

## **Effectivity of Hepa Filters in the Dental Clinics in Covid Times Systemic Review and Meta Analysis.**

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### **Abstract**

**Introduction:** The outbreak of SARS-CoV-2 has made us all think critically about hospital indoor air quality and the approaches to remove, dilute, and disinfect pathogenic organisms from the hospital environment. While specific aspects of the coronavirus infectivity, spread, and routes of transmission are still under rigorous investigation, it seems that a recollection of knowledge from the literature can provide useful lessons to cope with this new situation. As a result, a systematic literature review was conducted on the safety of air filtration and air recirculation in healthcare premises. This review targeted a wide range of evidence from codes and regulations, to peer-reviewed publications, and best practice standards.

**Materials and methods:** PUBMED, EMBASE, MEDLINE, the Cumulative Index to Nursing and Allied Health Literature, and the Cochrane Collaboration.

**Results:** The literature search resulted in 394 publications, of which 109 documents were included in the final review. We identified 10 relevant randomized controlled trials that examined the influence of a residential air filtration system on patients with COVID19. Air filters were associated with significantly lower total symptom scores (weighted mean difference of 0.47; 95% confidence interval [CI], 0.69 to 0.25) on a 10-point scale, and lower sleep disturbance score (weighted mean difference of 0.93; 95% CI, 1.44 to 0.42); however, heterogeneity of results weakens the inferences from these trials. Air filtration systems were not associated with any differences in medication use or morning peak expiratory flow values. None of these trials employed validated scales to measure clinical symptoms or quality of life.

**Conclusion:** Overall, even though solid evidence to support current practice is very scarce,

proper filtration remains one important approach to maintain the cleanliness of indoor air in hospitals. Among patients with allergies and COVID-19, use of air filters is associated with fewer symptoms. Rigorous sufficiently powered randomized clinical trials are needed to more precisely define the influence of air filtration on health-related quality of life and symptom control for COVID-19 patients.

**Keyword:** HEPA, COVID-19, Allergies, Meta-analysis, Air filtration.

## **Introduction**

The prevention of healthcare associated infections (HAIs) has long been a top strategic priority for the Center for Disease Control and Prevention (CDC).<sup>1,2</sup> The recent pandemic manifested an urgent need to better understand and implement design, maintenance, and operations that ensure indoor air quality in healthcare facilities. Specifically for the SARS-CoV-2 virus, the CDC recognizes three main routes of transmission: (1) direct large droplet transmission between people within close proximity; (2) indirect respiratory droplet deposition on surfaces and objects and subsequent transmission via the contaminated fomite; and (3) the airborne transmission via small particle aerosols containing viable virus. Although the portion each route contributes to disease transmission is under close investigation, one can reasonably assume that lowering the number of virus particles in the indoor space would result in lower rates of transmission. Engineering tools can be instrumental to remove, contain, and dilute virus concentrations in the spaces where the COVID-19 patients are evaluated and treated, and air filtration–recirculation is a long-lasting method used to remove and dilute contaminants.<sup>3–5</sup> Infection may transfer via air from one person to another and become epidemic.<sup>6</sup> Although it is accepted that the airborne route exists, its attributed contribution to the spread of infectious diseases is less certain.<sup>7</sup> Most recently, a review of scientific evidence on hospital buildings studied the temperature, relative humidity, and ventilation system. The current state of healthcare ventilation management stems from two complementary schools of thought around minimizing both recirculation of indoor air and energy demands. Various studies demonstrate the importance of the airborne route of infection transmission in the hospital setting.<sup>8</sup> On one hand, it seems unreasonable to allow recirculation of return air into patient care environments. On the other hand, it seems reasonable to take advantage of the energy in the return air to dilute contamination through air recirculation, while ensuring that the return air is clean and comfortable. With recent advancements in technology, the latter can also be achieved via energy recovery techniques, and recirculation is no longer the sole option. However, these techniques are not always a feasible and affordable retrofit response to the emergence of COVID-19, especially in existing facilities while replacing the filtration system, and altering the air distribution system could be more convenient. The objective of this systematic review is to critically appraise and summarize the current randomized trial evidence about the effect of residential air filters on signs and symptoms of COVID-19, and to inform patients, clinicians, and researchers of our findings.

