

Household air pollution from domestic combustion of solid fuels and health



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List of Design Committee Members: John R. Balmes, MD (author); Zuhair K. Ballas, MD (editor)

Disclosure of Significant Relationships with Relevant Commercial Companies/Organizations: The author declares that he has no relevant conflicts of interest. Z. K. Ballas (editor) disclosed no relevant financial relationships.

Activity Objectives:

1. To understand that household air pollution from cooking and heating with solid fuels is an important contributor to outdoor air pollution.
2. To learn that household air pollution is a major risk factor contributing to the global burden of disease.
3. To become aware of the strength of the evidence in support of associations between household air pollution and cardiopulmonary disease outcomes.

Recognition of Commercial Support: This CME activity has not received external commercial support.

List of CME Exam Authors: John R. Balmes, MD

Disclosure of Significant Relationships with Relevant Commercial Companies/Organizations: The exam authors disclosed no relevant financial relationships.

Inefficient cooking and heating with solid fuels in poorly ventilated homes are a major source of exposure to indoor air pollution in developing countries. Household air pollution from cooking and heating with solid fuels also is an important contributor to outdoor air pollution. The combustion of organically derived solid fuel is qualitatively similar to the burning of tobacco in terms of emissions of particulate matter and gases, and the mechanisms by which solid fuel smoke causes adverse health effects in human subjects are likely similar. The public health effect of domestic cooking and heating with solid fuels is great. The World Health Organization estimates that

there are 3.8 million deaths globally per year attributable to household air pollution. This estimate is based on the strength of the evidence, primarily meta-analyses of epidemiologic studies of acceptable scientific quality, although for cardiovascular disease, the evidence is more inferential. The greatest burden of household air pollution-related premature deaths is in children with pneumonia exposed to biomass smoke. The greatest estimated burden in adults is cardiovascular disease, but chronic obstructive pulmonary disease and lung cancer are important causes of disability and premature death in women, who are the primary cooks and tend not to smoke tobacco in developing countries. Research gaps and opportunities for interventions to reduce effects of solid fuel smoke on public health are identified. (*J Allergy Clin Immunol* 2019;143:1979-87.)

Key words: Household air pollution, indoor air pollution, biomass smoke, solid fuel, global burden of disease

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Disclosure of potential conflict of interest: The author declares that he has no relevant conflicts of interest.

Received for publication April 10, 2019; revised April 29, 2019; accepted for publication April 29, 2019.

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0091-6749/\$36.00

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<https://doi.org/10.1016/j.jaci.2019.04.016>

Inefficient combustion of solid fuels in poorly ventilated homes is a major source of exposure to indoor air pollution in the developing world, and such exposures also continue to occur in the developed world. Levels of exposure to particulate matter (PM) from smoke in such homes are often at least an order of magnitude greater than the greatest concentrations that occur in

Abbreviations used

ALRI:	Acute lower respiratory tract infection
COPD:	Chronic obstructive pulmonary disease
DALY:	Disability-adjusted life year
GBD:	Global Burden of Disease
ITT:	Intention-to-treat
LMIC:	Low- and middle-income country
OR:	Odds ratio
PM:	Particulate matter
PM _{2.5} :	Fine particulate matter less than or equal to 2.5 μm in mass median aerodynamic diameter
RCT:	Randomized controlled trial
WHO:	World Health Organization

ambient air of the developed world.^{1,2} Household air pollution from cooking and heating with biomass fuels also is an important contributor to outdoor air pollution, accounting for an estimated 10% of ambient fine particulate matter of less than or equal to 2.5 μm in mass median aerodynamic diameter (PM_{2.5}).³

Biomass fuel refers to any recently living plant- and/or animal-based material that is deliberately burned by human subjects as fuel, including wood, crop residues, and animal dung.¹ The term solid fuel includes charcoal and coal in addition to biomass. The number of persons cooking with solid fuels is approximately 3 billion.^{4,5} Most of these persons are poor and live in rural areas of low- and middle-income countries (LMICs).⁴

Cooking with biomass fuels is generally done on unvented stoves typically consisting of such simple arrangements as 3 rocks, a U-shaped hole in a block of clay, or a pit in the ground (Fig 1).³ Cooking and heating with coal or charcoal is also usually done indoors with inefficient stoves. Incomplete combustion occurs under such conditions because the supply of oxygen is relatively poor, causing carbon monoxide, black carbon, and complex organic carbon compounds to be produced. This typically leads to extremely high pollutant concentrations in the vicinity of the stove. Pollutant concentrations are further exacerbated by the lack of ventilation that characterizes many of the kitchens in rural areas of developing countries.

High levels of smoke from cooking indoors with solid fuels commonly contain up to 1000 $\mu\text{g}/\text{m}^3$ PM, and much greater values have been reported.^{3,6} These concentrations are orders of magnitude greater than either the US Environmental Protection Agency national ambient air quality standard for PM or the World Health Organization (WHO) guidelines. In addition to PM, carbon monoxide, nitrogen oxides, formaldehyde, and a number of toxic organic compounds (eg, benzene; 1,3 butadiene; benzo[α]pyrene; and other polycyclic aromatic hydrocarbons) are present in biomass smoke, depending on the type of fuel that is burned.⁷ Combustion of wood and other biomass is qualitatively similar to the burning of tobacco in terms of emissions of PM and gases, although without the nicotine.

In rural areas of less developed countries, women often spend many hours a day cooking, and therefore duration of exposure to smoke from solid fuel combustion is often considerable. The potential for exposure to children is further increased by common cultural practices. Infants and toddlers are often carried on the mother's back while she cooks so that from early infancy, children spend hours breathing smoke from cooking or heating fires. In temperate climates and highland areas people spend more time



FIG 1. Traditional open 3-stone fire in a rural village home in the western highlands of Guatemala, where kitchen 48-hour PM_{2.5} levels are in the range of 600 to 1200 $\mu\text{g}/\text{m}^3$.

indoors to protect themselves from the cold, and the cold temperatures that characterize these areas require fires that burn over extended periods and tighter house construction (ie, less ventilation) for space heating.⁴ Thus both pollution levels and exposure times increase.

The public health effect of the relatively high exposures to PM in homes where cooking is done with inefficient and poorly ventilated stoves using solid fuels remains high despite progress that has been made over the past several decades to reduce this effect. A recent WHO report estimated that 3.8 million persons a year die prematurely from illness attributable to household air pollution caused by the inefficient use of solid fuels and kerosene for cooking.⁵ Estimates are based on the strength of the evidence, primarily meta-analyses of observational epidemiologic studies.

