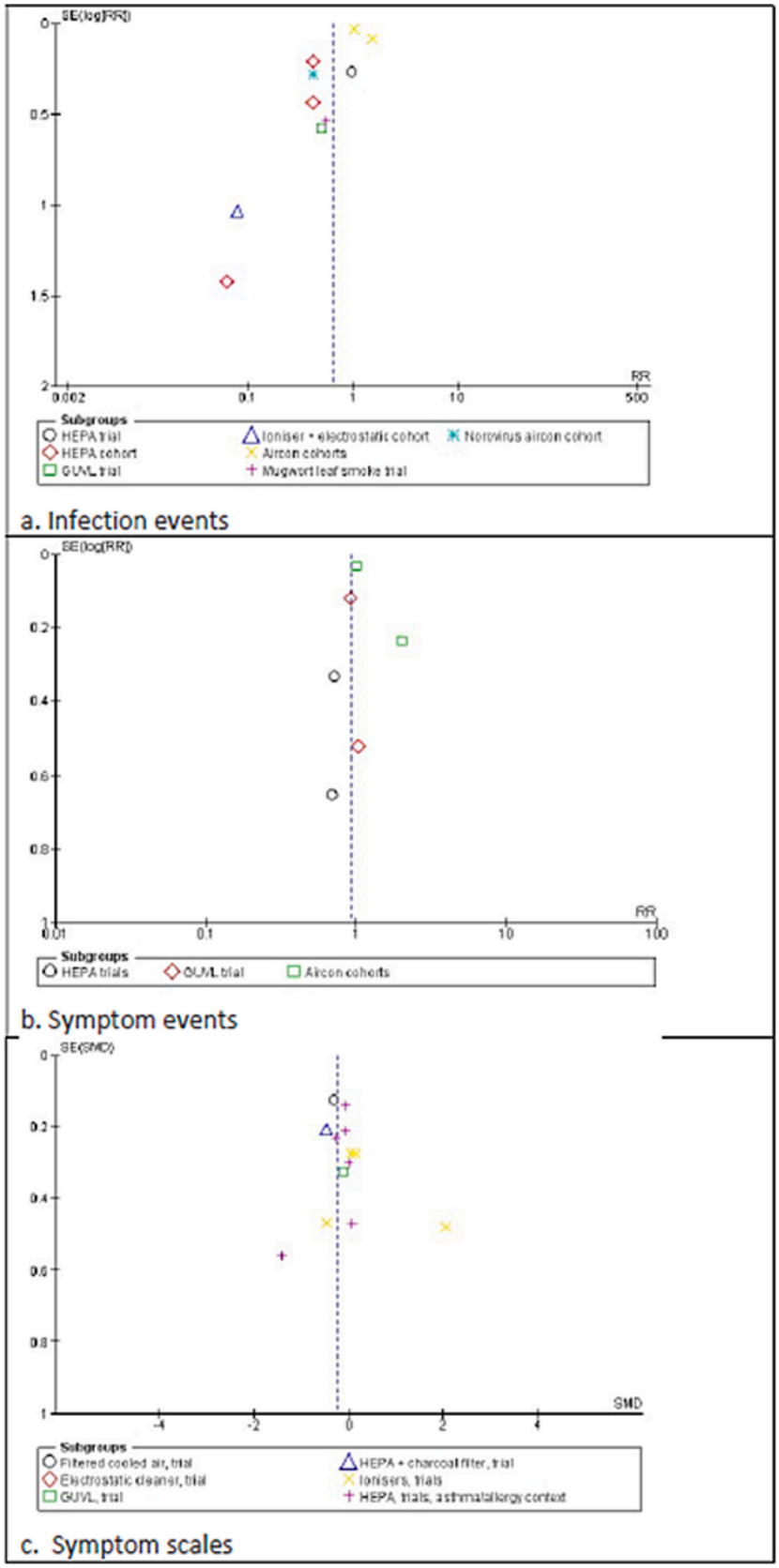


**Fig. 2.** Funnel plots for studies shown with infection events (2a: Fig. 3 data), symptom events (2b: Fig. 4 data) or symptom scales (2c: Fig. 5 data).

