Indoor Air Pollution and Asthma in Children

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The purpose of this article is to review indoor air pollution factors that can modify asthma severity, particularly in inner-city environments. While there is a large literature linking ambient air pollution and asthma morbidity, less is known about the impact of indoor air pollution on asthma. Concentrating on the indoor environments is particularly important for children, since they can spend as much as 90% of their time indoors. This review focuses on studies conducted by the Johns Hopkins Center for Childhood Asthma in the Urban Environment as well as other relevant epidemiologic studies. Analysis of exposure outcome relationships in the published literature demonstrates the importance of evaluating indoor home environmental air pollution sources as risk factors for asthma morbidity. Important indoor air pollution determinants of asthma morbidity in urban environments include particulate matter (particularly the coarse fraction), nitrogen dioxide, and airborne mouse allergen exposure. Avoidance of harmful environmental exposures is a key component of national and international guideline recommendations for management of asthma. This literature suggests that modifying the indoor environment to reduce particulate matter, NO_2, and mouse allergen may be an important asthma management strategy. More research documenting effectiveness of interventions to reduce those exposures and improve asthma outcomes is needed.

Keywords: particulate matter; air pollution; pediatric; urban; bronchial hyperreactivity

According to the World Health Organization, 24% of the global disease burden and 23% of all deaths are attributable to environmental factors (1). The causal pathway from exposure to disease and death is often complex and poorly understood. These risks are not evenly distributed across all age groups. Children may be particularly susceptible to the adverse environmental effects, as the proportion of deaths among children attributed to the environment is as high as 36% (1).

While there is a large literature linking ambient air pollution and cardiopulmonary disease (2–6), less is known about the impact of indoor air pollution on morbidity and mortality. Children, the elderly, and women are the most vulnerable with respect to potential indoor air pollution health effects because they spend more time in the home environment. Time activity studies have estimated that children and the elderly can spend as much as 90% of their time indoors (7). This observation underscores the substantial contribution that indoor exposures can make to an individual's total exposure.

There are many sources of indoor air pollution in the home environment. Air pollution inside homes consists of a complex mixture of agents penetrating from ambient (outdoor) air and agents generated by indoor sources. Indoor pollutants can vary in their potential health effects and intensity, as well as in their distribution across geographic areas, cultural backgrounds, and socioeconomic status. Indoor pollutants include products of combustion, including particulate matter (PM) and oxides of nitrogen, as well as airborne allergens and endotoxin. Exposure to indoor air pollutants can cause health effects ranging from sneezing and coughing to outcomes such as cancer and exacerbation of chronic respiratory disorders such as asthma.

Asthma, a complex disease influenced by both environmental and genetic factors, is common and the prevalence is increasing worldwide (8). Childhood asthma is the most common chronic disease in children. The International Study of Asthma and Allergies in Childhood (ISAAC) estimates the asthma prevalence by country as ranging from 2% to 40% (9). Indoor environmental factors thought to modify asthma severity include pollutants such as PM, nitrogen oxides, secondhand smoke, and allergens from pests, pets, and molds (10). In contrast to the outdoor environments, people may have a greater ability to modify indoor environmental exposures. The ability to modify indoor environments makes addressing indoor air pollution an attractive target for disease prevention.

The purpose of this article is to present an overview of research on indoor pollution and asthma focusing on studies conducted by the Johns Hopkins Center for Childhood Asthma in the Urban Environment.

INDOOR PARTICULATE MATTER

Particulate matter is a principal component of indoor air pollution in homes. PM originates from a variety of human-made and natural sources. Natural sources include pollen, spores, bacteria, plant and animal debris, and suspended crustal materials. Human-made sources consist of industrial emissions and combustion by-products from incinerators, motor vehicles, and power plants. Indoor sources include cigarette smoking, cooking, wood and other biomass burning in stoves and fireplaces, cleaning activities that re-suspend dust particles (e.g., sweeping), and penetration of outdoor particles into the indoor environment (11, 12). Indoor PM differs from outdoor PM in source, composition, and concentration (11, 13–16). As a result, the health effects of indoor PM cannot be readily extrapolated from studies of outdoor air pollution. Figure 1 presents the time-dependent PM concentrations determined using a light scattering nephelometer (MIE pDR 1000; ThermoElectron, Franklin, MA) measured simultaneously inside a home, immediately outside the home, and at a central monitoring site. In this instance, PM

(*Received in original form August 5, 2009; accepted in final form February 9, 2010*)

Supported by grants from the U.S. Environmental Protection Agency (R82672401) and the National Institute for Environmental Health Sciences grant numbers (ES09606 to P.N.B., ES03819 to J.G., and K23 ES 016819 to M.C.M.).