The greatest burden of household air pollution–related premature deaths is in children with pneumonia. The greatest estimated burden of disability and death in adults is for cardiovascular disease. However, the estimated burden of premature mortality caused by cardiovascular diseases is based on inference from epidemiologic data for outdoor particulate pollution, secondhand tobacco smoke, and active smoking, as well as the assumption that particles emitted from domestic cooking and heating with solid fuels have similar cardiovascular toxicity to particles from these other sources. For the typically nonsmoking women cooking with solid fuels in rural areas of LMICs, chronic obstructive pulmonary disease (COPD) is also a major cause of morbidity and mortality. Household air pollution also contributes to the burden of cataracts, the leading cause of blindness, and lung cancer, especially among women. Asthma and tuberculosis have not been included in the burden of disease estimates for household air pollution, but there is substantial evidence of associations with each of these conditions.^{8,9}

The Global Burden of Disease (GBD) comparative risk assessment uses disability-adjusted life years (DALYs) as the primary metric of health effect. Although the latest version of the GBD undertaken in 2017 found the percentage of DALYs attributable to household air pollution from solid fuel use to

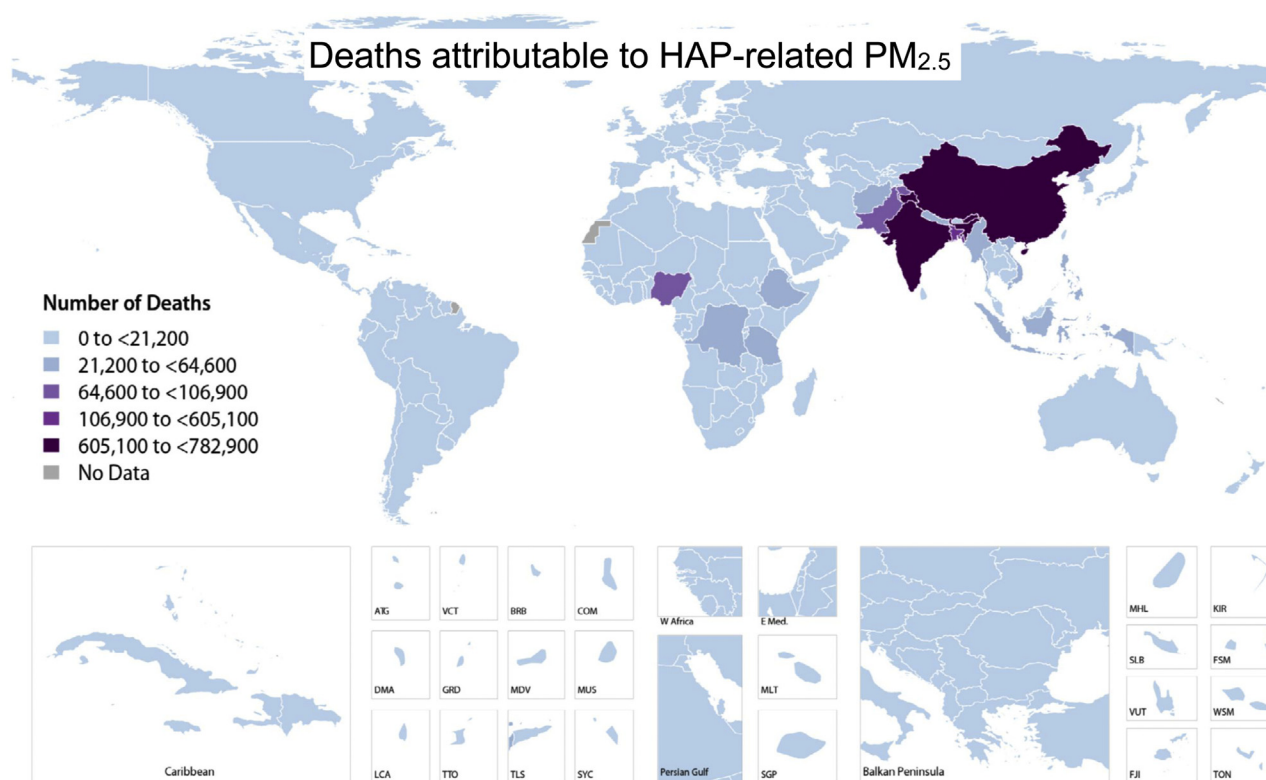


FIG 2. Global map of deaths attributable to household air pollution (HAP)-related PM_{2.5}.

have decreased by more than 40% since 1990, in certain parts of the world, the observed risk related to this exposure is actually increasing.¹⁰ Ambient PM is the 10th leading risk factor for DALYs and the most important environmental factor. Regions where this risk is greatest are Sub-Saharan Africa and Southeast Asia. In these regions a considerable percentage of the global burden of disease attributed to ambient PM pollution comes from household combustion of solid fuel and falls hardest on the most impoverished populations (Fig 2).

The latest WHO and GBD risk estimates did not include lighting with nonsolid fuels, such as kerosene, because of lack of data, but combustion of this fuel for lighting is often done with wick lamps in poor households, which leads to high levels of emissions. Kerosene is similar to diesel fuel as a petroleum distillate, and therefore exposures of children and adults crowded around such lamps at night in a poorly ventilated home can be quite high.¹¹ In particular, there is evidence for increased risk of tuberculosis with household use of kerosene.¹²

MECHANISMS

The mechanisms by which solid fuel smoke causes adverse health effects in human subjects are likely similar to those involved in tobacco smoke and combustion-generated PM pathogenic processes.¹³ Oxidative stress in the airways and alveoli leads to stimulation of alveolar macrophages and injury to the epithelial lining, which in turn attracts inflammatory cells from the circulation.¹⁴ This local lung inflammatory reaction can spill over into the systemic circulation and contribute to adverse effects in other organs, such as the cardiovascular system, and the fetus in pregnant women. Alveolar macrophages laden

with carbon particles from smoke can contribute to increased risk of respiratory tract infections.^{15,16} The pathways involved in solid fuel smoke-induced lung carcinogenesis are probably identical to those by which tobacco smoke induces lung cancers.

Although the toxicological literature for biomass smoke is much less rich than for tobacco smoke and ambient PM, a number of animal and *in vitro* studies have been reported. Pulmonary outcomes have been best studied in animal models, including airway responsiveness, lung function, effects on surfactant, epithelial damage, inflammation, edema, and antibacterial activity.^{13,14,16-19} Extrapulmonary outcomes have included effects on the cardiovascular system, adjuvant activity, p450 enzyme activity, glutathione depletion, and tumor/cancer growth.^{18,19}

A growing number of reports of controlled human exposure studies of wood smoke have been published. These studies are limited to acute effects and are specific to the fuels and burn conditions used, but evidence of systemic oxidative stress and inflammation, airway inflammation, and arterial stiffness has been observed after short-term exposure to wood smoke.²⁰⁻²³ However, not all studies have found adverse effects.²⁴⁻²⁶

ACUTE LOWER RESPIRATORY TRACT INFECTION (CHILDHOOD PNEUMONIA)

Acute lower respiratory tract infection (ALRI) is a leading contributor to the global burden of disease.¹⁰ Pneumonia is also the primary cause of death in children younger than 5 years, and the incidence and mortality are generally greatest in those countries and regions where solid fuel use is greatest.²⁷ The relative risk of ALRIs for children exposed to household solid fuel smoke has been quantified in a number of studies, the majority