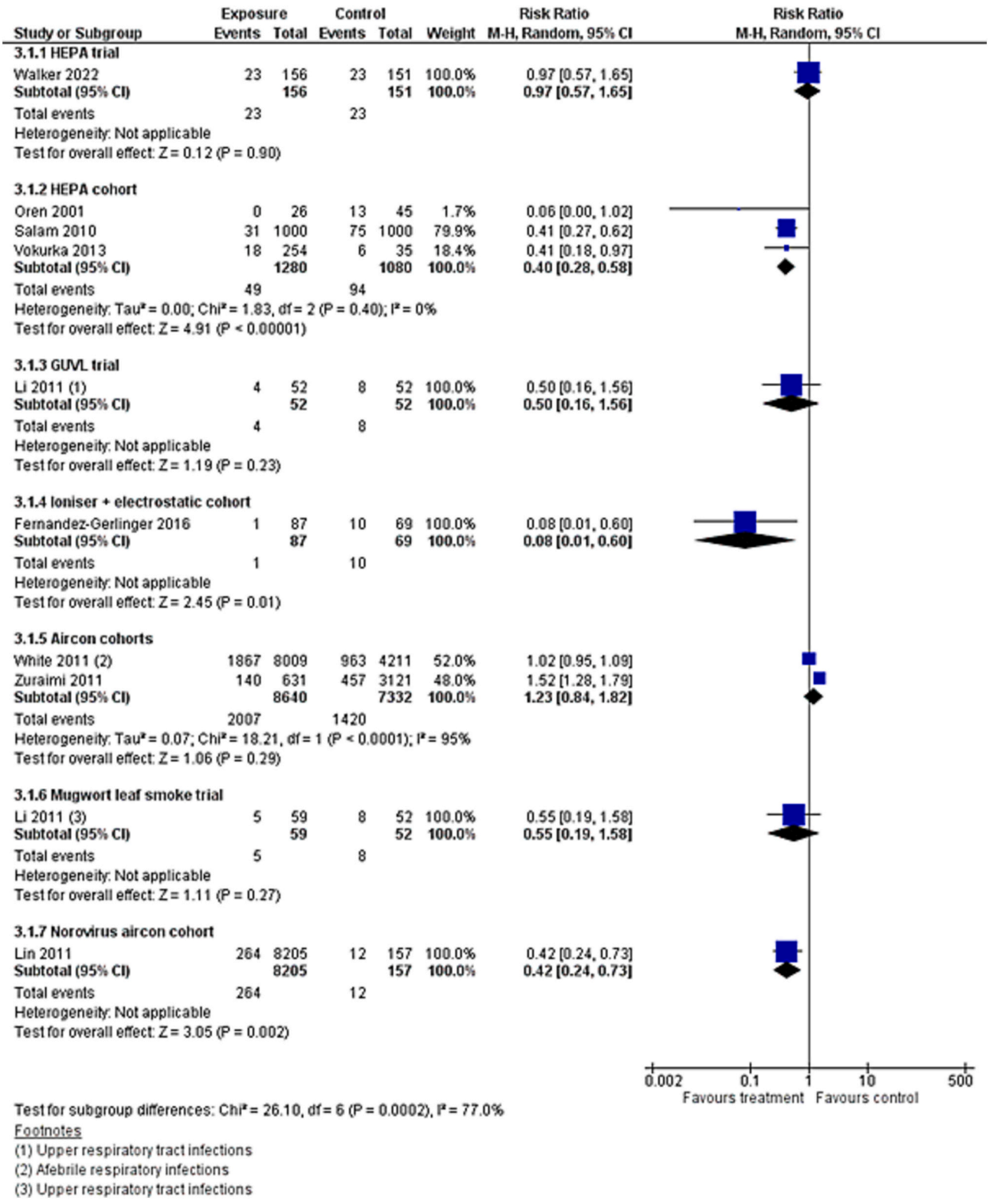


**Fig. 3.** Infection outcomes after exposure to air filtering or treatment.

study found that elderly care home residents in 2014 spent an average 95% of their time indoors (Almeida-Silva et al., 2014). Care home residents spend much of their time in doors and are usually frail, and are thus especially vulnerable to respiratory infections. Therefore, in such settings, technologies that try to stop disease transmission by disinfecting air have the greatest chance of success.