## **Materials and methods**

Data mining:

Online data from the MEDLINE, Cochrane, PUBMED, EMBASE and Cumulative Index to Nursing and Allied Health Literature from 2019 to 2021 using the following text words and key words: “COVID-19,” “quality of life,” “air filter,” “indoor air quality,” and “randomized controlled trials.”, were searched.

To identify additional potentially relevant studies, we corresponded with experts in the field

of COVID19 research, manufacturers of air filtration systems, and the authors of the primary studies included in this review. We also reviewed the citation lists or bibliographies of all the relevant studies and reviews, and retrieved any article that looked relevant to this systematic review.

### Study Selection

Two reviewers independently selected the articles based on the titles, abstracts and full texts. Then, two reviewers independently extracted the following data from included studies: (1) design, randomized controlled trials; (2) population, children or adults with a diagnosis of COVID19; (3) intervention, use of a residential air filtration system; and (4) patient-oriented outcomes, as reported in each study such as COVID19 signs and symptoms, physiologic, laboratory, and other end points (ie, measurement and documentation of particulate). Two reviewers independently assessed the risk of bias of the selected RCTs using the Cochrane Risk of Bias tool.<sup>9</sup>

All statistical analyses were performed using Review Manager (RevMan) version 5.3. Comparable data from studies with similar interventions and outcomes were pooled using forest plots. Relative risk (RR) with 95% confidence intervals (CIs) for dichotomous data was used as the effect measure. Between-study heterogeneity was assessed using the  $I^2$  for each pooled estimate.<sup>10</sup> We adopted a random-effects model for heterogeneity  $P < 0.10$ . We performed a subgroup analysis based on the settings (hospital, community) due to the possibility of clinical heterogeneity. A sensitivity analysis was conducted to evaluate the robustness of the results by excluding individual studies for each forest plot. Funnel plots were planned to assess publication bias. Because of the small number of studies available for each pooled estimate, we failed to assess publication bias.

## Results

### Study Selection

Flow chart explaining the data search and final selection are shown in figure 1. Our search strategies identified 14 randomized trials evaluating the effect of air filtration systems in patients with COVID19.

