

Air pollution and lung function in children



Erika Garcia, PhD,^a Mary B. Rice, MD, MPH,^b and Diane R. Gold, MD, MPH^{c,d}

Los Angeles, Calif; and Boston, Mass

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1. To summarize literature on air pollution exposures affecting pediatric lung function and lung function growth.
2. To describe effects of various air pollutants including wildfires, indoor biomass and coal burning, gas and wood stove use, and volatile organic compounds on pediatric lung function.
3. To discuss individual/household, local/regional, and national level efforts to reduce air pollution exposures to improve child lung function.

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In this narrative review, we summarize the literature and provide updates on recent studies of air pollution exposures and child lung function and lung function growth. We include exposures to outdoor air pollutants that are monitored and regulated through air quality standards, and air pollutants that are not routinely monitored or directly regulated, including wildfires, indoor biomass and coal burning, gas and wood stove use, and volatile organic compounds. Included is a more systematic review of the recent literature on long-term air pollution and child lung function because this is an indicator of future adult respiratory health and exposure assessment tools have improved dramatically in recent years. We present “summary observations” and “knowledge gaps.” We end by discussing what is known about what can be done at the individual/household, local/regional, and national levels to overcome structural impediments, reduce air pollution

exposures, and improve child lung function. We found a large literature on adverse air pollution effects on children’s lung function level and growth; however, many questions remain. Important areas needing further research include whether early-life effects are fixed or reversible; and what are windows of increased susceptibility, long-term effects of repeated wildfire events, and effects of air quality interventions. (*J Allergy Clin Immunol* 2021;148:1-14.)

Key words: Children, lung function, FEV₁, FVC, air pollution, wildfire, gas stoves, biomass

The adverse acute effects of ambient air pollution from traffic, fossil fuel combustion, industrial facilities, and other sources on child respiratory health have been well documented in decades of research. This research has directly informed national ambient

From ^athe Department of Preventive Medicine, University of Southern California, Los Angeles; ^bthe Division of Pulmonary and Critical Care Medicine, Department of Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, ^cthe Department of Environmental Health, Harvard T.H. Chan School of Public Health, and ^dthe Channing Division of Network Medicine, Brigham and Women’s Hospital, Harvard Medical School, Boston.

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Corresponding author: Erika Garcia, PhD, Keck School of Medicine of USC, Department of Preventive Medicine, 2001 N. Soto St, SSB1 Rm 225F MC 9237, Los Angeles, CA 90089. E-mail: garc991@usc.edu.

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Abbreviations used

FVC:	Forced vital capacity
NO ₂ :	Nitrogen dioxide
NO _x :	Nitrogen oxide
O ₃ :	Ozone
PEF:	Peak expiratory flow
PM:	Particulate matter
PM ₁₀ :	Particulate matter <10 μm
PM _{2.5} :	Particulate matter <2.5 μm
US EPA:	United States Environmental Protection Agency

air quality standards for ground-level ozone (O₃), fine particulate matter (PM_{2.5} [particulate matter <2.5 μm]), and other criteria pollutants regulated by the United States Environmental Protection Agency (US EPA)¹ per the Clean Air Act, which mandates that the standard be designed to protect sensitive subpopulations including children. In the 1980s and 1990s, child lung function was assessed as a subclinical marker of acute pollution health effects in panel studies of children with and without asthma, and short-term decrements in lung function were observed with short-term increases in ambient air pollution.²⁻⁴ These early panel studies contributed biologic plausibility to the time-series studies of clinically sensitive children that demonstrated short-term increases in air pollution to be related with increases in adverse clinical events (eg, urgent care visits and hospitalization for respiratory illnesses).^{5,6} Air pollution and lung function studies also have direct clinical import for stepwise management of childhood asthma, because level of FEV₁ and FEV₁/forced vital capacity (FVC) percent predicted are used in assessment of level of asthma severity.⁷

In addition to studies showing acute effects of air pollution on lung function, a growing number of longitudinal studies have suggested adverse effects of early-life or lifetime long-term air pollution exposures on lung function growth during childhood. In contrast to lung function level, which is assessed at a single point in time, lung function growth is assessed on the basis of repeated measurements, with the difference between first and last lung function measure (size of increase) often used as a proxy for lung function development. As a body of evidence, these studies suggest that long-term childhood air pollution exposures may shift the entire population distribution of childhood lung function and lung function growth downward. This is portrayed in the hypothetical child lung function growth trajectories (Fig 1),⁸⁻¹⁰ where air pollution exposures in the prenatal period or during early childhood could result in reduced lung function growth (Fig 1: scenario b or d). Persistent or additional exposures could compound the injury by increasing the risk of early, and potentially steeper lung function decline after the plateau in early adulthood (Fig 1: scenario c or e). The consequence of either scenario could be lung function that is below the threshold for chronic obstructive pulmonary disease (postbronchodilator FEV₁/FVC below 0.70) in later adulthood.

We provide a narrative review of air pollution exposures and their associations with child lung function and lung function growth in general pediatric populations (Box 1). We primarily focus on ambient air pollutants that are primary and secondary

products of fossil fuel combustion and regulated by the US EPA (eg, PM_{2.5} and PM₁₀ [particulate matter <10 μm], nitrogen dioxide [NO₂], and O₃), reporting results separately for short- and long-term exposures. We include a more systematic review of the recent literature on long-term exposure to ambient air pollution and child lung function. We also include separate summaries of the literature on air pollution that is not currently regulated or covered by the Clean Air Act but may have adverse child lung function effects. Specifically, we focus on air pollution from wildfires, indoor biomass and coal burning, gas and wood stove use, and volatile organic compounds (VOCs) from household products. Exposure data and research on child lung function outcomes are much sparser for these pollutants compared with the large body of evidence on the outdoor criteria pollutants. For each section, we provide boxed statements of “summary observations” and “knowledge gaps.”

Although some families may have a few options to improve their children’s health by reducing air pollution exposures at home and during the school day, for consequential exposure reduction across the population, structural changes and regulations at national, regional, and local levels are required. As neighbors and citizens, individual families can influence structural change and regulation, for example, by advocating for electric buses, traffic-free zones, wildfire mitigation strategies, or public housing upgrades (eg, ventilation and new stoves)—we acknowledge, however, that not all are empowered to do so. In the final segment of this review, we share summary observations (and knowledge gaps) about what can be done at the individual/household, local/regional, and national levels to reduce air pollution exposures and improve child lung function, thereby improving child and subsequent adult respiratory health. In addition, suggestions for future research are made.