We found just four reports about experiments (rather than observational study designs) that collected data about infection status in humans after ATT were deployed to deactivate or remove pathogens from indoor air. Lack of rigorous experimental trials is problematic because of the greater biases in cohort (observational) study designs. Even in randomised controlled trials (RCT) study designs, biases introduced by poor randomisation, blinding and allocation concealment may exceed the apparent preventive effects suggested by cohort studies

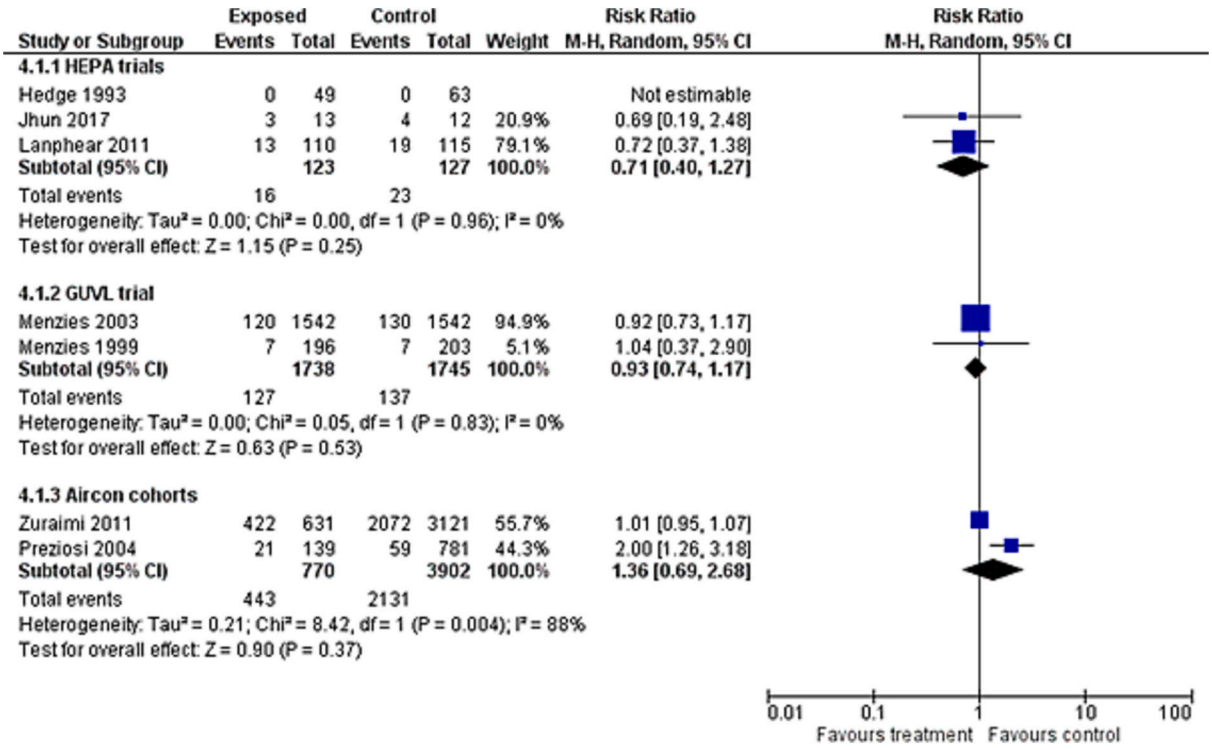


**Fig. 4.** Symptoms as dichotomous outcomes after exposure to air filtering or treatment.

(Wood et al., 2008; Savović et al., 2012). Unfortunately, we found evidence of publication bias in the existing evidence base. It is excellent that five cluster RCTs were registered since 2020, in four different countries, to evaluate deployment of ATT to reduce respiratory infections. These trials will have evaluated both HEPA ($n = 3$) and GUVL ($n = 2$). According to registrations, two school-based trials (ISRCTN46750688; NCT05016271) were scheduled to finish data collection by late 2022; while three experiments in care home settings (NCT05084898; ACTRN12621000567820; ISRCTN63437172) will finish data collection in 2023 and 2024. Because each environment is unique in terms of its physical infrastructure, ventilation system design, size, occupancy, and occupant behaviour, the trials due to report should have collected data under a variety infrastructures and concurrent infection control policies.

We found many studies undertaken in the context of allergenic response or asthma. We included these studies unless the authors said they had excluded infection as a cause of symptoms (which they did not). We included for full text review all studies about respiratory or gastrointestinal outcomes in people where a relevant technology was tested in an eligible setting. Even if our outcomes were not mentioned in the article abstract, these data were sometimes collected and reported in the full report. Reviewing full text of so many articles exceeded our initial resource allocation. We also decided that it was undesirable to confine our review to only dichotomous outcomes as stated in the original protocol. These are among the many reasons for deviating from our original protocol (Prospero CRD42020208109).

ATT can be expensive (Wightwick, 2021; Zimmer, 2021). Resource limits are an uncomfortable reality with regard to any medical or public health intervention: data on implementation costs, operational costs and energy efficiency (Settimo and Avino, 2021) should be included in published evaluations.