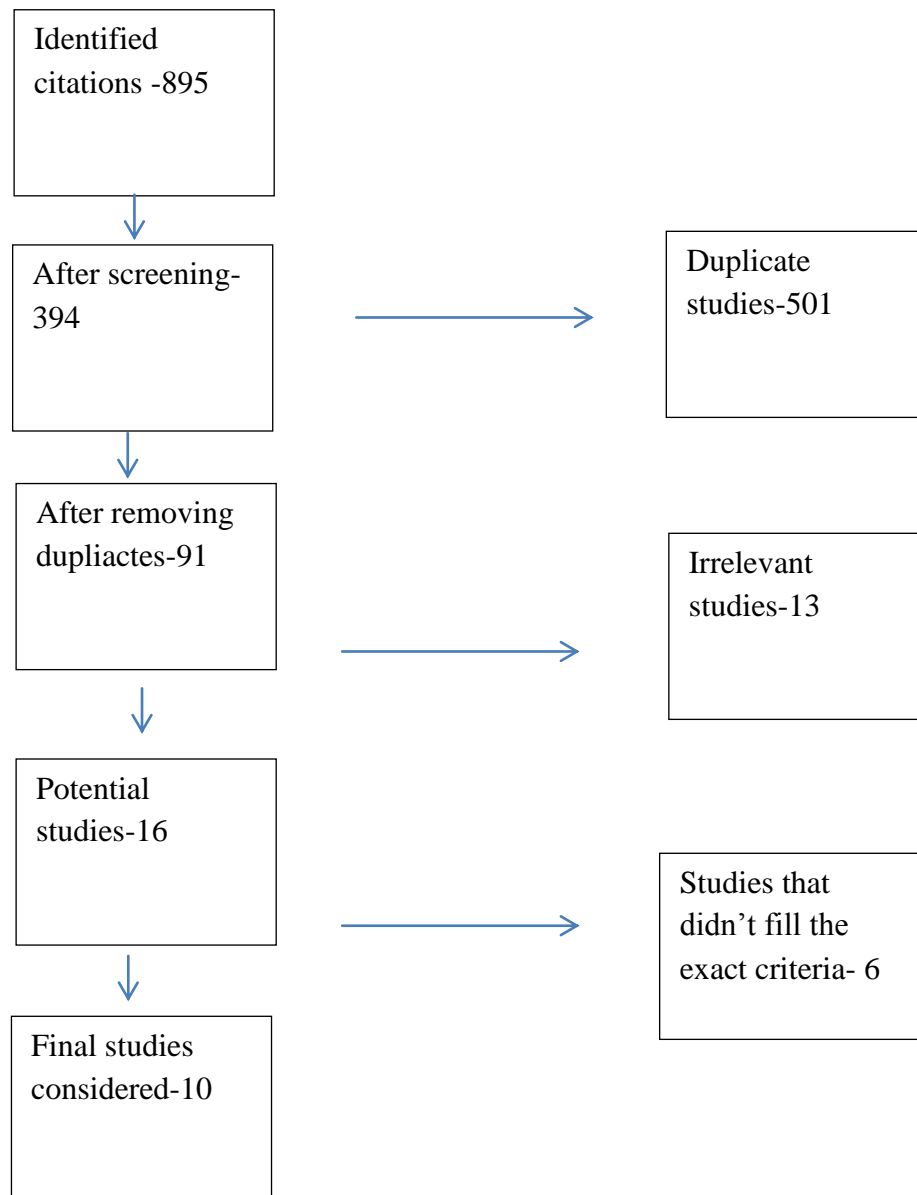
### Clinical Characteristics

Five of 14 trials enrolled exclusively adults, while 1 trial enrolled exclusively children (Table 2). The sample size ranged from 9 to 45 participants in each study, for a total of 216 patients across all studies. Multiple outcome measures were used to determine the effectiveness of air filters in each study (Table 2). All but one study used a subjective measure of symptoms. However, none of these trials employed validated scales to measure clinical symptoms or quality of life. Five studies reported allergen levels. Air filtration systems were not associated with any differences in medication use or symptom/ medication scores. Two trials showed that air filters were associated with significantly fewer symptoms. Two studies reported a statistically significant decrease in airway responsiveness associated with air filter exposure. There was a trend toward lower total symptom scores as shown by a weighted mean difference of 0.76 (95% confidence interval [CI], 2.17 to 0.65;  $p < 0.29$ ) on a 10-point scale using the random-effects model. Using the fixed-effects model, the symptom improvement was statistically significant (weighted mean difference of 0.47; 95% CI, 0.69 to 0.25;  $p < 0.01$ ). However, the magnitude of this apparent benefit on symptoms differed across studies ( $p$  value for heterogeneity  $< 0.01$ ). The most conservative estimate of the effect of HEPA

filters on symptoms is shown by the random-effects model and the associated wide CI. Figure 2.

Air filters were not associated with any improvement in nasal symptoms. We also found a trend toward less sleep disturbance associated with air filters, as shown by a weighted mean difference of 1.08 (95% CI, 2.78 to 0.62;  $p < 0.21$ ) using a random-effects model, or 0.93 (95% CI, 1.44 to 0.42;  $p < 0.01$ ) using a fixed-effects model. However, these study results were also heterogenous, weakening the inferences we can draw from this meta-analysis ( $p$  value for heterogeneity  $< 0.01$ ). Table 1.