We briefly describe our review methods. We searched the database PubMed with combinations of the following search terms: “lung function,” “pulmonary function,” “pollution,” “pollutant,” “traffic,” “child,” “children,” “childhood,” “adolescent,” “adolescence,” “in utero,” “prenatal,” and “early life.” We also searched using the following MeSH terms in combination: “lung function test,” “air pollutants, environmental,” and “children.” Studies not in English were excluded, but we did not restrict by country—the scope was global. We conducted our search on October 15, 2020. We also reviewed the most recent US EPA Integrated Science Assessments for nitrogen oxide (NO_x), PM, and O₃ for additional citations.¹¹⁻¹³ The Integrated Science Assessments were also helpful in providing context for interpretation of individual citations, because they provided a committee-based comprehensive review of experimental, toxicologic, and epidemiologic data to evaluate the specificity, temporality, and plausibility of associations of specific pollutants with a large range of child and adult health outcomes. Studies of household air pollution and wildfire smoke are not consistently reported as studies of pollution, and therefore we extracted studies from the above PubMed search and performed additional targeted literature searches using the terms “wildfire,” “smoke,” “household air pollution,” “gas stove,” “wood stove,” “biomass burning,” and “volatile organic compounds” to review the sparser literature on household/indoor and wildfire pollution and child lung function. In select cases in which epidemiologic evidence is scant and toxicologic data were compelling to us (eg, O₃ effects on lung development relevant to growth), we drew from the toxicology literature. We provide a complete summary of all studies

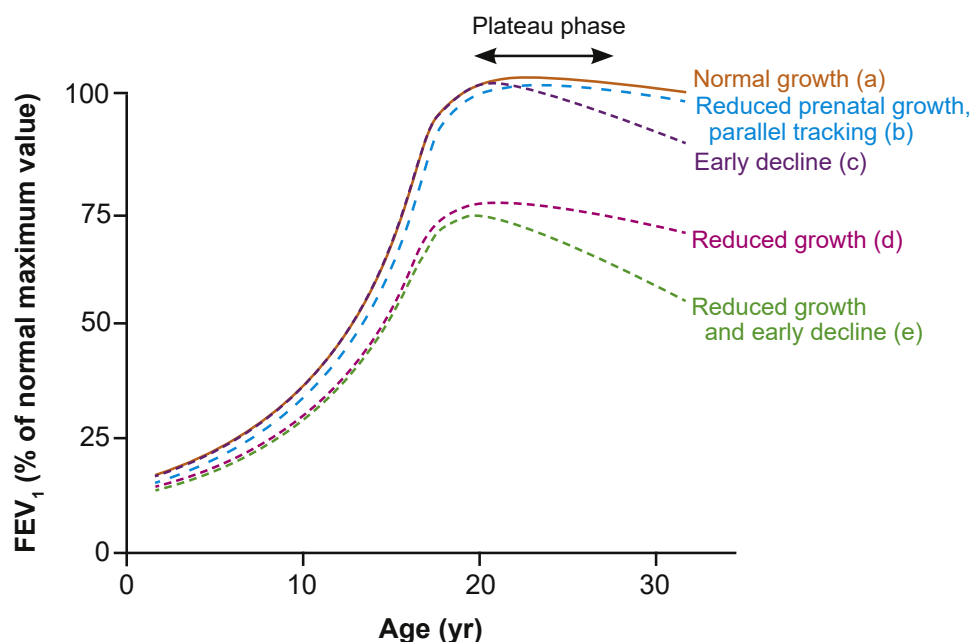


FIG 1. Hypothetical lung function trajectories depicting normal and reduced growth and early decline.⁸⁻¹⁰ (a) Normal pattern of lung function growth. (b) Reduced prenatal growth, with postnatal growth tracking at a fixed percent predicted lower than normal. (c) Normal growth until late teen years, when peak lung function growth is reduced, and lung function begins to decline early. (d) Reduced growth and (e) reduced growth with early decline. Both (d) and (e) can result in levels of lung function consistent with diagnosis of chronic obstructive lung disease. Adapted from McGeachie et al.¹⁰

found in our search that were published 2018 or later only for long-term ambient air pollution exposure and lung function level or growth because long-term exposure assessment has improved in the past several years due to satellite data availability, child lung function level and growth is a key indicator of future adult respiratory health, and these most recent studies have not previously been included in previous reviews.

SHORT-TERM AMBIENT AIR POLLUTION EXPOSURE AND CHILD LUNG FUNCTION

A large literature indicates that short-term air pollution exposures can acutely reduce lung function in children. This literature has been previously reviewed,¹¹⁻¹⁶ and we will briefly summarize the findings here, focusing on studies of acute effects of ambient gases and particles in general pediatric populations. See [Box 2](#) for a summary of this section. It is important to recognize that in panel studies of children—as well as any observational air pollution study—, inhalation exposure is to a mixture of air pollutants; thus, the responses being measured are responses to that mixture. Air pollutant mixtures, however, may be dominated by one pollutant, or another, depending on the source of the mixture and whether the pollutant mixture is dominated by local sources (eg, local traffic or nearby industries with ground-level emissions of primary pollutants), or regional pollution, with exposure to transported primary and secondary pollutants. Nevertheless, below we report a summary of studies that focused on specific pollutants, sometimes interpretable as representing sources or mixtures, and their acute influences on children's lung function.

Higher O₃ exposure has been linked with lower levels of lung function (both FEV₁ and FVC) in healthy children and those

with asthma, with much evidence coming from panel studies of children attending schools or summer camps.^{12,14,17-20} Short-term PM_{2.5} exposure has been associated with acute decrements in lung function, including lower FEV₁/FVC, in healthy pediatric populations.^{13,21} Short-term PM₁₀ exposure has also been linked with acute lung function decrements in children.^{22,23}

Epidemiologic studies have found associations between higher short-term ambient NO₂ (often considered as an indicator of exposure to traffic-related air pollution) and acute lung function decrements in children,^{11,16,24,25} although not all studies support this relation.^{26,27} For observed NO₂ associations, there is uncertainty as to whether NO₂ is the causal factor, there is confounding by correlated pollutants (eg, PM_{2.5}), or NO₂ serves as a representation of a pollution mixture (eg, traffic pollution) that is the causal factor.¹¹

Often at significantly higher levels of exposure than in the United States, recent panel studies of schoolchildren from sub-Saharan Africa, Bangladesh, and China add supporting evidence for acute lung function impacts of NO₂²⁸ and PM_{2.5}²⁹⁻³¹ and PM₁₀.^{29,31} Air pollution concentrations at study locations are important to consider (ie, whether concentrations are below or well above recommended US EPA/European standards). In settings of low air pollution levels, greater sample size is needed to detect associations should they exist.