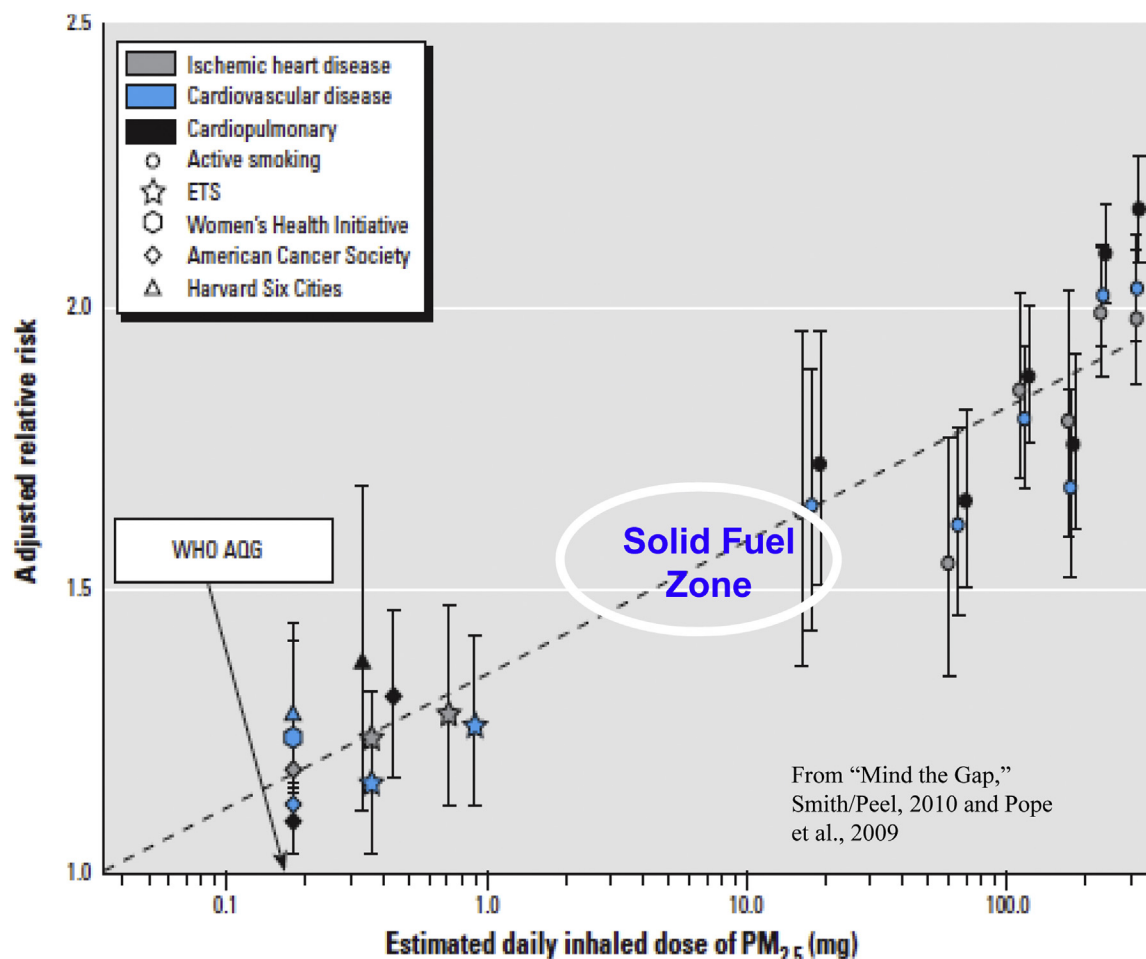


FIG 3. Adjusted relative risks (95% CIs) of cardiovascular and cardiopulmonary mortality and estimated dose of $PM_{2.5}$ across studies of outdoor air pollution, environmental tobacco smoke (ETS), and active cigarette smoking (adapted with permission from Pope et al).⁶⁸ Exposure was measured as daily inhaled dose of $PM_{2.5}$ (plotted on a log scale), which was calculated assuming an 18 m³/d breathing rate. Active cigarette smoking was quantified as 3 or less, 4 to 7, 8 to 12, 13 to 17, 18 to 22, and 23 or more cigarettes per day (relative to never smokers). Also shown is the equivalent dose for the WHO (2006) Air Quality Guidelines for $PM_{2.5}$ (10 µg/m³ annual average).⁶⁹

from developing countries, but also from the United States.²⁸ Most of these studies have used a case-control design, although several cohort studies have also been conducted. Taken together, these observational epidemiologic studies show a consistent association between solid fuel use and an increase in the risk of ALRIs in exposed children. The overall estimate of the risk of ALRIs from a meta-analysis of 24 studies published before 2008 conducted in preparation for the 2010 GBD comparative risk assessment was a pooled odds ratio (OR) of 1.79 (95% CI, 1.26-2.21) for children younger than 5 years.³ The OR for children younger than 2 years was 1.96 (95% CI, 1.36-2.82). A problem with most of the studies was lack of direct measurement of exposure, with use of fuel type as the usual proxy. Outcome definitions varied from parental recall of WHO signs of ALRIs to chest x-ray confirmation and included severe and fatal outcomes; some evidence of an increased risk for more severe pneumonia was found. Impaired respiratory tract defense mechanisms, such as decreased mucociliary clearance and alveolar macrophage function, provide biological plausibility for the observed association between biomass smoke exposure and ALRI risk in children.^{19,29}

Only 2 randomized controlled trials (RCTs) of an intervention to reduce exposure to biomass smoke to prevent childhood ALRIs have been completed,³⁰ one involving slightly more than 500 infant rural Guatemalan children and a chimney wood stove intervention and the other involving more than 10,000 rural Malawian children and cleaner-burning gasifier stoves. In the Guatemala trial, where cooking was primarily indoors, child exposure was reduced by 50%, and the intention-to-treat (ITT) analysis showed a relative risk of 0.67 (95% CI, 0.45-0.98) for severe (defined by low oxygen saturation) physician-diagnosed pneumonia. Adjusted exposure-response analysis found significant relationships for both all and severe pneumonia (Fig 3). In the Malawi trial, where cooking was primarily outdoors, the ITT analysis showed no protective effect, but exposures might not have been substantially reduced by the intervention.³¹

Although there are abundant observational epidemiologic data that support an association between early childhood exposure to household air pollution and pneumonia, the 2 published RCTs report conflicting results regarding whether reduction of exposure is linked to the outcome. Given the burden of childhood

pneumonia, better exposure-response data are needed to assess the potential benefit of stove and/or clean fuel interventions. An important gap in knowledge is how much emissions need to be reduced to have substantial benefit in reduction of early childhood pneumonia.³² A large multicountry intervention trial of liquefied petroleum gas stoves has been funded by the National Institutes of Health and the Gates Foundation to assess the efficacy of this cleaner fuel intervention on pneumonia in children.³³

Insufficient data exist to support a clear association between household air pollution and adult pneumonia. However, one small study from Kenya showed a significant exposure-response relationship.³⁴ Another mechanistic study using primary human alveolar macrophages harvested from healthy Malawian adults reported that *in vitro* exposure to wood smoke decreased phagocytosis.²⁹ The strong evidence of a biomass smoke effect in children and the known effects of other sources of combustion-sourced particle exposure (eg, smoking and ambient air pollution) together suggest that exposure to solid fuel smoke increases the risk of adult ALRIs. Further research is required to confirm and quantify this risk.