**Figure 1:** Flowchart of retrieved studies.

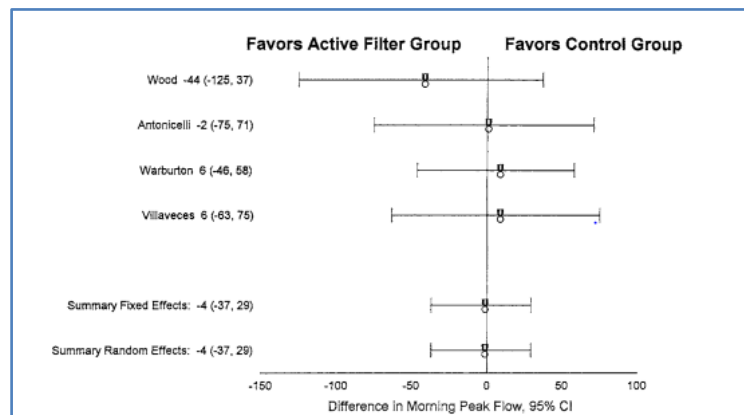


**Table 1: Selected studies and their features.**

Reference	Quality level	Methodology	Remarks	Setting
Shirani et al. (1986)	2	burn units	Observational study of 318 patients	Significant improvement was observed in the cohort of patients admitted to a renovated unit. The renovation consisted of adding handwashing sinks, partitions to provide individual rooms, and HEPA filters on the air supply.
Sheretz et al. (1987)	3	BMT	Observational study of 113 patients	Placing patients in a room with a whole-wall HEPA filtration unit reduced the risk of nosocomial aspergillus up to 10 times.
Barnes and Rogers (1989)	2	BMT	Observational study of 19 children	The introduction of laminar airflow plus HEPA filtration terminated the outbreak of invasive pulmonary aspergillosis.
Marier et al. (1993)	3	AIRR	Experiments in controlled environment	The combination of UV lights and Ultra Low Particulate Air (ULPA) filters efficiently removed particles from the air.
McManus et al. (1994)	2	Burn units	Observational study of 2519 patients over ten years	Isolation of burn patients in separate rooms equipped with new filters reduced mortality ratio to one-third of predicted ratio. Authors attributed the improvements to the use of single-bed rooms, rather than the filtration system. However, these two effects were not decoupled.
Miller-Leiden et al. (1996)	2	Test Chamber	Experiments in controlled environment.	Ceiling mounted filters reduced the concentration of synthetic aerosols tracer particles by 90%. Non-HEPA filters were as effective as HEPA filters.
Passweg et al. (1998)	2	PE	Observational study of 5065 patients	LAF+HEPA filtration significantly reduced the mortality rate in the first 100 days. The combination of LAF and HEPA filtration was effective. The influence of LAF from HEPA filtration was not decoupled.

Cornet et al. (1999)	2	PE	1047 prospective air sampling during 2-year period	Efficiency of HEPA filtration and LAF+HEPA in preventing Aspergillus contamination was assessed. It was shown that HEPA filtration alone may not be sufficient under severe release due to construction/renovation activities.
Hahn et al. (2002)	2	PE	Retrospective cohort study of 90 patients	An outbreak of invasive aspergillosis was documented in a hematologic oncology unit with no HEPA filter. The contamination source was determined in the non-BMT wing of the setting.
Alberti et al. (2001)	2	BMT	prospective study of 3100 air and 9800 surface samples	Fungal contamination was never found in air and on surfaces of rooms with HEPA+LAF. Separate effects of HEPA and LAF were not decoupled.
Olmsted et al. (2008)	3	OR	Experiments in controlled environment	Using a freestanding HEPA unit inside the OR resulted in a surge of synthetic particles into the sterile zone. Using it outside of the room could effectively remove the particles.
Johnson et al. (2009)	3	AIIRs		Experiments in controlled environment The effect of HEPA filtered air recirculation with AIIR was assessed. In the presence of abundant particles, some might escape through the HEPA unit.
Stephens et al. (2013)	4	Waiting Room	Numerical	The Well-Riley equation was modified to include the removal efficiency of filters. The influenza infection risk was not mitigated using a filter rating higher than MERV 13.
Emmerich et al. (2013)	4	General Ward	Numerical	A well-mixed condition was assumed. Concentration of TB was reduced by 3 orders of magnitude when HEPA filters were used. The use of HEPA filters led to significant decrease in contaminant concentrations compared to MERV 15