Wildfires

Air quality regulations, technological advances such as improved catalytic converters, and a transition away from coal burning in many regions of Europe and the United States have contributed to a downward trend in outdoor PM pollution. Despite

Box 1. Why study effects of ambient air pollution on lung function in children?**Why children?**

- More susceptible to pollution effects due to developing physiology
- Increased exposure due to size and behavior

Why lung function?

- Subclinical marker with short- and long-term clinical implications for lung health across the lifespan
- Clinical outcome measure in children with asthma, cystic fibrosis, and other chronic lung diseases

these advances, in the Northwestern United States and Northern California, air quality has in fact *worsened* between 1988 and 2016 as a result of wildfire activity in the United States and Canada.³² In the United States, wildfires have become the number 1 single source of PM and contribute more than a third of the total annual burden of PM_{2.5} in the atmosphere according to the US EPA Emissions Inventory.³³

North America has experienced a sharp increase in the frequency of large, devastating wildfires as a result of longer, hotter fire seasons due to climate change, and years of fire suppression that have led to an overaccumulation of fire-prone organic matter.³⁴ Many other parts of the world, including Australia, Brazil, Southeast Asia, and Russia, are also grappling with increased wildfire activity—a worrisome trend that will continue globally due to climate change.

The composition of wildfire smoke varies depending on the type of fuel burned (eg, forests, grasslands, peat bogs, and human-made structures). Wildland smoke includes not only high levels of particles from organic sources but also gases such as carbon monoxide, NO_x (which also lead to O₃ formation), and VOCs including carcinogens such as benzene, benzo[a]pyrene, formaldehyde, and acetaldehyde.^{34,35} Even though wildfire smoke events may be relatively short in duration (eg, days to weeks), the pollution levels can be extremely high. For example, PM_{2.5} levels in San Francisco exceeded 200 µg/m³ during the Camp Fire, whereas the average PM_{2.5} level for the city is about 9 µg/m³. In addition, smoke travels great distances. Children living in wildfire-prone areas today are exposed to smoke pollution from multiple regional fires during each wildfire season, which now continues for weeks to months longer than the wildfire season of a generation ago.

The respiratory effects of individual wildfire smoke pollutants (eg, PM_{2.5}, NO_x, and O₃) are likely to be similar to the effects of those pollutants as identified in epidemiologic and mechanistic studies without regard for emission source. However, the composition of PM_{2.5} emitting by burning wildlands is different from that of PM_{2.5} emitted by fossil fuel combustion, and there are likely to be unique airway toxicities of the complex wildfire-generated smoke mixture of gases and particles. Among children (and adults) with asthma, for example, PM_{2.5} from wildfires appears to be more likely to trigger an asthma exacerbation per unit mass than PM_{2.5} from other sources, suggesting a possible enhanced inflammatory effect of the wildfire smoke mixture on asthmatic airways.^{36,37} There is evidence that healthy children who have smaller airways, as determined by a low ratio of the forced expiratory flow at 25% to 75% of the pulmonary volume to the FVC, are more likely to experience respiratory symptoms

Box 2. Short-term ambient air pollution exposure and children's lung function**Summary observations**

- Short-term exposure to O₃ and particle pollution (PM_{2.5} and PM₁₀) has been associated with lower lung function, including lower FEV₁, FVC, and FEV₁/FVC, in generally healthy children and in those with asthma
- Large wildfires are occurring at increasing frequency and are a major source of PM and other pollutants
- PM_{2.5} levels during wildfires can reach extreme concentrations that far exceed air quality standards and are associated with acute decrements in peak expiratory flow
- Short-term elevations in NO₂ levels outdoors and indoors have been associated with reduction in child lung function

Knowledge gaps

- Need to improve understanding of the extent to which observed acute effects of NO₂ on child lung function are causal, due to confounding by correlated pollutants (eg, PM_{2.5}), or represents a pollution mixture that is causal (eg, traffic pollution)
- Need to evaluate the long-term consequences of repeated exposure to wildfire smoke on child lung function

when exposed to wildfire smoke than children with normal lung function.³⁸ These findings suggest an acute inflammatory effect of wildfire smoke on small airways.

Relatively few studies have examined the acute effects of short-term exposure to wildfire smoke on child lung function. A panel study measuring daily peak flow among 234 generally healthy schoolchildren aged 6 to 15 years exposed to seasonal wildfires in the Brazilian Amazon found that higher levels of PM₁₀ and PM_{2.5} in the preceding 5 days were associated with lower peak flow.³⁹ In this study, younger children (aged 6-8 years) experienced greater decrements in peak expiratory flow rate in association with wildfire-PM than older children. A panel study of 309 schoolchildren exposed to smoke from biomass burning in the Brazilian Amazon also found associations between short-term PM_{2.5} exposure and daily peak expiratory flow rate, with greater effects for children without asthma.⁴⁰ In one of very few studies of chronic effects of wildfires on child lung function, infants exposed to a 6-week coal mine fire had lower lung reactance as measured by forced oscillation technique at age 3 years in association with their level of PM_{2.5} exposure during the fire.⁴¹ A study of rhesus macaque monkeys exposed as infants to ambient smoke from a series of Northern California wildfires in 2008 while housed in an outdoor colony had lower lung function at age 3 years compared with unexposed monkeys.⁴² These studies suggest that such extreme fire pollution events may have long-term sequelae for lung function growth. However, there is a need for more studies on the chronic effects of long-term and repeated exposure to wildfire smoke on child lung function level and lung function growth.