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Proc Am Thorac Soc Vol 7. pp 102–106, 2010
DOI: 10.1513/pats.200908-083RM
Internet address: www.atsjournals.org

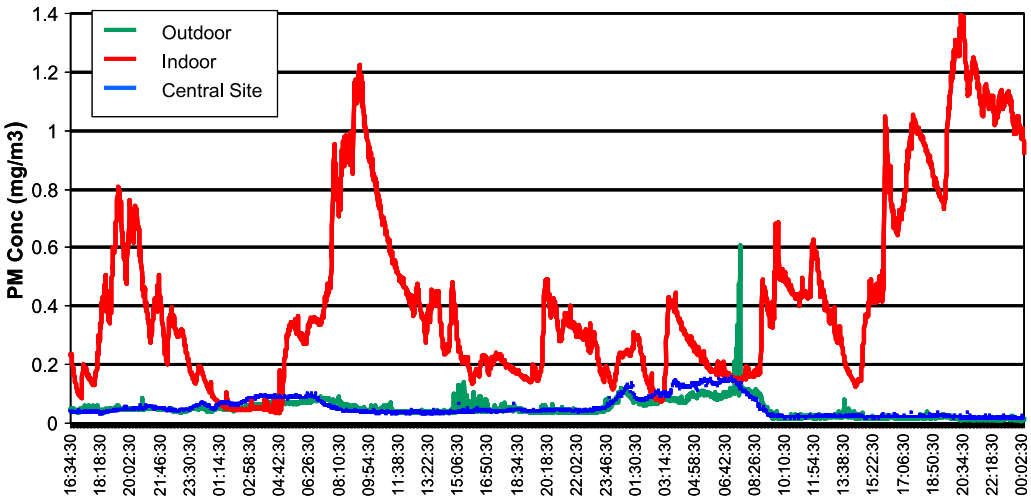

Figure 1. Comparison of particulate matter (PM) concentrations simultaneously measured indoors, immediately outdoors, and at a central monitoring site.

measured inside the home is clearly higher and more variable than outside either at the home or a central monitoring site, demonstrating the importance and complexity of addressing the health effects of indoor airborne particles.

There are relatively few studies of indoor PM and asthma. Studies of school-age children in Seattle found that indoor $PM_{2.5}$ exposure was associated with decreased pulmonary function in a subgroup of 10 children not using inhaled corticosteroids (17). In this study, Koenig and coworkers (17) also found that $PM_{2.5}$ originating from indoor sources was more potent in decreasing lung function than was outdoor-derived PM. A California study of 19 predominantly white children found significant decrements in lung function (FEV_1) associated with indoor PM. While this study found associations between ambient PM and lung function, they found stronger associations for indoor than outdoor central site PM concentrations (18).

A longitudinal study of 150 inner city preschool children with asthma, conducted as a part of the Johns Hopkins Center for Childhood Asthma (Baltimore Indoor Environment Study of Asthma in Kids [BIESAK] Study) investigated the impact of indoor fine ($PM_{2.5}$) and coarse PM ($PM_{2.5–10}$) on asthma morbidity (Figure 2). The mean indoor $PM_{2.5}$ concentration in the BIESAK study was roughly twice as high as the indoor coarse PM fraction ($PM_{2.5–10}$) concentration, 40.3 ± 35.4 μg/m^3 and 17.4 ± 21.1 μg/m^3, respectively. The in-home $PM_{2.5}$ and $PM_{2.5–10}$ concentrations were significantly higher than the respective average ambient measurements made over the same time period, 12.4 ± 6.2 μg/m^3 and 10.3 ± 21.0 (Figure 2).