COPD

COPD is a leading cause of morbidity and mortality (approximately 3.2 million deaths per year) worldwide and results in an economic and social burden that is both substantial and increasing, especially among women.³⁵ In less developed countries a substantial proportion of COPD occurs in persons who have never smoked tobacco products, especially among women cooking with stoves that emit high levels of a wide variety of pollutants similar to those present in tobacco smoke. Multiple case-control and cross-sectional studies have found an association between cooking with biomass fuel and chronic bronchitis or COPD when compared with lower exposure/cleaner fuels. Exposure was often assessed as present or absent or by daily hours spent by the stove. Like the studies of childhood ALRIs, most studies did not include direct measurements of specific pollutants. Studies that have measured kitchen particulate levels from solid fuel use have confirmed very high concentrations,^{36,37} but until recently, personal measurements of exposure have not been used. Only a few cross-sectional studies measured lung function, and these studies showed an association between solid fuel use and chronic airflow obstruction.^{37,38}

Several systematic reviews and meta-analyses of the studies reported before 2010 have been published.^{3,39-41} The pooled ORs from these meta-analyses were similar, ranging from 1.94 to 2.80, which should be no surprise because the same set of studies, give or take a few, were included. Stratified analysis by sex in all of the meta-analyses showed a stronger association between exposure to solid fuel smoke and COPD in women. The stronger association in women might be due to their greater exposure from doing most of the cooking.

A major weakness of the published literature on household air pollution and COPD reviewed above is the lack of an objective definition of the outcome, especially the lack of postbronchodilator spirometry. Recently, 2 large-scale meta-analyses of studies from multiple countries with high-quality spirometry, including postbronchodilator testing, were published.^{42,43} Unfortunately, like the conflicting RCTs for childhood pneumonia, these 2 studies produced conflicting results.⁴⁴

Longitudinal studies of the effect of biomass smoke exposure on the development of COPD are lacking, but one study did

follow women with COPD associated with biomass smoke exposure in terms of mortality risk.⁴⁵ Survival analysis over a 7-year follow-up period showed that women with COPD associated with biomass smoke exposure had mortality rates similar to those of men with COPD caused by tobacco smoking. One interesting autopsy study from Mexico found that women with biomass smoke-induced COPD had more peribronchial fibrosis and less emphysema than a matched group of women with tobacco smoke-induced COPD.⁴⁶ Another study from China found greater dyspnea and more allergic rhinitis in women with biomass smoke-induced COPD than in those with tobacco smoke-induced COPD.⁴⁷

Intervention studies to prevent COPD from biomass smoke exposure have been limited. A retrospective Chinese study found significant reductions in COPD incidence in homes where coal was used in improved stoves with chimneys, the effect increasing with time since adoption.⁴⁸ Another prospective Chinese study showed that replacing solid fuel with biogas for cooking and improving kitchen ventilation are associated with a reduced decrease in FEV₁ and risk of COPD.⁴⁹ Two recently published studies of the efficacy of reducing wood smoke exposure with the use of an improved chimney stove were limited by short follow-up time (12-18 months).⁵⁰⁻⁵²

Thus although studies suggest lower solid fuel smoke exposure can be associated with lower COPD risk, several key questions remain, including whether the development or progression of COPD can be prevented by reducing smoke exposure in these settings and the nature of the exposure-response relationship between smoke and the rate of decrease in lung function? Similar to childhood pneumonia, an important gap in knowledge is how much emissions need to be reduced to have a substantial benefit regarding adult COPD.³² It also might be that the exposure-response relationships are different for an acute effect (pneumonia) compared with a chronic effect (COPD). Prospective cohort studies that have adequate statistical power, follow participants for a sufficient duration to accurately measure the rate of decrease in lung function, and actually measure exposures are needed to answer these questions. Ideally, intervention studies with clean stoves will be conducted.

ASTHMA

Given the airway-irritating effects of solid fuel smoke, it is reasonable to suspect that exposure might increase the risk for asthma, especially because exposure to secondhand tobacco smoke has been associated with development of asthma in children.⁵³ On the other hand, there is a rural-urban gradient for asthma. The disease is generally much more prevalent in urban areas than in largely rural areas, where exposure to solid fuel smoke is more common.⁵⁴ The protective effect of living on a farm, especially with livestock, has been well documented.⁵⁵ Because the evidence for an effect of solid fuel smoke on COPD is strong and both asthma and COPD involve airway inflammation, the relationship between exposure to solid fuel smoke and risk of asthma remains a topic of considerable research interest.

A systematic review and meta-analysis of the association between exposure to biomass smoke and asthma in children and women by Po et al⁴¹ was published in 2011. Nine studies were selected for the meta-analysis, 4 involving children, and 5 involving women. The pooled OR for the 4 studies on asthma

Integrated Exposure Response Curves

fit from Burnett et al data, 2014

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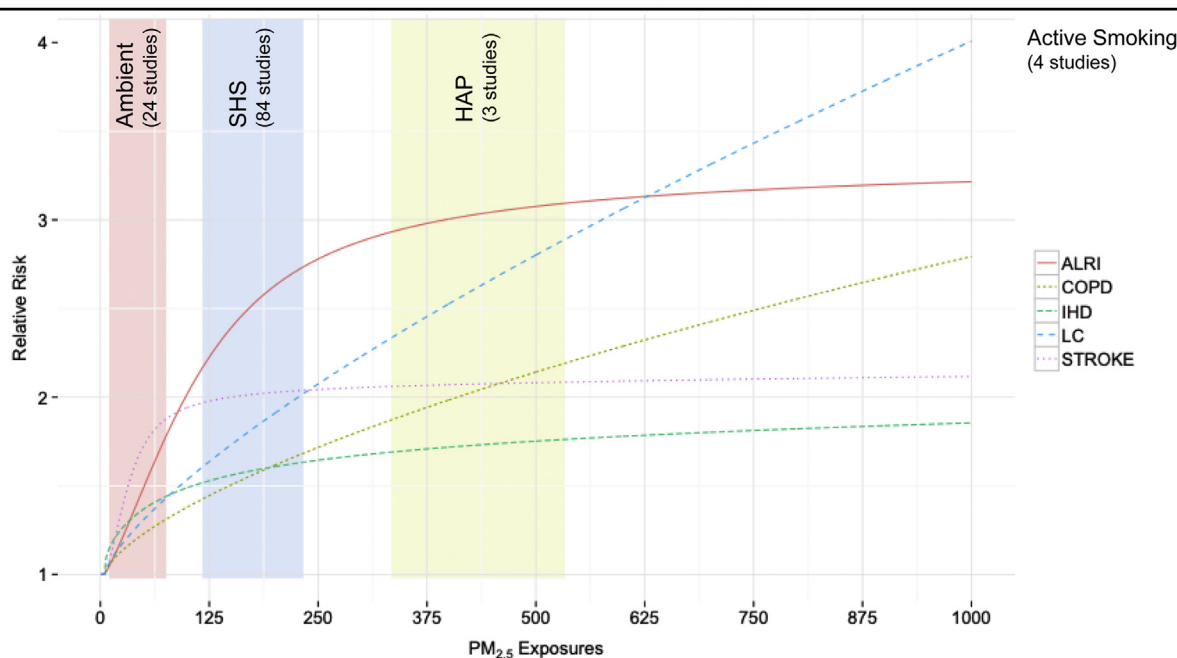


FIG 4. Integrated exposure-response curves for the relative risk for ALRI, COPD, ischemic heart disease (IHD), lung cancer (LC), and stroke with exposure to PM_{2.5} in micrograms per cubic meter from various combustion sources, ambient air pollution, secondhand tobacco smoke (SHS), household air pollution (HAP), and active smoking.⁷⁰

in children exposed to biomass smoke was 0.50 (95% CI, 0.12-1.98). For the 5 studies of women, the pooled OR was 1.34 (95% CI, 0.93-1.93).