LONG-TERM AMBIENT AIR POLLUTION EXPOSURE AND CHILD LUNG FUNCTION**Associations with subsequent level and growth of lung function**

We first summarize the literature on long-term air pollution exposure and children's lung function in general pediatric

Box 3. Long-term ambient air pollution and children's lung function

Summary observations

- A large number of studies support a relation between early-life or long-term air pollution exposures and subsequent children's lung function level, with the most epidemiologic evidence for PM_{2.5} and NO₂
- There is inconsistent evidence of an effect of early-life or long-term exposure to O₃ on subsequent children's lung function, although animal model studies suggest prenatal or early-life O₃ effects on lung development
- Associations with long-term exposures are more consistent for FEV₁ compared with for FVC, which may indicate greater impacts on airway caliber/airflow obstruction than overall lung size or growth

Knowledge gaps

- Although there is evidence that air pollution exposure at all ages in childhood can have adverse lung function effects, few studies have evaluated whether timing or cumulative period of exposure influences whether pollution effects are fixed or reversible
- Long-term consequences of air pollution on reduced lung function development/growth/trajectories in childhood are not fully understood; studies need to investigate impacts of childhood exposures on lung function in adulthood as well as risk for later respiratory health, such as chronic obstructive pulmonary disease, emphysema, fibrosis, or pulmonary vascular disease
- Need to further assess the toxicity of specific PM components and sources on lung function

populations and then present the findings from our systematic review of studies since 2018. Studies up to through approximately 2018 have been previously reviewed or summarized.^{11-14,43} See [Box 3](#) for a summary of this section. A range of exposure windows, both in duration and in timing, have been considered in previous studies. In studies of chronic air pollution exposure, lung function outcomes have often been assessed either (1) at a single time point (eg, at age ~12 years; "lung function level") or (2) at relatively few repeated time points with the difference (size of increase) between first and last lung function measure sometimes used as a proxy for lung function development (eg, change in FVC between ages 8 and 16 years; "lung function growth"). We should note, however, that the use of only 2 to 3 repeated measures to represent lung function growth over time may lead to limitations in interpretation of the outcome (see below).

In their recent comprehensive review that extended beyond examination of the literature on traffic exposure and lung function to include pollution exposures from other sources, Schultz et al⁴³ concluded that regardless of the timing of exposure, early-life and school-age exposure to traffic-related air pollution adversely affects children's lung function. The authors did not find firm evidence from the studies evaluated that exposure during certain age windows was more relevant for subsequent lung function. They instead concluded that exposure over the entire childhood period is of importance but suggested that more studies may be needed to define whether children were more vulnerable at specific life stages.⁴³

Defining effects of specific long-term pollutant exposures by particle size fraction, particle component, or level of pollutant gases

A large number of studies provide evidence that long-term PM_{2.5} is associated with lower lung function levels and slower lung function growth in children.¹³ Studies have been conducted in multiple cohorts from several locations, with differing exposure assessment methods and from different time periods, adding to the robustness of the evidence. The evidence for the larger size range of PM₁₀—which includes road dust (tire and brake wear, road salt), wildfires smoke, and aeroallergens—is less robust due to lower availability of long-term PM₁₀ models.¹³ Two studies that have been conducted, both in Europe, have found null associations between long-term PM₁₀ exposure and child lung function.^{44,45} Recently, there is a renewed interest in the study of the coarse particle fraction (2.5-10 μm; PM_{10-2.5}),⁴⁶ which is primarily composed of organic debris, crustal elements, and suspended road dust metals.⁴⁷ The effects of particles in this size fraction on child lung function, possibly mediated through their effects on the upper airway, including the nose, is an area of active investigation.⁴⁸

Associations between long-term NO₂ exposure and decrements in lung function levels in children are also well documented in the epidemiologic literature from studies in various locations with varied follow-up time and using different methods for exposure assessment and lung function measurements.¹¹ The evidence for adverse NO₂ effects is stronger for FEV₁, representing airway mechanical properties and/or airway caliber, compared with that for FVC, representing lung volume.¹¹ Uncertainty, however, remains as to whether NO₂ is the causal agent, whether results are confounded by copollutant exposure, or whether NO₂ represents a source that is the causal factor. Results from NO₂ models with adjustment for PM_{2.5} are mixed, and it is therefore difficult to conclude whether the NO₂ associations with lung function are explained by effects of traffic particles that are imperfectly measured by NO₂ and PM_{2.5}.¹¹

Based on epidemiologic studies previously reviewed, studies with evidence supporting associations of long-term O₃ exposure with lower lung function levels and growth are inconsistent, suggesting perhaps that this pollutant may have its greatest chronic effects in regions of the world where exposure is more constantly elevated and where indoor penetration of outdoor air is greater.^{12,49-55} Toxicologic studies involving rodents and primates, in contrast, provide support of prenatal or early-life effects of O₃ exposure on lung development, with suggestive evidence in Shore et al's rodent models of interactions among O₃, diet/obesity, and allergen exposures in their influences on the risk of airflow obstruction.^{12,56-62}

Following up on these previous thorough reviews and summaries, in [Table I](#) and in the text below we present a summary of recent lung function studies of general pediatric populations and long-term air pollution exposure assessment published since 2018, using the literature search methodology described in the Introduction section. We defined long-term air pollution exposure as exposure in some earlier time period (ie, not concurrent, and not only the preceding 12 months). Lung function assessment must have included one of the following measures: FEV₁, FVC, or forced expiratory flow at 25%-75% of the pulmonary volume (the latter being the same as mean flow between 25% and 75% of FVC and maximum midexpiratory flow). We identified 8

TABLE I. Summary of studies on long-term air pollution and lung function in healthy or population-based children published since 2018