Significant determinants of indoor PM concentrations included smoking, sweeping, and stove use (19), activities that are modifiable and provide opportunities for exposure reduction. Smoking has been consistently described as a major source of indoor particulates over the last several decades, with more than 30% of all U.S. children exposed to secondhand smoke (20). Our results suggest that smoking continues to be a significant contributor to PM exposure in the inner city. The

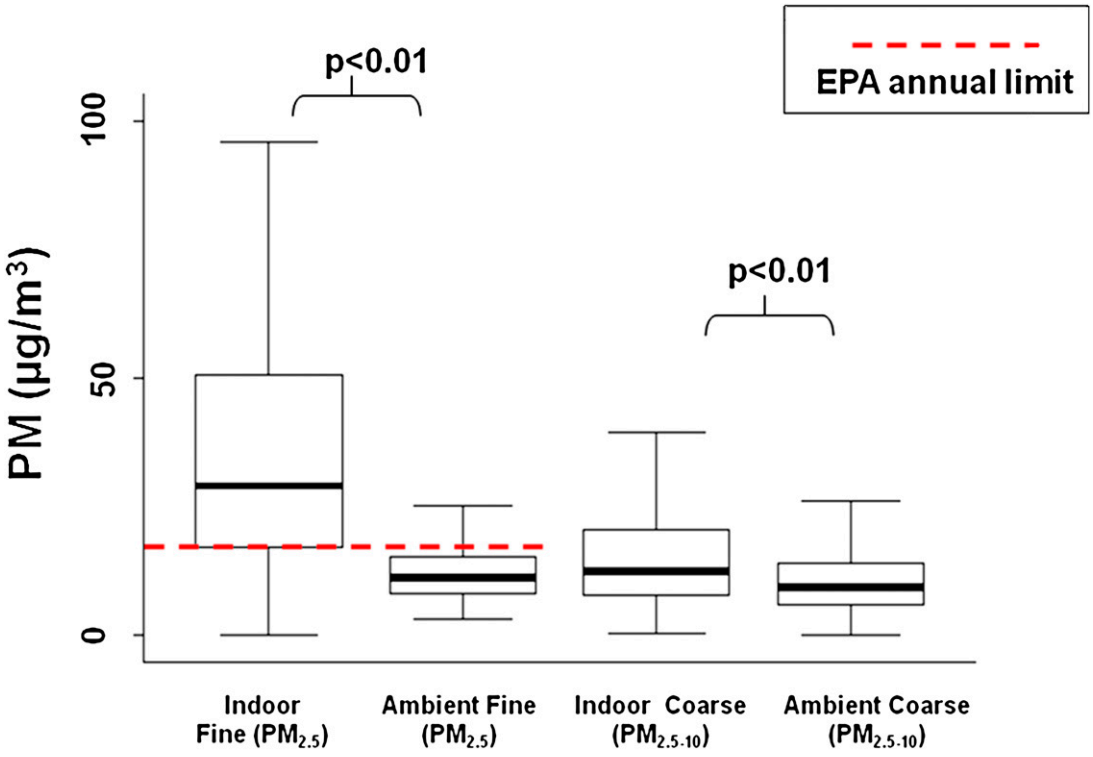

Figure 2. Distributions of indoor PM in the child's bedroom.

difference in $PM_{2.5}$ between smoking and nonsmoking households of 26 $\mu g/m^3$ is similar to the range of 25 to 45 $\mu g/m^3$ that has been previously reported (11, 16, 21, 22).

Indoor coarse PM concentrations were associated with substantial increases in asthma symptoms (Figure 3). For example, for every 10-$\mu g/m^3$ increase in indoor $PM_{2.5–10}$ concentration, there was a 6% increase in the number of days of cough, wheeze, or chest tightness, after adjusting for age, race, sex, socioeconomic status, season, indoor fine PM, and ambient fine and coarse PM concentrations. In adjusted models, higher indoor coarse PM concentration was also significantly associated with increased incidence of symptoms severe enough to slow a child's activity, wheezing that limited speaking ability, nocturnal symptoms, and rescue medication use. Outdoor coarse PM was not associated with increased asthma symptoms or rescue medication use.

Fine PM was also positively associated with respiratory symptoms and with rescue medication use (Figure 3). For example, for every 10-$\mu g/m^3$ increase in $PM_{2.5}$ measured indoors, there was a 7% increase in days of wheezing severe enough to limit speech and a 4% increase in days on which rescue medication was needed, after adjustment for potential confounders. Both indoor and ambient fine PM concentrations were also associated with exercise-related respiratory symptoms. In multivariate models adjusting for participant characteristics that were potential confounders as well as for simultaneous indoor and ambient coarse PM, for every 10-$\mu g/m^3$ increase in indoor and ambient $PM_{2.5}$, there was a 7% and a 26% (data on ambient PM not shown in Figure 3) increase in days of exercise-related symptoms, respectively. In contrast, neither indoor nor ambient coarse PM concentrations were associated with exercise-related symptoms.