Since the Po et al⁴¹ review was published, the results of several new studies have been reported. A survey of 508 adults in southeastern Kentucky found a significant association with asthma when wood and coal were burned for cooking.⁵⁶ A much larger population survey from India found that adult women living in households using biomass and solid fuels had a significantly greater risk of asthma than those living in households using cleaner fuels, even after controlling for the effects of a number of potentially confounding factors.⁵⁷ A study from China of exposures to ambient PM_{2.5} and doctor-diagnosed asthma found a stronger association in rural populations with greater exposure to household air pollution than in urban populations,⁵⁸ and a study from Brazil found that exposure to household air pollution was associated with poorer asthma control, greater proportion of severe asthma, and lower lung function compared with those without such exposure.⁵⁹

Additional evidence supporting an increased risk of asthma from cooking with solid fuels was reported by the International Study of Asthma and Allergy in Children, which surveyed almost 513,000 children from 1999-2004.⁹ The sole use of an open fire for cooking (assessed by questionnaire) was associated with an increased risk of wheeze in the past year in both young children (ages 6-7 years; OR, 2.17; 95% CI, 1.64-2.87) and older children (ages 13-14 years; OR, 1.35; 95% CI, 1.11-1.64). ORs for wheeze in the past year and use of an open fire in combination with other fuels for cooking were slightly lower but still significant for both age groups.

Not all recent studies have reported positive associations between exposure to biomass smoke and asthma outcomes. For example, a recent study of 299 children from rural villages in Nigeria reported smoke exposure was not associated with an increased risk of asthma symptoms or airway obstruction.⁶⁰ An RCT of an air-filter intervention that improved indoor air quality did not affect asthma quality of life, although ITT analysis did show an improvement in the secondary measure of diurnal peak flow variability.⁶¹ A recent GBD risk assessment was not able to quantify the risk of asthma caused by exposure to household air pollution because the published evidence is mixed.⁶² Further research is needed to better understand the nature of the relationship between exposure to solid fuel smoke and asthma in both children and adults and for both new-onset disease and disease exacerbations. Studies that actually measure exposure and are thus able to develop an exposure-response relationship would be particularly helpful.

LUNG CANCER

Emissions generated by combustion of the main solid fuels used for cooking and space heating, biomass and coal, can be associated with differential cancer risk because of differences in chemical composition. The International Agency for Research on Cancer has concluded household use of coal is a group 1 carcinogen, whereas biomass is classified as a group 2(a) or probable carcinogen because of more limited epidemiologic evidence.⁶³

Several recent systematic reviews and meta-analyses of household use of coal and lung cancer risk have been

conducted.^{64,65} Few studies were conducted in countries other than mainland China and Taiwan. Household coal use for cooking and heating was associated with a pooled OR for lung cancer of approximately 2. In both reviews the risk for women was somewhat greater than the risk for men.

Because the great majority of the approximately 3 billion solid fuel users globally are exposed to biomass rather than coal smoke, the issue of the carcinogenic risk associated with the former is an important one. A systematic review and meta-analysis of studies primarily conducted in Asia, although some from Europe and North America, of cooking and/or heating with biomass found a pooled OR of 1.17 (95% CI, 1.01-1.37).⁶⁶ A case-control study from Nepal published after this review found a somewhat greater OR of 1.77 (95% CI, 1.00-3.14).⁶⁷ Most studies find that women have a somewhat greater risk than men.

CARDIOVASCULAR DISEASE

In contrast to the other health outcomes discussed above, the epidemiologic evidence for an association between exposure to solid fuel smoke and cardiovascular disease is quite limited. That said, a remarkably consistent nonlinear relationship between estimated inhaled dose of combustion-sourced particles measured as PM_{2.5} and cardiovascular disease mortality was first demonstrated by Pope et al.⁶⁸ This dose-response relationship was remarkable for a noncancer outcome in that it covered at least 3 orders of magnitude of dose from lowest to highest (exposure to ambient air pollution, exposure to secondhand tobacco smoke exposure, and active cigarette smoking). Exposures to PM_{2.5} from solid fuel cooking lie in the range between those from secondhand smoke and active smoking, and given that tobacco is a kind of biomass, Smith and Peel postulated that the relative risk for CVD from biomass fuel smoke exposure would be on the order of 1.3 to 1.6 (Fig 3).⁶⁹

The GBD estimates for the burden of cardiovascular disease DALYs attributable to household air pollution use interpolation on what are now called integrated exposure-response curves (Fig 4).⁷⁰ The curve derived for risk of ischemic heart disease in relation to combustion-sourced fine particles generates a relative risk of 1.5 for high household air pollution exposure.^{3,70} The integrated exposure-response curve for stroke is similar but appears to flatten off at levels well within the household air pollution range at a maximum relative risk of just over 2.0. The population attributable risk for ischemic heart disease associated with household air pollution exposure estimated by the integrated exposure-response curve method generally goes down with economic development as the attributable risk for ambient PM_{2.5} from other mobile and power-generation sources goes up.

Although direct epidemiologic evidence remains relatively sparse, several recent studies have provided more support for increased risk of cardiovascular outcomes with exposure to household air pollution. A cross-sectional Chinese study involving more than 14,000 men and women aged 18 years or older showed that solid fuel use (biomass and coal) for heating and/or cooking as assessed by questionnaire showed increased adjusted ORs (2.6) for self-report of physician-diagnosed ischemic heart disease for ever versus never use of solid fuels and significant trends across duration of use for stroke, hypertension, and diabetes.⁷¹ Sex-stratified analysis found stronger effect estimates for women, which is consistent with their greater exposure, as well as among nonsmokers. Other studies from

China, Honduras, and Peru have also reported associations between household air pollution and blood pressure.⁷²⁻⁷⁴ A meta-analysis of data from 12 demographic and health surveys from 10 countries showed that women who primarily cooked with solid fuel had greater systolic blood pressure compared with those who primarily used clean fuel.⁷⁵ One study measured exposures to household air pollution in China and provided some evidence that clean stove and fuel interventions might reduce the burden of cardiovascular disease.⁷⁶

Exposure to ambient PM_{2.5} has been shown to be associated with metabolic dysfunction.⁷⁷ Given the epidemiologic transition from morbidity/mortality caused by infectious diseases to non-communicable chronic conditions, such as metabolic syndrome and diabetes, which are occurring with economic development in many LMICs, the effect of exposure to solid fuel smoke on these conditions remains of public health concern because lifestyle and diet can change before cleaner fuels are available.

RESEARCH GAPS

Although RCTs of the efficacy of improved biomass stoves compared with an open fire for the prevention of early childhood pneumonia have been published,^{30,31} and related studies have suggested benefit regarding low birth weight, cognitive development, and respiratory symptoms in adult women, more studies of stove interventions are needed. In particular, the exposure-response data from the Guatemala trial provide evidence that stoves which are cleaner than the chimney stove studied would provide greater reduction in childhood pneumonia. The ongoing multicountry RCT of a liquified petroleum gas should contribute data to fill the gap in our knowledge about the added benefit of cleaner-burning stoves beyond those with chimneys.