Reference	Population (location, cohort name)	Study design	Exposure focus	Exposure assessment	Lung function assessment	Results
Cai et al, ⁴⁴ 2020	5276 children at age 8 y, 3446 children at age 15 y (Avon in southwest England, ALSPAC)	Prospective birth cohort	Prenatal and childhood air pollution	PM ₁₀ during each trimester, 0-6 mo, 7-12 mo, and up to age 15 y	FEV ₁ % predicted and FVC% predicted at ages 8 and 15 y	- At age 8 y, PM ₁₀ was associated with lower FEV ₁ % predicted and FVC% predicted - At age 15 y, no observed adverse association with lung function
Usemann et al, ⁶³ 2019	232 children at age 6 y (Bern, Switzerland, BILD)	Prospective birth cohort	Low to moderate air pollution levels, from pregnancy until school-age	NO ₂ , O ₃ , PM ₁₀ during each pregnancy, first year of life, sixth year of life, and birth until follow-up	FEV ₁ , FVC, FEV ₁ /FVC ratio, and FEF ₂₅₋₇₅ measured at age 6 y	- NO ₂ exposure during pregnancy and first year of life was associated with decreased FEV ₁ - Null associations observed for O ₃ and PM ₁₀
He et al, ⁶⁴ 2019	2942 children at age ~17.5 y (Hong Kong, "Children of 1997" cohort)	Prospective birth cohort	Prenatal and childhood air pollution	NO, NO ₂ , PM ₁₀ , and SO ₂ during pregnancy, age 0-2 y, and age 2-8 y	FEV ₁ , FVC, FEF ₂₅₋₇₅ , and FEV ₁ /FVC ratio measured at age ~17.5 y	- Higher NO and NO ₂ <i>in utero</i> , age 0-2 y and age 2-8 y were consistently associated with lower FEV ₁ , FEV ₁ /FVC, and FEF ₂₅₋₇₅ in multipollutant analysis - SO ₂ and PM ₁₀ were not associated with lung function
Milanzi et al, ⁴⁸ 2018	915 children for the age 8-16 y growth analysis, 721 for the age 16-y analysis (The Netherlands, PIAMA)	Prospective birth cohort	Air pollution exposure from birth	NO ₂ , PM _{2.5} , PM ₁₀ , and PM coarse during preschool, primary school, and secondary school time windows	FEV ₁ and FVC measured at age 16 y, and FEV ₁ and FVC growth from ages 8 to 16 y based on repeated measures at ages 8, 12, and 16 y	- Exposure during the preschool period was associated with reduced FEV ₁ growth for all pollutants - No association with FVC growth, except for a positive association with PM _{2.5} - Across pollutants and time periods, higher air pollution was associated with lower FEV ₁ at age 16 y - Inverse associations were also observed for FVC at age 16 y, but these were not statistically significant
Tsui et al, ⁶⁵ 2018	1016 children age 6-15 y (Taiwan)	Nationwide, cross-sectional, school-based survey	Lifetime residential exposure to air pollution	PM ₁₀ , O ₃ , SO ₂ , NO ₂ , and CO during first year of life, age 2-6 y, and lifetime	FEV ₁ , FVC, FEF ₂₅₋₇₅ , and FEV ₁ /FVC ratio measured once among children at mean age 11.9 y (SD, 2.4)	- Lifetime PM ₁₀ and O ₃ was associated with lower FEV ₁ , FVC, and FEF ₂₅₋₇₅ - NO ₂ was associated with FEV ₁ and FVC in all exposure windows examined - CO showed some association with lower lung function - SO ₂ was not associated with lung function

(Continued)

TABLE I. (Continued)

Reference	Population (location, cohort name)	Study design	Exposure focus	Exposure assessment	Lung function assessment	Results
Bougas et al, ⁶⁶ 2018	788 children age 8-9 y (Paris, France, PARIS)	Prospective birth cohort	Traffic-related air pollution	NOx during each trimester and entire pregnancy, first year of life, and lifetime	FEV ₁ , FVC, and FEF ₂₅₋₇₅ measured at age 8-9 y	- Prenatal NOx exposure during the entire pregnancy was associated with a lower FEF₂₅₋₇₅, but there were no significant associations with FEV₁, FVC, or FEV₁/FVC ratio - Associations were similar for NOx exposure during the second trimester, but associations were null for the first and third trimesters - Null associations for first year of life and lifetime exposure
Bose et al, ⁶⁷ 2018	191 children age 5-8 y (Boston, USA, ACCESS)	Prospective birth cohort	Prenatal NO ₃ - exposure	NO ₃ - during pregnancy by gestational week	FEV ₁ , FVC, FEF ₂₅₋₇₅ , and FEV ₁ /FVC ratio measured once among children at mean age 7.0 y (SD, 0.89)	- No statistically significant sensitive window was identified in the overall population - Shape of the associations across gestation suggests an early window in pregnancy during which higher exposure to nitrates may be associated with reduced FEV₁ - Cumulative effect over entire gestation suggested an inverse association, but results were not statistically significant
Bergstra et al, ⁶⁸ 2018	424 children age 7-13 y (East Vliissingen in southwest of The Netherlands)	Cross-sectional study	Long-term air pollution from heavy industry	PM _{2.5} and NOx during previous 5 y	FVC, FEV ₁ , PEF, FEF ₂₅₋₇₅ , FEV ₁ /FVC ratio measured once among children between the ages of 7 and 13 y	- PM_{2.5} and NOx were associated with lower PEF - Higher NOx was associated with lower FVC and FEV₁

ACCESS, Asthma Coalition on Community, Environment and Social Stress study; ALSPAC, Avon Longitudinal Study of Parents and Children; BILD, Basel Bern Infant Lung Development birth cohort; CO, carbon monoxide; FEF₂₅₋₇₅, forced expiratory flow at 25%-75% of the pulmonary volume; NO₃-, nitrate; PARIS, Pollution and Asthma Risk: an Infant Study birth cohort; PEF, peak expiratory flow; PIAMA, Prevention and Incidence of Asthma and Mite Allergy birth cohort; SO₂, sulfur dioxide.

studies fitting these criteria. Five of the studies were based in Europe,^{44,48,63,66,68} 2 in Asia,^{64,65} and 1 in the United States.⁶⁷ Of these 8 studies, 4 included exposure to NO₂, all of which found a negative association with lung function; 2 included O₃, of which 1 found a negative association with lung function; 1 included PM_{2.5}, which found a negative association with lung function; and 5 included PM₁₀, of which 3 found a negative association with lung function. Although all studies examined lung function levels, only 1 study⁴⁸ also examined lung function

growth. This study, the Dutch Prevention and Incidence of Asthma and Mite Allergy cohort, assessed associations between air pollution exposure from birth to age 4 years and lung function growth between ages 8 and 16 years in 721 children. They included into their models an exposure-age interaction term—which can be interpreted as the association of pollution exposure with annual rate of change in lung function.⁴⁸ They reported that PM_{2.5} exposure was related to reduced FEV₁ growth.⁴⁸

Our review of recent literature highlights the small number of assessments of lung function growth in studies of long-term air pollution at contemporary levels of exposure. As illustrated with hypothetical growth curves in Fig 1, the trajectories of lung function growth can be tracked throughout childhood, with assessment of whether children attain normal peak growth and avoid a steep decline that could lead to chronic obstructive pulmonary disease or other respiratory deficits shown to be predictive of higher morbidity or mortality (Fig 1). More frequent longitudinal outcome measurements and more precise exposure estimates during critical childhood life stages offer more opportunities for investigators to assess whether and when air pollution perturbs lung function growth, and whether any deficit in growth can be recovered with reduced air pollution exposure (eg, through regulation to reduce emissions or limit exposure to pollution sources at school, or interventions to purify the air). Single measures of lung function during adolescence are particularly challenging, because estimates of lung function growth during this period need to consider height growth and where the children are in their growth spurt, which differs by sex.⁶⁹ Although challenging to perform, studies with repeated pulmonary function testing across childhood and adolescence would add important data to the literature by enabling evaluation of more nuanced aspects of the pollution-lung function growth relation, such as pollution effects on lung function growth velocity (ie, time-varying rate of growth); whether effects are fixed or reversible; or whether effects differ by timing of exposure (eg, during puberty—a period of great somatic growth related to lung development).