These findings demonstrate that both indoor coarse and fine PM distinctly affect respiratory health in children with asthma. There are physiologic reasons that can explain why PM of these different size fractions can contribute separately to asthma morbidity. Although fine PM may be capable of reaching the alveoli, the regions responsible for gas exchange, the deposition of coarse PM in upper airways and subsequent bronchial hyperreactivity may be responsible for the symptomatic response measured in these preschool children.

The strong relationship between indoor and ambient fine PM exposure and exercise-related symptoms was striking in this study. Previous investigators have indicated that exercise may play a role in asthma by modifying the effect of environmental stimuli and pollutants (18). Increased exercise symptoms in response to fine PM exposure may be attributable to increased minute ventilation and an increased dose of fine PM in the distal airways and the pulmonary circulation. The increased fine PM doses in the distal airways may be more potent in eliciting exercise-related symptoms than the doses of coarse PM that deposit in the more proximal airways.

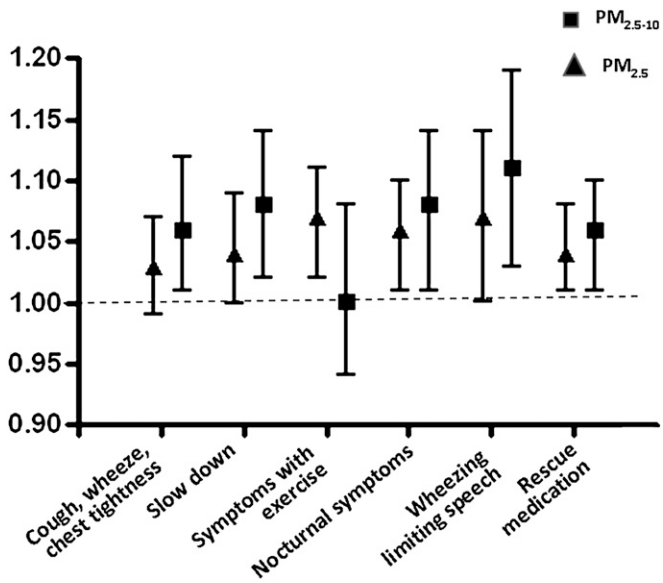

Figure 3. Indoor PM concentrations, asthma symptoms, and rescue medication use: multivariate models (coarse module adjusted for age, sex, race, parent education level, season, indoor fine PM, ambient fine PM, ambient coarse PM; fine module adjusted for age, sex, race, parent education level, season, indoor coarse PM, ambient coarse PM, ambient fine PM).

INDOOR NITROGEN DIOXIDE AND ASTHMA MORBIDITY

Nitrogen dioxide is a product of high-temperature combustion. The principal indoor source of NO_2 is unvented gas appliances (stoves and furnaces). NO_2 may be particularly problematic in the inner city, where gas stoves are common and proper venting rare and using stoves for heating is commonly reported. Results from the BIESAK Study have demonstrated high indoor NO_2 concentrations in inner city Baltimore homes (21, 23).

NO_2 is an irritant gas and has been linked to respiratory effects. Although some studies (24–29) have found adverse respiratory health effects from indoor NO_2, other studies have failed to confirm that association (30–34). For example, data from the National Health and Nutrition Examination Survey III did not suggest any impact from gas stoves on pulmonary function or respiratory symptoms in adults with asthma (34). In contrast, the National Cooperative Inner City Asthma Study (NCICAS) conducted in eight inner cities across the United States showed a link between higher concentrations of indoor NO_2 and increased symptoms and decreased peak flows in children with asthma (35).

Hansel and colleagues (36) recently reported on the effect of indoor NO_2 concentrations and asthma in the BIESAK longitudinal cohort. Most of the homes in the BIESAK study were row homes (homes that share adjacent walls; 79%) and close to the street (within 25 ft; 71%). The overall mean (± SD) indoor NO_2 concentration was 30.0 ± 33.7 ppb (range, 2.9–394.0 ppb).