Another gap is the lack of a well-designed longitudinal study of the effect of improved stoves on the development of COPD in adults exposed to biomass smoke from cooking and heating. Although the study from Guatemala conducted in the context of the RCT designed to prevent childhood pneumonia found no protective effect of the chimney stove on rate of decrease in lung function in the ITT analysis, in an exposure-response analysis there was a protective effect.⁵² This finding highlights the need to actually measure exposure to PM_{2.5} and not just use a questionnaire-based surrogate.

Perhaps the greatest research gap involves the lack of epidemiologic evidence to support the concept that biomass smoke exposure leads to increased risk of cardiovascular disease consistent with other combustion-sourced particle exposures, outdoor PM_{2.5}, secondhand tobacco smoke, and active smoking. The National Institutes of Health- and Gates Foundation-funded RCT is studying blood pressure in adults as one of its primary outcomes.³³ The exposure-response relationship might be different for cardiovascular compared with respiratory outcomes and acute compared with chronic cardiovascular outcomes.

More research is needed with regard to the associations between solid fuel smoke exposure and adult pneumonia, asthma, and tuberculosis, either because of a paucity of data (adult pneumonia) or conflicting results. Another unresolved issue is the toxicity of kerosene as an alternative fuel, especially given the recently published evidence that it substantially increases the risk of tuberculosis.⁷⁸

Because adoption of new stoves can be a difficult transition for households in the developing world because of both financial and

cultural factors, more research is needed to improve our understanding of these potential barriers to the effectiveness of intervention programs.

Toxicological studies (*in vitro*, animal, and controlled human exposure) are needed to improve our mechanistic understanding of the pathways by which biomass smoke causes or contributes to disease pathogenesis. Such studies can also assist in the development of biomarkers of both exposure and effects.⁷⁹

CONCLUSION

Cleaner cooking solutions are needed to improve the health of the roughly 40% of the world's population that still cooks with solid fuel because even the most efficient stoves that burn solid fuels emit more PM_{2.5} than the gas and electric stoves that are used by developed world households. This has led some experts to suggest that electrification of developing countries, perhaps through local solar power generation and the use of relatively inexpensive induction cookers, might be the most effective way to reduce exposure to household air pollution in LMICs.

A final policy note is that black carbon generated from biomass combustion is an important short-lived climate-forcing agent.⁸⁰ Interventions to improve the efficiency of combustion of solid fuels or better, which eliminate combustion of solid fuels altogether, would provide a major climate change mitigation cobenefit in addition to the public health benefits described above.

REFERENCES

- Bruce N, Perez-Padilla R, Albalak R. Indoor air pollution in developing countries: a major environmental and public health challenge. *Bull World Health Organ* 2000;78:1078-92.
- Diette GB, Accinelli RA, Balmes JR, Buist AS, Checkley W, Garbe P, et al. Obstructive lung disease and exposure to burning biomass fuel in the indoor environment. *Glob Heart* 2012;7:265-70.
- Smith KR, Bruce N, Balakrishnan K, Adair-Rohani H, Balmes J, Chafe Z, et al. Millions dead: how do we know and what does it mean? Methods used in the comparative risk assessment of household air pollution. *Annu Rev Public Health* 2014;35:185-206.
- Smith KR, Frumkin H, Butler CD, Chafe Z, Fairlie I, Kinney P, et al. Energy and human health. *Annu Rev Public Health* 2013;34:1-30.
- World Health Organization. Household air pollution and health. Geneva: World Health Organization. Available at: <https://www.who.int/news-room/fact-sheets/detail/household-air-pollution-and-health>. Accessed May 8, 2018.
- Balakrishnan K, Ghosh S, Ganguli B, Sambandam S, Bruce N, Barnes DF, et al. State and national household concentrations of PM_{2.5} from solid cookfuel use: results from measurements and modeling in India for estimation of the global burden of disease. *Environ Health* 2013;12:77.
- Warwick H, Doig A. Smoke—the Killer in the Kitchen. London: ITDG Publishing; 2004.
- Sumpter C, Chandramohan D. Systematic review and meta-analysis of the associations between indoor air pollution and tuberculosis. *Trop Med Int Health* 2013;18:101-8.
- Wong GW, Brunekreef B, Ellwood P, Anderson HR, Asher MI, Crane J, et al. ISAAC Phase Three Study Group. Cooking fuels and prevalence of asthma: a global analysis of phase three of the International Study of Asthma and Allergies in Childhood (ISAAC). *Lancet Respir Med* 2013;1:386-94.
- GBD 2017 Risk Factor Collaborators. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet* 2018;392:1923-94.
- Lam NL, Muhwezi G, Isabirye F, Harrison K, Ruiz-Mercado I, Amukoye E, et al. Exposure reductions associated with introduction of solar lamps to kerosene lamp-using households in Busia County, Kenya. *Indoor Air* 2018;28:218-27.