**Figure 2. The pooled analysis using both the fixed- and random-effects analysis show no benefit of air filtration on values.**



## Discussion

In this systematic review of 14 randomized clinical trials among adults and children with COVID19 and allergy symptoms, we found a small but statistically significant difference in total symptoms and sleep disturbance associated with use of domestic air filters. We did not identify any benefit conferred by air filters with respect to nasal symptoms, medication use. We adhered to rigorous systematic review methods (26) in this review. Jadad and colleagues 27 previously summarized the clinical, methodologic, and reporting aspects of systematic reviews and meta-analyses on the treatment of asthma that can be implied to present COVID19, highlighting how serious methodologic flaws limited their usefulness.

Strengths of this systematic review include a focused clinical question, a comprehensive search for published and unpublished research, explicit selection criteria, validity assessments conducted in duplicate independently, and reporting of the heterogeneity of study results. In critically appraising review articles, it is important to distinguish between the quality of the review methods and the quality of the studies included in the review. Accordingly, we evaluated and reported the randomized trial methodology in detail,26 thereby allowing readers to make their own inferences about the primary evidence. None of the studies explicitly reported on concealment of treatment allocation. Few studies reported strategies to maintain the blinding of participants, caregivers, clinicians, and outcome assessors; however, eight studies used sham air filters in the control period.

Of the 14 randomized trials included in this systematic review, only few trials evaluated COVID19 symptoms, but none included a validated generic or disease-specific quality-of-life instrument. At the time that many of these trials were conducted, few such instruments were available. Some simple symptom measures used in these trials may be insensitive to detect clinically important improvements due to environmental modifications. This hypothesis is supported by the observation that a reduction in airborne particulate matter associated with air filters did not always correlate with an improvement in symptoms. The dearth of randomized trials evaluating the effect of air filters in children merits comment. Only one study enrolled exclusively children, despite the high and growing prevalence of COVID19 in this population. The Seattle-King County Healthy Homes Project, which surveyed low-income urban caregivers of children with asthma, found that 12% used a vacuum with a HEPA quality filter.38 This can be similarly for the COVID19. However, the random-effects model meta-analysis in this review that gives smaller studies proportionally greater weight in the pooled estimate, and results in more conservative interpretation of the effect of HEPA

filters, suggests no overall benefit in terms of symptoms and sleep disturbance. These findings, and the fact that disease-specific outcomes were not measured, precludes making guidelines or policy recommendations about the use of air filters. However, the epidemiologic trend of increased COVID19 and allergy symptoms, the growing importance of patient empowerment through symptom control, and the need to measure outcomes that are important to patients suggest that further large rigorous randomized trials of environmental interventions such as air filters are warranted.

### **Conclusion**

There is substantial evidence that contaminated air can result in disease spread, and that the combination of air filtration and recirculation can reduce this risk. Observational and animal studies suggest that air recirculation alone may result in the airborne transmission of pathogens.<sup>28-30</sup> The experimental setup is mostly designed for extreme cases to prove the airborne route, which is far from realistic in the healthcare setting. There are a few outstanding findings from the literature that can be used to minimize the adverse impact of the SARS-CoV-2 virus on medical personnel who spend many hours of their time inside the hospital as well as reduce risk of nosocomial infections.

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