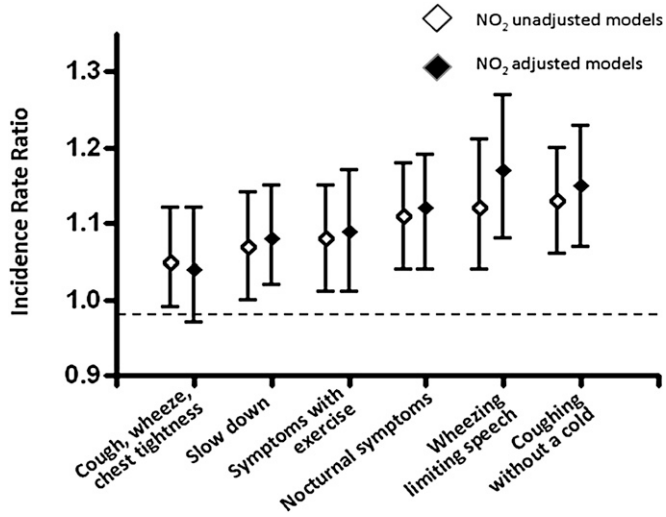

Figure 4. Risk of asthma symptoms per 20-ppb increase in NO_2 exposure, adjusted for $PM_{2.5}$; second hand smoke; distance from the curb; type of street in front of house; season of sampling; age, sex, and race of child; and mother's education level.

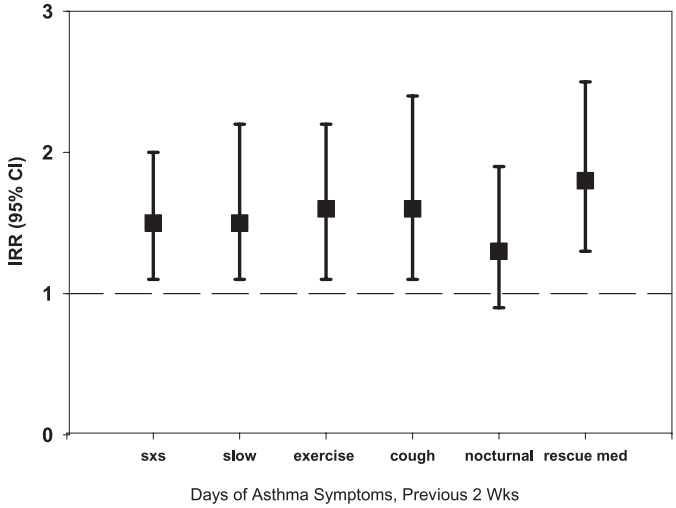

Figure 5. Recent asthma symptoms and rescue medication use among mouse-sensitized, highly exposed children. Adjusted for age, sex, atopy, cockroach sensitization and exposure, public health insurance, and study visit.

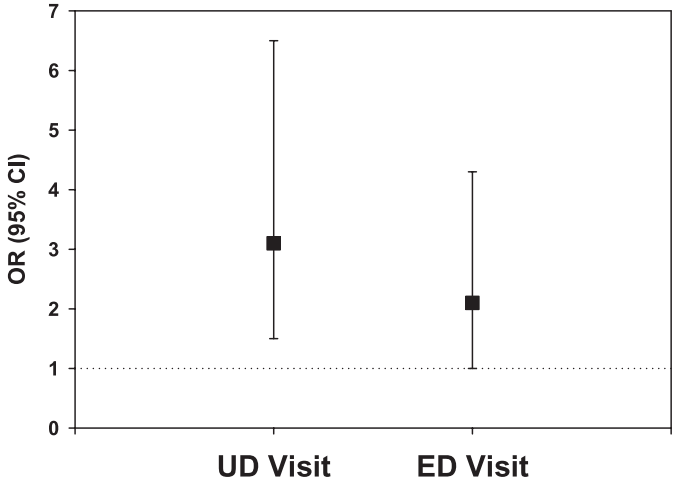

Figure 6. Asthma health care use among mouse-sensitized, highly exposed children adjusted for age, sex, atopy, cockroach sensitization and exposure, public health insurance, and study visit.

NO_2 concentrations were significantly lower in summer (15.9 ± 14.0 ppb) than in any other season. The mean ambient NO_2 concentration during the study period was 25.7 ppb, and there was minimal correlation ($r^2 = 0.056$, $P < 0.01$) between ambient and indoor NO_2 concentrations. NO_2 concentrations were higher in homes with a gas stove (mean, 33.1 ppb) compared with those without a gas stove (mean, 16.8 ppb). Similarly, the mean indoor NO_2 concentrations were 7.2 ppb higher in homes with a gas heater compared with those without a gas heater, and the presence of a gas heater had a greater effect on indoor NO_2 concentrations during the winter months.