There are no studies addressing aerosols and gastrointestinal infections. Aerosol transmission for gastrointestinal infections can follow projectile vomiting often associated with norovirus illness (Makison Booth, 2014). Norovirus outbreaks have been linked to air travel in spite of HEPA filtration being routinely fit on nearly all commercial aircraft manufactured in recent decades (Thornley et al., 2011). Experiments evaluating effective protection from ATT should consider multiple pathogens, which could establish greater benefits.

Potential adverse effects in most studies were not addressed. Noise sometimes led to trial withdrawal. Noise nuisance is likely to reduce with technological developments. Technological developments have also led to GUVL being developed to be much safer to deploy for chronic exposure in recent years (Narita et al., 2020). Technological developments are ongoing with all forms of ATT. For instance, electrostatic cleaners combined with ionisers may be viable ATT developments that will reduce the ozone generation risk associated with earlier design ionisers (Lee et al., 2020).

### 4.1. *Strengths and limitations*

We undertook a very large search in diverse bibliographic sources (engineering, environmental, medical and health sciences), including three trial registries. We checked full text of seemingly relevant studies even when the abstract did not mention eligible outcomes. About a third of our included studies came from thorough forward and backward citation searches. We searched nine systematic reviews for additional studies.

Many decisions influenced our findings. We excluded studies published before 1970; we are aware of 1940s–1950s studies with both encouraging and equivocal results using GUVL (Reed, 2010). We did not wait for results from five very modern trials (initiated ≥2020) that have yet to report. Contacting original authors for additional information exceeded our resource capacity. We excluded articles that did not report primary raw (unadjusted) outcomes. We excluded multifactorial experiments, such as Eggleston et al. (2005), which had HEPA filters as well as environmental actions in the only intervention arm. We found many studies that collected symptom outcome data related to ATT but did not report unadjusted results. For instance, Shao et al. (2017) collected data about shortness of breath in participants, but did not report this information. In models adjusted for participant age and gender, Noonan et al. (2017; RCT in homes) found no improvement in