Studies evaluating effect of air pollutant mixtures

Continued child lung function research should consider the context of air pollution mixtures when examining health effects. Such considerations can refer to a number of different research questions, such as Which pollutant is the causal agent in this mixture? Do pollutants interact in their health effect? What is the overall effect of the mixture?⁷⁰ Air pollution studies often examine one pollutant at a time due to statistical realities regarding multicollinearity for highly correlated pollutants. Some studies of child lung function have implemented multipollutant models examining the effects of multiple pollutants in a single model (eg, PM_{2.5} and NO₂ together as explanatory variables in a single model), often just 2 pollutants,^{25,71,72} although some studies have included more.⁴⁹ This type of approach is often used to answer the first question above, “Which is the causal agent or dominant mixture/cluster associated with the adverse outcome?”⁷⁰ There have been several recent advancements in mixture model approaches^{70,73,74}—a research area of great interest in environmental epidemiology—that could be implemented in studies of child lung function to improve understanding of air pollution effects. Overall, however, disentangling the effects of individual pollutants is challenging and often not possible in observational studies in children, as compared with toxicologic studies and controlled human exposure studies in adults, which themselves have limitations in terms of size, generalizability, and potential to measure long-term as opposed to short-term exposure responses. Nevertheless, complementary studies from these and other fields will continue to be needed to evaluate causality and understanding potential biologic mechanism. In some cases, removing or reducing the exposure and witnessing the

Box 4. Indoor sources of air pollution and children’s lung function

Summary observations

- Worldwide, young children are often highly exposed to smoky household air pollution from biomass burning for heating and cooking at a very critical age when their lungs are developing
- There are a few trial studies providing evidence that installation of clean chimney stoves in infancy may lead to more rapid lung function growth
- Installation of clean stoves can improve indoor air pollution, but levels of indoor/outdoor pollution may remain elevated (though lower than previously) and these reductions are inconsistently associated with improvements in lung function

Knowledge gaps

- Gas stoves
 - Need to understand who is more susceptible to the adverse lung function effects of gas stove pollution
 - Need to understand the extent to which gas stove-related lung function decrements are improved or prevented with improved kitchen ventilation
- Biomass and coal burning cook stoves
 - Need to assess what additional exposures or factors in the use of multiple fuel sources or lack of stove maintenance are responsible for the inconsistencies in effects of provision of clean stoves and improved indoor ventilation on child lung function
- Additional research is needed on the effects of VOCs on child lung function to corroborate the few existing studies that provide evidence of adverse effects

improvement in health have been the strongest evidence for causality.

INDOOR SOURCES OF AIR POLLUTION AND CHILD LUNG FUNCTION

Young children often spend most of their time at home, where they are exposed to household air pollution (from household sources such as cooking and heating) and ambient pollution (from outdoor sources) that penetrate inside the home. Here, we review the literature on 3 major sources of household air pollution—biomass burning, gas stove use, and VOCs—and child lung function. See Box 4 for a summary of this section.

Indoor biomass and coal burning

In low- and middle-income countries, biomass burning for cooking or heating is a major source of air pollution inside the home, and in the neighborhood if vented to the outdoors. The few studies of indoor biomass or coal burning for cooking or heating have generally found that these exposures are associated with lower lung function in children.^{75–80} The largest of these followed more than 3000 children aged 6 to 13 years with repeated lung function measures in 4 Chinese cities and found that use of coal as a household fuel was associated with a 16.5 mL/y (95% CI, –23.6 to –9.3) lower annual growth of FEV₁ and a 20.5 mL/y (95% CI, –28.3 to –12.7) lower growth of FVC.⁷⁸ This study also found that household ventilation improved lung function growth. A small number of intervention studies in low-income countries have examined the effect of placing clean cookstoves

in homes to improve indoor air quality. Most of these have examined childhood pneumonia as the primary outcome, with mixed results.⁸¹ The Randomized Exposure Study of Pollution Indoors and Respiratory Effects (RESPIRE) trial placed clean chimney stoves in households with pregnant women and infant children in Guatemala either at baseline or 18 months later. Among the 440 children with longitudinal spirometry testing, delayed (18 months) chimney stove placement was associated with slower peak expiratory flow growth of 173 mL/min/y (95% CI, -341 to -7) and slower FEV₁ growth of 44 mL/y (95% CI, -91 to 4).⁸² This suggests an effect of early-life indoor air quality on lung function growth that may not be fully reversible with a subsequent air quality intervention, and that household air quality interventions during infancy may have lasting lung function benefits.

Indoor biomass burning is a phenomenon not only in low- and middle-income countries. Wood-burning stoves are a common source of heating in many high-income countries. In the United States, wood stove use has been increasing over the past 2 decades, and it has been estimated that 11 million households and more than 3 million children are exposed to higher levels of indoor particulate matter due to the use of wood-burning stoves for heating.⁸³ In a recent narrative review of 36 studies conducted in developed countries on the pediatric health effects of wood smoke exposure, estimated community-level wood smoke exposure was consistently associated with child respiratory symptoms, whereas findings on wood stove use were less consistent.⁸⁴ There are few studies of wood stove use and child lung function. The recent review identified a single study, which was conducted in Turkey among 617 schoolchildren aged 9 to 12 years and found lower average child lung function among those living in households using wood stoves.⁸⁵ Pediatric research on wood stove use has relied on self-reported questionnaire data, and there is a clear need for studies that measure wood smoke pollution in the home to arrive at a more precise estimate of household air pollution exposure.⁸⁴