As summarized in Figure 4, higher NO_2 concentrations were associated with statistically significant increases in respiratory symptoms in preschool children with asthma. After adjusting for potential confounders, increasing NO_2 concentrations were significantly associated with increasing frequency of limited speech due to wheezing, coughing without a cold, and nocturnal awakenings due to cough, wheeze, and shortness of breath or chest tightness during the daytime and while running. There was no significant relationship between NO_2 concentration and rescue medication use in the previous two weeks or health care utilization. In general, the presence of atopy did not modify the effect of NO_2 exposure on asthma symptoms, except that individuals with atopy were more likely to experience nocturnal symptoms with increasing NO_2 concentration (Incidence Rate Ratio [IRR] = 1.13 per 20-ppb increase in NO_2) compared with nonatopic individuals (IRR = 1.03). In addition, daily use of inhaled corticosteroids (ICS) did not modify the association of NO_2 concentrations and asthma symptoms, and mean ambient NO_2 concentrations were not significantly associated with any respiratory symptoms.

MOUSE ALLERGEN AND ASTHMA

Asthma is an allergic and inflammatory disease, and exposure to indoor allergens is a widely recognized risk factor for asthma morbidity (37). Allergens can be produced from pests (mites, cockroaches, rodents), pets (cats, dogs), plants (pollen), and fungi (mold spores). Allergens as risk factors for asthma have been widely studied (38, 39). Mouse allergen, a well-recognized occupational allergen, has only recently been identified as a common household allergen. Matsui and coworkers investigated the role of mouse allergen exposure in the BIESAK cohort and other homes in Baltimore, MD (39, 40), reporting that 100% of homes in inner city Baltimore had detectable mouse allergen in settled dust samples. In addition, airborne mouse allergen was detected in greater than 80% of the bedrooms sampled. Settled dust concentrations of mouse allergen that exceeded 0.5 μg/g were found to be predictive of having detectable airborne mouse allergen (39).

In the BIESAK cohort, both asthma symptoms and asthma-related health care use were more common among mouse-sensitized participants who had greater than 0.5μg/g of mouse allergen in their bedroom dust sample than in the others (Figures 5 and 6). The associations between mouse allergen exposure and asthma outcomes were found to be independent of cockroach sensitization/exposure, public health insurance, atopy, age, and sex.

CONCLUSIONS

Analyses of exposure outcome relationships in the BIESAK cohort and other studies mentioned in this review demonstrate the importance of evaluating indoor home air pollution sources as risk factors for asthma morbidity. Results presented indicate that indoor particulate matter (particularly the coarse fraction), NO_2, and mouse allergen exposure are important determinants of asthma morbidity in urban environments.

Avoidance of harmful exposures is a key component of national and international guideline recommendations for management of asthma (41, 42). Guidelines identify PM and NO_2 as pollutants of concern, but specific recommendations are limited and focused mostly on avoiding exposure to elevated outdoor concentrations. Objective measure of indoor air exposures may be indicated for children with uncontrolled asthma. These results from the BIESAK and other studies suggest that modifying the indoor environment to reduce PM, NO_2, and mouse allergen may be an important asthma management strategy. More research documenting effectiveness of interventions to reduce those exposures and improve asthma outcomes is needed.

Conflict of Interest Statement: P.N.B. does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript. G.B.D. served as a consultant for Merck & Co., Inc, GlaxoSmithKline ($1,001–$5,000), and Healthways ($10,001–$50,000). He served on the Board or Advisory Board for Merck & Co, Inc. ($1,001–$5,000) and received lecture fees from AstraZeneca, Pfizer ($10,001–$50,000), Boehinringer Ingelheim ($1,001–$5,000), and Schering Plough ($5,001–$10,000). He served as an expert witness for Firminich ($50,001–$100,000) and received grant support from Hill-Rom, Inc. (former Adanced Respiratory) ($10,001–$50,000), Eumdedic ($50,001–$100,000),

Asthmatix ($100,001 or more), Novartis (up to $1,000), the National Institutes of health (NIH), the Environmental Protection Agency, and Housing and Urban Development ($100,001 or more). His institution served as a consultant for Healthways ($100,001 or more). E.C.M. received grant support from the NIH ($100,001 or more). A.M.B. does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript. N.N.H. served as a consultant for Pfizer ($1,001–$5,000) and received grant support from Pfizer and the NIH ($100,001 or more). M.C.M. received lecture fees from Pfizer (Up to $1,000). Her spouse received grant support from Gilead Sciences Research Scholars Program ($50,001–$100,000). She has received grant support from the National Institute for Environmental Health Sciences and the NIH ($100,001 or more).

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