

in vitro studies and RCTs that support the use of particular types of spacer devices. Our own study cites several RCTs that did not find side effects without spacer use. All of this highlights the need for continued research of varying designs as described above.

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Reducing the burden of allergy and asthma in schoolchildren: Air cleaning solutions and microbial diversity—the dark side of the moon?



To the Editor:

The article "School Environmental Intervention to Reduce Particulate Pollutant Exposures for Children with Asthma" by Jhun et al¹ elegantly showed, similarly to other intervention studies in different environments, that high-efficiency particulate arrestance (HEPA) filters in schools are able to significantly reduce the indoor concentrations of particulate matter, which may potentially reduce exacerbations in children with asthma. In this age group, allergic asthma is the prevalent phenotype; therefore, the study's intervention may also impact allergic diseases. This interventional approach has been referred as a highly effective indoor environmental control methodology,² but is "air cleaning the school indoor environment" really the best approach?

Recently, we reported evidence supporting the association between high concentrations of particulate matter and the

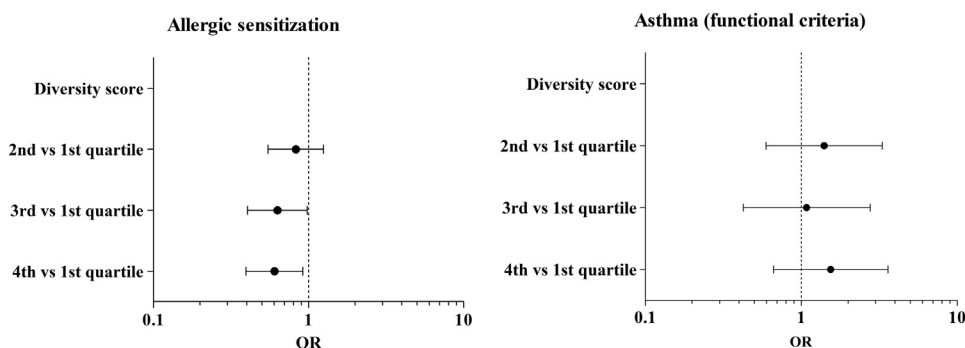


FIGURE 1. The influence of microbial diversity in schools on the development of allergy and asthma in children has been investigated. A microbial diversity score was defined as the sum of all the detected fungi groups/species, categorized into quartiles, with the classrooms with lower diversity score in the first quartile, whereas the fourth quartile included those with higher diversity scores. The graphics represent the logistic regression between fungal diversity scores and the prevalence of allergic sensitization (left) and asthma (right). The results are expressed as odds ratios (ORs) with 95% CI in logarithmic scale. Although a clear tendency for a lower risk of allergic sensitization may be observed as the fungal diversity increases in classrooms, the same was not observed for asthma. Figure adapted from Figure 2 of Cavaleiro Rufo et al.⁷

exacerbation of wheezing.³ In face of these results, air purification methods such as the HEPA filters used in the aforementioned study may appear as an effective preventive measure for allergic and respiratory symptoms. However, we must keep in mind the effects of their use on other indoor air parameters. Air cleaners and HEPA filters have been found to promote the growth of certain fungal species such as *Cladosporium* and *Penicillium*.⁴ However, polyurethane coatings containing ammonium have been developed to render bactericidal properties to the HEPA filters.⁵ Either way, these air purification methods may significantly impact the diversity of microorganisms in the indoor environment.

Recent evidence suggests that environmental biodiversity and human microbiome may have a major role in allergic sensitization development.⁶ It is now recognized that early contact with multiple microbiological agents appears to contribute to a preventive immunomodulation, inducing tolerance to allergens through both adaptive and innate immune mechanisms. We have also observed the beneficial role of a biodiversified exposure in a study comprising 858 children attending 20 primary schools, where classrooms with higher fungal diversity had a significantly lower prevalence of sensitized children, although no significant associations were observed for the prevalence of asthma⁷ (Figure 1).

It is important to understand that a “totally cleansed air” may not be the perfect strategy for the prevention of allergies. This does not mean that air purifiers and filters should be disregarded, but should rather be used in situations in which the benefits surpass the risk of possible microbiome disruption, such as in highly polluted indoor environments or when the immunomodulation is no longer possible and exposure avoidance is recommended. Conversely, a balanced exposure to the natural environment may be a more cost-effective approach to prevent allergy development in children.

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Reply



To the Editor:

The interaction between environmental biodiversity and human microbiome is complex and their impacts on allergic sensitization and asthma are far from being fully elucidated. The latest literature provides mixed evidence on the effect of microbial diversity and asthma outcomes among children. Farm-related microbial exposures in early life have been associated with protection against allergic diseases.¹ Similarly, an urban study found that higher exposure to specific allergens and diverse bacteria during the first year of life among inner-city children reduced the risk of recurrent wheeze and allergic sensitization.² However, in established asthma, increased asthma severity has been associated with exposures to microbes, including bacterial endotoxin and fungal glucan, with a recent study demonstrating that increased microbial diversity in the home environment is associated with more severe asthma symptoms.³ Furthermore, responses to microbial agents vary with allergic status. For instance, children with allergy exposed to sensitizing allergens experience increased asthma severity, whereas nonallergic asthma may be influenced by bacterial endotoxin.⁴

Rufo et al⁵ point out that “totally cleansed air” may not be the panacea for allergy prevention and that high-efficiency particulate arrestance (HEPA) filters can compromise environmental biodiversity. There are several important considerations. First, HEPA filters do not yield “totally cleansed air” because their efficiency varies by particle size. Studies have shown that the relative abundance of fungal phyla varies by the size fraction of particles collected, with pathogenic fungal species predominating in fine particles—the particle size most efficiently filtered by HEPA filters.⁶ Similarly, the relative abundance of bacteria differs by particle size.⁷ It is premature to assume that the use of HEPA filters will lower the diversity of indoor fungi and bacteria without further investigation. Furthermore, we do not yet know what constitutes a “healthy” indoor microbiome, and whether it is based on diversity measures or the presence or absence of certain microbial taxa. We are just beginning to parse out the health effects of microbial “dose” (as measured by cell wall components such as beta glucans or endotoxin) and microbial “identity” (as measured by sequencing to identify microbial community structure and function).

Literature suggesting that exposure to beta glucans or yeasts in early life may reduce asthma development should not be used as a rationale to discourage the creation of healthy indoor spaces without mold problems. Although HEPA filtration is certainly not

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