Gas cooking

Gas cooking is a common source of indoor NO₂ in low-, middle-, and high-income countries, with peak indoor NO₂ levels during cooking far exceeding exposure to NO₂ from outdoor sources that penetrates indoors.⁸⁶ In fact, it has been estimated that more households are exposed to indoor NO₂ levels above the 1-hour US EPA national ambient air quality standard for NO₂ due to use of unvented gas stoves than NO₂ emitted by outdoor pollution sources that enters the home.⁸⁷ Although controlled human exposure studies have yielded inconsistent results regarding the acute effects of NO₂ gas alone on lung function at typical outdoor NO₂ exposure concentrations (up to 20 ppb), indoor NO₂ concentrations can exceed 100 ppb (especially in the absence of outdoor kitchen ventilation),⁸⁷ and among adults such concentrations have been linked to oxidative stress and acute decrements in lung function.⁸⁸ Numerous individual studies have examined whether gas stove cooking is associated with lower lung function in children, with inconsistent findings.^{89,90} Inconsistencies may vary in part by whether the gas stove has a continuously burning pilot light, whether it is vented to the outdoors, whether it is used for heating the home, and also by the amount of air exchange in the home. A meta-analysis combining data from 24,000 children in Europe and North America concluded that gas stove cooking is

associated with a small but significant reduction in FEV₁ (0.7%) and FVC (0.6%), with evidence of greater effect sizes among children with atopy.⁹¹ This suggests a reduction in average lung function among healthy children with gas stoves in the home, and that children with allergic phenotypes may be more susceptible. If true, this would add to a very long and complicated literature on the effect of gas stove use on risk of childhood asthma and respiratory symptoms among children with asthma or atopy.^{92,93}

There is also some evidence that gas stove ventilation can mitigate the effect of gas stoves on lung function: in National Health and Nutrition Examination Survey (NHANES) III, girls living in households with gas stoves using ventilation had higher FEV₁ and FEV₁/FVC than those with gas stoves and no ventilation.⁹⁴ This suggests an opportunity to improve child lung function through household interventions such as improved ventilation or replacement of gas stoves with electric models.

Volatile organic compounds

VOCs include a wide range of chemicals, and although emission sources are numerous and varied, most are emitted from indoor sources such as paints and floor coverings, building materials and furnishings, and consumer products (eg, cleaning supplies, air fresheners, and hobby supplies).⁹⁵⁻⁹⁷ Outdoor sources (eg, industrial facilities, dry cleaners, and gasoline stations) and attached garages can also contribute to residential VOC exposure.^{96,98} Concentrations of many VOCs are often higher indoors compared with outdoor levels.^{96,99}

Adverse effects of VOCs on children's respiratory health have been reported,¹⁰⁰⁻¹⁰² but there are very few studies examining associations with lung function in children.¹⁰³⁻¹⁰⁶ A Canadian study measured 84 VOCs in residential indoor air and report that among the 709 participants aged 6 to 16 years there were significant reductions in lung function observed for 9 VOCs.¹⁰³ The largest associations were a 9.0% decrease in FEV₁ (95% CI, -15.4 to -2.6), associated with an interquartile range change in nonanal, and a 5.1% change in FEV₁ (95% CI, -9.2 to -1.0), associated with an interquartile range change in 2-furancarboxaldehyde.¹⁰³ A study of 772 Mexican preschoolers examined prenatal VOC exposure and lung function measured with forced oscillation tests at age 36, 48, and 60 months.¹⁰⁴ Negative associations between prenatal exposure to xylene and respiratory reactance were reported, but null associations for benzene and toluene were found.¹⁰⁴ Data from a South African birth cohort with lung function measured at age 6 to 10 weeks among 645 infants demonstrated higher levels of household benzene to be associated with lower early lung function as measured by the forced oscillation technique.¹⁰⁵ Higher levels of prenatal exposure to benzene were associated with clinically significant deficits in FEV₁ among 620 Spanish preschoolers (aged 4.5 years); however, this study used estimates of outdoor (not indoor) benzene levels at residential address.¹⁰⁶ Given the expansive sources of VOCs and their ubiquitous presence in the air, especially indoors, coupled with this small literature, their effects on child lung function merit further research.

WHAT CAN BE DONE?

There are several actions that can be taken to reduce children's exposure to air pollution, implemented at a range of control levels from individuals and families to national policies (Fig 2).

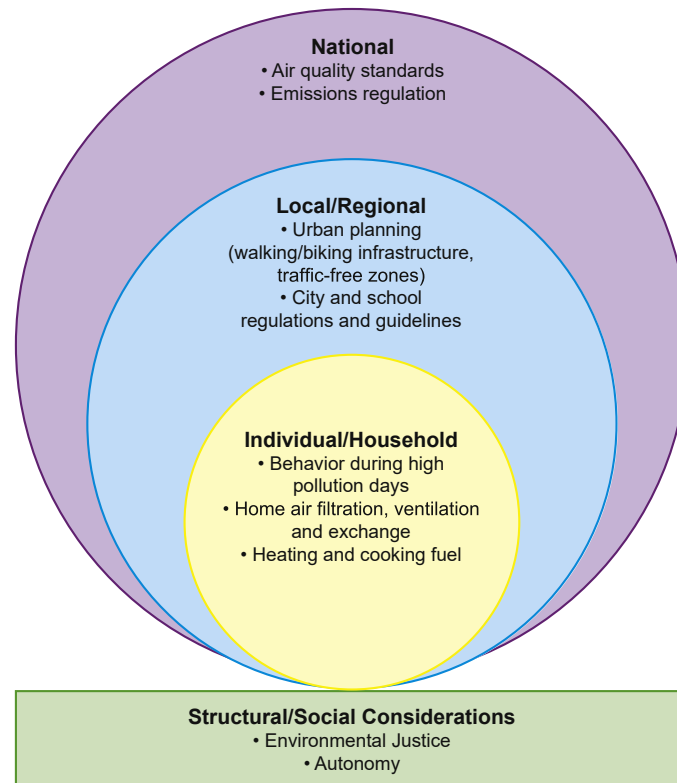


FIG 2. Examples of current or potential air pollution interventions at various intervention levels.

Interventions at higher levels (eg, national air quality standards) would impact a larger number of people compared with actions taken at smaller scales (eg, an air filtration unit will reduce exposure only for those within the household). To be clear, we are not recommending each of the interventions; instead, when there is sufficient or reasonable evidence, then such interventions could be considered and implemented.