- Pokhrel AK, Bates MN, Verma SC, Joshi HS, Sreeramareddy CT, Smith KR. Tuberculosis and indoor biomass and kerosene use in Nepal: a case-control study. *Environ Health Perspect* 2010;118:558-64.
- Mehra D, Geraghty PM, Hardigan AA, Foronjy R13. A comparison of the inflammatory and proteolytic effects of dung biomass and cigarette smoke exposure in the lung. *PLoS One* 2012;7:e52889.
- Mondal NK, Saha H, Mukherjee B, Tyagi N, Ray MR. Inflammation, oxidative stress, and higher expression levels of Nrf2 and NQO1 proteins in the airways of women chronically exposed to biomass fuel smoke. *Mol Cell Biochem* 2018;447:63-76.
- Lee A, Kinney P, Chillrud S, Jack D. A systematic review of innate immunomodulatory effects of household air pollution secondary to the burning of biomass fuels. *Ann Glob Health* 2015;81:368-74.
- Whitehouse AL, Miyashita L, Liu NM, Lesosky M, Flitz G, Ndamala C, et al. Use of cleaner-burning biomass stoves and airway macrophage black carbon in Malawian women. *Sci Total Environ* 2018;635:405-11.
- McCarthy CE, Duffney PF, Gelein R, Thatcher TH, Elder A, Phipps RP, et al. Dung biomass smoke activates inflammatory signaling pathways in human small airway epithelial cells. *Am J Physiol Lung Cell Mol Physiol* 2016;311:L1222-33.
- Migliaccio CT, Mauderly JL. Biomass smoke exposures: toxicology and animal study design. *Inhal Toxicol* 2010;22:104-7.
- Zelikoff JT, Chen LC, Cohen MD, Schlesinger RB. The toxicology of inhaled woodsmoke. *J Toxicol Environ Health B Crit Rev* 2002;5:269-82.
- Barregard L, Sällsten G, Andersson L, Almstrand AC, Gustafson P, Andersson M, et al. Experimental exposure to wood smoke: effects on airway inflammation and oxidative stress. *Occup Environ Med* 2008;65:319-24.
- Sehlfeldt M, Dove R, Boman C, Pagels J, Swietlicki E, Löndahl J, et al. Antioxidant airway responses following experimental exposure to wood smoke in man. *Part Fibre Toxicol* 2010;7:21.
- Stockfelt L, Sällsten G, Olin AC, Almerud P, Samuelsson L, Johannesson S, et al. Effects on airways of short-term exposure to two kinds of wood smoke in a chamber study of healthy humans. *Inhal Toxicol* 2012;24:47-59.
- Unosson J, Blomberg A, Sandström T, Muala A, Boman C, Nyström R, et al. Exposure to wood smoke increases arterial stiffness and decreases heart rate variability in humans. *Part Fibre Toxicol* 2013;10:20.
- Riddervold IS, Bønløkke JH, Olin AC, Grønberg TK, Schlünssen V, Skogstrand K, et al. Effects of wood smoke particles from wood-burning stoves on the respiratory health of atopic humans. *Part Fibre Toxicol* 2012;9:12.
- Forchhammer L, Møller P, Riddervold IS, Bønløkke J, Massling A, Sigsgaard T, et al. Controlled human wood smoke exposure: oxidative stress, inflammation and microvascular function. *Part Fibre Toxicol* 2012;9:7.
- Stockfelt L, Sällsten G, Almerud P, Basu S, Barregard L. Short-term chamber exposure to low doses of two kinds of wood smoke does not induce systemic inflammation, coagulation or oxidative stress in healthy humans. *Inhal Toxicol* 2013;25:417-25.
- Nair H, Simões EA, Rudan I, Gessner BD, Azziz-Baumgartner E, Zhang JSF, et al. Global and regional burden of hospital admissions for severe acute lower respiratory infections in young children in 2010: a systematic analysis. *Lancet* 2013;381:1380-90.
- Dherani M, Pope D, Mascarenhas M, Smith KR, Weber M, Bruce N. Indoor air pollution from unprocessed solid fuel use and pneumonia risk in children aged under five years: a systematic review and meta-analysis. *Bull World Health Organ* 2008;86:390-8.
- Rylance J, Fullerton DG, Scriven J, Aljurayyan AN, Mzinza D, Barrett S, et al. Household air pollution causes dose-dependent inflammation and altered phagocytosis in human macrophages. *Am J Respir Cell Mol Biol* 2015;52:584-93.
- Smith KR, McCracken JP, Weber MW, Hubbard A, Jenny A, Thompson LM, et al. Effect of reduction in household air pollution on childhood pneumonia in Guatemala (RESPIRE): a randomised controlled trial. *Lancet* 2011;378:1717-26.
- Mortimer K, Ndamala CB, Njunje A, Malava J, Katundu C, Weston W, et al. A cleaner burning biomass-fueled cookstove intervention to prevent pneumonia in children under 5 years old in rural Malawi (CAPS): a cluster randomized controlled trial. *Lancet* 2016;389:167-75.
- Gordon S, Mortimer K, Grigg J, Balmes J. In control of ambient and household air pollution—how low should we go? *Lancet Respir Med* 2017;5:918-20.
- Fandiño-Del-Río M, Goodman D, Kephart JL, Miele CH, Williams KN, Moazzami M, et al. Effects of a liquefied petroleum gas stove intervention on pollutant exposure and adult cardiopulmonary outcomes (CHAP): study protocol for a randomized controlled trial. *Cardiopulmonary outcomes and Household Air Pollution trial (CHAP) Trial Investigators. Trials* 2017;18:518.
- Ezzati M, Kammen DM. Quantifying the effects of exposure to indoor air pollution from biomass combustion on acute respiratory infections in developing countries. *Environ Health Perspect* 2001;109:481-8.
- World Health Organization. Chronic obstructive pulmonary disease (COPD). Geneva: World Health Organization. Available at: [https://www.who.int/news-room/fact-sheets/detail/chronic-obstructive-pulmonary-disease-\(copd\)](https://www.who.int/news-room/fact-sheets/detail/chronic-obstructive-pulmonary-disease-(copd)). Accessed April 13, 2019.