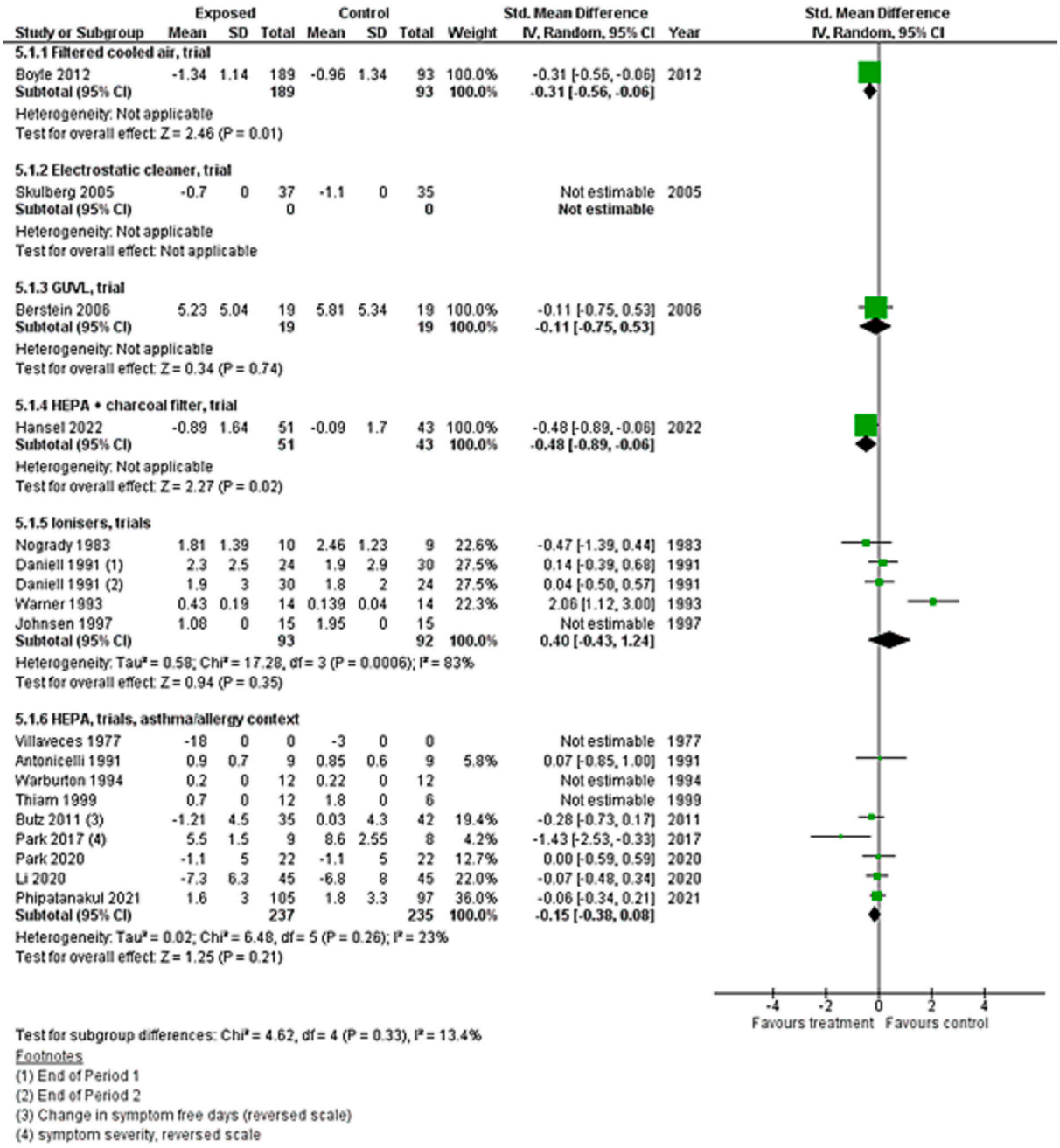


**Fig. 5.** Respiratory severity scores after exposure to air filtering or treatment.

(asthmatic) symptom severity related to HEPA filtration. In models adjusted for 13 other covariates, Abd Razak et al. (2020; cohort study in child care centres) found greater symptom severity related to air conditioning rather than natural ventilation. Gent et al. (2022; RCT in homes) found reduced symptomatic illness related to HEPA filtration in homes of asthmatics, after adjusting for measured $NO_2$ concentrations in same environment. These findings suggest that adjustment by many types of confounders may be warranted to find true effect size. Such adjustment requires access to individual participant data. We note that the lack of apparent consensus from adjusted outcomes is similar to our own findings.

There are potentially important factors which could affect study outcomes or findings but we did not summarise, partly because they are rarely reported. We did not adjust for relevant aspects such as participant vulnerability, participant ages, concurrent community prevalence of infection, device air flow rates, HEPA classification (e.g.e.g., standards like ISO 29463), concurrent risk mitigation measures, person-hours of exposure, adherence to trial protocol or vulnerabilities of target pathogens. It is likely that many other risk mitigation strategies operated simultaneously in most settings, but these were not well described. Guide or reference values for safe thresholds were not always reported when there was monitoring for air contaminants, and we note that these standards may have changed since the primary research was undertaken which complicates our ability to comment on safety outcomes. It is not ideal that our own study did not adhere to a pre-registered protocol.

## 5. Conclusions

Treatment of indoor air in public spaces was not shown to help prevent transmission of respiratory or gastrointestinal diseases. Our pooled data suggested no net benefits for symptom severity or symptom presence, in absence of confirmed infection. There is weak evidence that

ATT coincided with fewer confirmed infections, but these data evince strong publication bias. Although environmental and surface samples are often reduced by several air treatment strategies, especially germicidal lights and high efficiency particulate air filtration, robust evidence has yet to emerge to confirm that these technologies are effective in real world settings. Data from several relevant randomised trials have yet to report and will be welcome to the evidence base. Where such technology is trialled, costings and adverse events should be reported to contextualise any potential trade offs in public health protection decisions. We recommend that authors publish both raw unadjusted outcome measures as well as results from appropriately adjusted models, to facilitate multi-study synthesis.

## Approval to use the data to undertake the research

Approval was not required because this is secondary analysis of published data.

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## Author contributions

PRH conceived of the study. IRL and PRH secured funding. JB co-designed and ran the searches. JB integrated and de-duplicated bibliographic hits. JB, NRJ, ICS, EJA, AK, CL and KP screened titles and abstracts. ICS undertook backward and forward citation searches with confirmation by JB, who also checked references of systematic reviews for additional studies. JB and NRJ screened full text. JB and ICS initially extracted data from full text, confirmed by each other or NRJ. JB and PRH designed the synthesis strategy. JB and NRJ undertook quality assessment. JB wrote the first draft and assembled revisions with comments from all coauthors. All authors have read and approve of the final manuscript.

## Declaration of Competing interest

The authors declare that we have no conflict of interest.

## Data availability

Data will be made available on request.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ypmed.2023.107774.

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