Individual and household interventions

Several studies of air pollution interventions at the household and individual levels have identified subsequent improvements in child respiratory health (though not always including lung function as an outcome). As discussed above, improved kitchen ventilation and placement of clean cookstoves appear to benefit child lung function, especially if done early in life. Short-term use of indoor air purifiers has been found to lower airway resistance in adults¹⁰⁷ and appears to improve asthma symptoms,¹⁰⁸ but any long-term benefits of indoor air filtration on child lung function or lung function growth remains unknown.

National and local policies to improve outdoor air quality

Several studies have taken advantage of changes—usually reductions—in air pollution levels to investigate subsequent impacts on children's lung function. These studies add to the evidence of a causal relationship between air pollution and respiratory health, directly relating to the “experiment” viewpoint of the Bradford Hill criteria for causality.¹⁰⁹ If lung function

is adversely impacted by higher air pollution exposure—and these relations are truly causal—then it is expected in situations of improved air quality that benefits in lung function would be observed. Here, we provide a brief review of studies that have used this approach.

During the 1990s, the reunification of Germany saw marked declines in air pollution levels, including for total suspended particles and sulfur dioxide, and several studies of schoolchildren from East and West Germany reported associated improvements in lung function primarily based on consecutive cross-sectional surveys between 1992 and 1999.^{110,111} Using multiple prospective cohorts consecutively recruited in the 1990s and early 2000s in the Southern California Children's Health Study, studies have reported observed improvements in air quality to be associated with improved lung function in schoolchildren.^{50,52,55,112} In the most recent of these Children's Health Study studies, which combined data from 3 cohorts spanning a 13-year period of air quality improvement, lower concentrations of NO₂, PM_{2.5}, and PM₁₀ across cohorts were related with improved lung function growth between the ages of 11 and 15 years.⁵² An evaluation of the Oxford Transport Strategy (implemented in 1999 to reduce city center congestion) did find improvements in lung function in schoolchildren as measured by peak expiratory flow after its implementation, but these improvements were not related to observed changes in traffic exposure.¹¹³ A 5-year study of London's low emission zones (implemented in 2008, restricts vehicle entry in urban areas and applies penalties on polluting vehicles) found reduced NO₂ and NO_x concentrations, although not PM₁₀, and that annual NO₂ and PM₁₀ exposures were inversely associated with FVC in 8- to 9-year-old children; however, no

change was observed in the proportion of children with small lung volumes for their age over the study period.¹¹⁴ Adoption of clean air technologies and fuels in school buses was found to reduce PM_{2.5} and ultrafine PM in buses, and ultralow-sulfur diesel adoption was associated with improved changes in FVC and FEV₁ school bus riders (aged 6–12 years).¹¹⁵ Other interventions that have been found to improve health (though child lung function was not a measured outcome) include public guidance for low-pollution walking/biking routes,^{116–119} idle-free zones,¹²⁰ and complete streets programs.¹²¹ Increasing neighborhood green space¹²² and the building of affordable “healthy housing”¹²³ may also reduce indoor and outdoor air pollution exposures. Future lung function research should continue to take advantage of “natural experiments” to improve understanding of the air pollution impacts on children’s respiratory health.

It is important to acknowledge that individuals may be limited in their ability to engage in pollution exposure reduction activities and advocacy due to structural or social constraints (Fig 2), which could lead to further disparities in pollution exposure. For example, individual families may not have the financial resources to undertake interventions such as replacement of stoves or installation of air purifiers, and instead structural changes (eg, in public and private housing and insurance coverage) would be needed to bring about such interventions. Some US communities have suffered an overt expression of structural racism through historical “redlining,” leading to the siting of communities, their homes, and their schools nearer to highways and sources of air pollution, which in turn have public health effects.^{124–126} Lastly, just as people are exposed to air pollutants as a mixture, people are exposed to several factors concurrently when one considers the wider realm of exposures, including other environmental exposure, individual characteristics including heritable factors, diet/nutrition, psychosocial stressors, structural racism, and so forth, which can interact to either adversely or beneficially impact health outcomes such as lung function.^{53,127–130}

CONCLUSIONS

There is a large literature supporting the link between air pollution exposure and adverse effects on children’s lung function level and growth; however, many questions remain, some relating to more nuanced understanding of air pollution effects and others to new or less studied exposures. Studies of repeated measures of pulmonary function in children as they grow—including into adulthood—would provide significant opportunity to expand our understanding of air pollution effects on children’s lung function. Important areas needing further study include identification of windows of increased susceptibility, whether early-life effects are fixed or reversible, evaluating the long-term effects of repeated wildfire events on child lung function, and the effect of air quality interventions at the individual, household, and local levels on child lung function and respiratory health. As additional studies are conducted to improve scientific knowledge about the adverse effects of air pollutants on children, simultaneous efforts at the individual, local/city, state, and national levels can be made to improve indoor and outdoor air quality, with assessment of the short- and long-term benefits to children and their families. Citizen and community engagement on the need for improved air quality and environmental justice may inspire ground-breaking policy changes with lasting health benefits.

What do we know?

- Short-term exposure to ozone, nitrogen dioxide, and particle pollution has been associated with lower child lung function
- Fine particulate matter levels can reach extreme concentrations during wildfires, and are associated with acute decrements in peak expiratory flow
- Long-term early childhood exposure to ambient pollutants, especially nitrogen dioxide and fine particulate matter, is associated with subsequent children’s lung function level
- Children worldwide are often highly exposed to smoky household air pollution at a very critical age of lung development

What is still unknown?

- Long-term consequences of repeated exposure to wildfire smoke on child lung function
- Whether timing or cumulative period of exposure influences whether pollution effects are fixed or reversible over time, as children reach adulthood
- Long-term consequences of air pollution on reduced lung function development in childhood are not fully understood. Studies need to investigate impacts of childhood exposures on lung function trajectories and later respiratory health in adulthood
- Need to understand (1) who is more susceptible to the adverse lung function effects of gas stove pollution and (2) the extent to which gas stove-related lung function decrements are improved or prevented with improved kitchen ventilation
- What factors, in trials for homes with biomass or coal burning cookstoves, are responsible for the inconsistencies in effects of provision of clean stoves and improved indoor ventilation on child lung function

The rate of lung function decline and level of lung function in later adulthood are strong predictors of overall morbidity and mortality. If reduction of air pollution exposures improves lung function growth, maximizes the peak lung function children attain as young adults, and minimizes population decline in lung function in adulthood, this will have significant long-term benefits for the health of the next generation.¹³¹

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