36. Albalak R, Frisnacho AR, Keeler GJ. Domestic biomass fuel combustion and chronic bronchitis in two rural Bolivian villages. *Thorax* 1999;54:1004-8.
37. Regalado J, Pérez-Padilla R, Sansores R, Páramo Ramirez JI, Brauer M, Paré P, et al. The effect of biomass burning on respiratory symptoms and lung function in rural Mexican women. *Am J Respir Crit Care Med* 2006;174:901-5.
38. Caballero A, Torres-Duque CA, Jaramillo C, Bolívar F, Sanabria F, Osorio P, et al. Prevalence of COPD in five Colombian cities situated at low, medium, and high altitude (PREPOCOL study). *Chest* 2008;133:343-9.
39. Kurmi OP, Semple S, Simkhada P, Smith WC, Ayres JG. COPD and chronic bronchitis risk of indoor air pollution from solid fuel: a systematic review and meta-analysis. *Thorax* 2010;65:221-8.
40. Hu G, Zhou Y, Tian J, Yao W, Li J, Li B, et al. Risk of COPD from exposure to biomass smoke: a meta-analysis. *Chest* 2010;138:20-31.
41. Po J, FitzGerald J, Carlsten C. Respiratory disease associated with solid biomass fuel exposure in rural women and children: systematic review and meta-analysis. *Thorax* 2011;66:232-9.
42. Amaral AFS, Patel J, Kato BS, Obaseki DO, Lawin H, Tan WC, et al. Airflow obstruction and use of solid fuels for cooking or heating: BOLD results. *Am J Respir Crit Care Med* 2018;197:595-610.
43. Siddharthan T, Grigsby MR, Goodman D, Chowdhury M, Rubinstein A, Irazola V, et al. Association between household air pollution exposure and chronic obstructive pulmonary disease outcomes in 13 low- and middle-income country settings. *Am J Respir Crit Care Med* 2018;197:611-20.
44. Balmes JR, Eisen EA. Household air pollution and chronic obstructive pulmonary disease. "A riddle, wrapped in a mystery, inside an enigma". *Am J Respir Crit Care Med* 2018;197:547-9.
45. Ramirez-Venegas A, Sansores RH, Pérez-Padilla R, Regalado J, Velázquez A, Sánchez C, et al. Survival of patients with chronic obstructive pulmonary disease due to biomass smoke and tobacco. *Am J Respir Crit Care Med* 2006;173:393-7.
46. Rivera RM, Cosío MG, Ghezzi H, Salazar M, Pérez-Padilla R. Comparison of lung morphology in COPD secondary to cigarette and biomass smoke. *Int J Tuberc Lung Dis* 2008;12:972-7.
47. Cheng LL, Liu YY, Su ZQ, Liu J, Chen RC, Ran PX. Clinical characteristics of tobacco smoke-induced versus biomass fuel-induced chronic obstructive pulmonary disease. *J Transl Int Med* 2015;3:126-9.
48. Chapman RS, He X, Blair AE, Lan Q. Improvement in household stoves and risk of chronic obstructive pulmonary disease in Xuanwei, China: retrospective cohort study. *BMJ* 2005;331:1050.
49. Zhou Y, Zou Y, Li X, Chen S, Zhao Z, He F, et al. Lung function and incidence of chronic obstructive pulmonary disease after improved cooking fuels and kitchen ventilation: a 9-year prospective cohort study. *PLoS Med* 2014;11:e1001621.
50. Smith-Sivertsen T, Díaz E, Pope D, Lie RT, Díaz A, McCracken J, et al. Effect of reducing indoor air pollution on women's respiratory symptoms and lung function: the RESPIRE Randomized Trial, Guatemala. *Am J Epidemiol* 2009;170:211-20.
51. Romieu I, Riojas-Rodríguez H, Marrón-Mares AT, Schilman A, Perez-Padilla R, Masera O. Improved biomass stove intervention in rural Mexico: impact on the respiratory health of women. *Am J Respir Crit Care Med* 2009;180:649-56.
52. Pope D, Díaz E, Smith-Sivertsen T, Lie RT, Bakke P, Balmes JR, et al. Associations of respiratory symptoms and lung function with measured carbon monoxide concentrations among nonsmoking women exposed to household air pollution: the RESPIRE trial, Guatemala. *Environ Health Perspect* 2015;123:285-92.
53. Vork K, Broadwin R, Blaisdell RJ. Developing asthma in childhood from exposure to secondhand tobacco smoke: insights from a meta-regression. *Environ Health Perspect* 2007;115:1394-400.
54. Addo-Yobo E, Woodcock A, Allotey A, Baffoe-Bonnie B, Strachan D, Custovic A. Exercise-induced bronchospasm and atopy in Ghana: two surveys ten years apart. *PLoS Med* 2007;4:355-60.
55. Ege M, Mayer M, Normand AC, Genuneit J, Cookson WO, Braun-Fahrlander C, et al. Exposure to environmental microorganisms and childhood asthma. *N Engl J Med* 2011;364:701-9.
56. Fagbule D, Ekanem E. Some environmental risk factors for childhood asthma: a case-control study. *Ann Trop Paediatr* 1994;14:15-9.
57. Agrawal S. Effect of indoor air pollution from biomass and solid fuel combustion on prevalence of self-reported asthma among adult men and women in India: findings from a nationwide large-scale cross-sectional survey. *J Asthma* 2012;49:355-65.
58. Chen F, Lin Z, Chen R, Norback D, Liu C, Kan H, et al. The effects of PM_{2.5} on asthmatic and allergic diseases or symptoms in preschool children of six Chinese cities, based on China, Children, Homes and Health (CCHH) project. *Environ Pollut* 2018;232:329-37.
59. Fernandes AGO, de Souza-Machado C, Pinheiro GP, de Oliva ST, Mota RCL, de Lima VB, et al. Dual exposure to smoking and household air pollution is associated with an increased risk of severe asthma in adults in Brazil. *Clin Transl Allergy* 2018;8:48.
60. Thacher JD, Emmelin A, Madaki AJ, Thacher TD. Biomass fuel use and the risk of asthma in Nigerian children. *Respir Med* 2013;107:1845-51.
61. Noonan CW, Semmens EO, Smith P, Harrar SW, Montrose L, Weiler E, et al. Randomized trial of interventions to improve childhood asthma in homes with wood-burning stoves. *Environ Health Perspect* 2017;125:097010.
62. GBD 2015 Chronic Respiratory Disease Collaborators. Global, regional, and national deaths, prevalence, disability-adjusted life years, and years lived with disability for chronic obstructive pulmonary disease and asthma, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet Respir Med* 2017;5:691-706.
63. International Agency for Research on Cancer. Household use of Solid Fuels and High-Temperature Frying: Evaluation of Carcinogenic Risks to Humans. Lyon (France): International Agency for Research on Cancer; 2010.
64. Hosgood HD 3rd, Wei H, Sapkota A, Choudhury I, Bruce N, Smith KR, et al. Household coal use and lung cancer: systematic review and meta-analysis of case control studies, with emphasis on geographic variation. *Int J Epidemiol* 2011;40:719-28.
65. Kurmi OP, Arya PH, Lam KB, Sorahan T, Ayres JG. Lung cancer risk of solid fuel smoke exposure: a systematic review and meta-analysis. *Eur Respir J* 2012;40:1228-37.
66. Bruce N, Dherani M, Liu R, Hosgood HD 3rd, Sapkota A, Smith KR, et al. Does household use of biomass fuel cause lung cancer? A systematic review and evaluation of the evidence for the GBD 2010 study. *Thorax* 2015;70:433-41.
67. Raspanti GA, Hashibe M, Siwakoti B, Wei M, Thakur BK, Pun CB, et al. Household air pollution and lung cancer risk among never-smokers in Nepal. *Environ Res* 2016;147:141-5.
68. Pope CA 3rd, Burnett RT, Krewski D, Jerrett M, Shi Y, Calle EE, et al. Cardiovascular mortality and exposure to airborne fine particulate matter and cigarette smoke: shape of the exposure-response relationship. *Circulation* 2009;120:941-8.
69. Smith KR, Peel JL. Mind the gap. *Environ Health Perspect* 2010;118:1643-5.
70. Burnett RT, Pope CA 3rd, Ezzati M, Olives C, Lim SS, Mehta S, et al. An integrated risk function for estimating the Global Burden of Disease attributable to ambient fine particulate matter exposure. *Environ Health Perspect* 2014;122:397-403.
71. Lee MS, Hang JQ, Zhang FY, Dai HL, Su L, Christiani DC. In-home solid fuel use and cardiovascular disease: a cross-sectional analysis of the Shanghai Putuo study. *Environmental Health* 2012;11:18.
72. Baumgartner J, Carter E, Schauer JJ, Ezzati M, Daskalopoulou SS, Valois MF, et al. Household air pollution and measures of blood pressure, arterial stiffness and central haemodynamics. *Heart* 2018;104:1515-21.
73. Young BN, Clark ML, Rajkumar S, Benka-Coker ML, Bachand A, Brook RD, et al. Exposure to household air pollution from biomass cookstoves and blood pressure among women in rural Honduras: a cross-sectional study. *Indoor Air* 2019;29:130-42.
74. Burroughs Peña M, Romero KM, Velazquez EJ, Davila-Roman VG, Gilman RH, Wise RA, et al. Relationship between daily exposure to biomass fuel smoke and blood pressure in high-altitude Peru. *Hypertension* 2015;65:1134-40.
75. Arku RE, Ezzati M, Baumgartner J, Fink G, Zhou B, Hystad P, et al. Elevated blood pressure and household solid fuel use in premenopausal women: Analysis of 12 Demographic and Health Surveys (DHS) from 10 countries. *Environ Res* 2018;160:499-505.
76. Snider G, Carter E, Clark S, Tseng JTW, Yang X, Ezzati M, et al. Impacts of stove use patterns and outdoor air quality on household air pollution and cardiovascular mortality in southwestern China. *Environ Int* 2018;117:116-24.
77. Wallwork RS, Colicino E, Zhong J, Kloog I, Coull BA, Vokonas P, et al. Ambient fine particulate matter, outdoor temperature, and risk of metabolic syndrome. *Am J Epidemiol* 2017;185:30-9.
78. Lam NL, Smith KR, Gauthier A, Bates MN. Kerosene: a review of household uses and their hazards in low- and middle-income countries. *J Toxicol Environ Health B Crit Rev* 2012;15:396-432.
79. Rylance J, Gordon SB, Naeher LP, Patel A, Balmes JR, Adetona O, et al. Household air pollution: a call for studies into biomarkers of exposure and predictors of respiratory disease. *Am J Physiol Lung Cell Mol Physiol* 2013;304:L571-8.
80. Jacobson MZ. Strong radiative heating due to the mixing state of black carbon in atmospheric aerosols. *Nature* 2001;409:695-7.