Millions Dead: How Do We Know and What Does It Mean? Methods Used in the Comparative Risk Assessment of Household Air Pollution

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Abstract

In the Comparative Risk Assessment (CRA) done as part of the Global Burden of Disease project (GBD-2010), the global and regional burdens of household air pollution (HAP) due to the use of solid cookfuels, were estimated along with 60+ other risk factors. This article describes how the HAP CRA was framed; how global HAP exposures were modeled; how diseases were judged to have sufficient evidence for inclusion; and how meta-analyses and exposure-response modeling were done to estimate relative risks. We explore relationships with the other air pollution risk factors: ambient air pollution, smoking, and secondhand smoke. We conclude with sensitivity analyses to illustrate some of the major uncertainties and recommendations for future work. We estimate that in 2010 HAP was responsible for 3.9 million premature deaths and ~4.8% of lost healthy life years (DALYs), ranking it highest among environmental risk factors examined and one of the major risk factors of any type globally.

INTRODUCTION

The Global Burden of Disease 2010 project (GBD-2010) was a large international effort, involving hundreds of investigators, to estimate the envelope of death, disease, and injury by age, sex, disease, and 21 world regions for 1990, 2005, and 2010 (1). As part of the project, dozens of expert groups conducted Comparative Risk Assessments (CRAs) to estimate the portion of the burden attributable to each of ~60 risk factors in the 21 regions (hereafter referred to as CRA-2010) (16).

The CRA for household air pollution (HAP) from use of solid fuels for cooking estimated that this risk factor was responsible for 3.5–4 million premature deaths in 2010 (16). The purpose of this article is to describe in detail how this estimate was derived. We summarize for HAP the framing of the CRA-2010; the evidence bases and modeling used; the distribution of burden by age, sex, and region; and comparison with results for other environmental risk factors. We end with a discussion of the impact of uncertainties and assumptions and the implications for future research and assessment. Because some elements of the HAP CRA were in progress at the time the GBD-2010 was published, we present here refinements that have appeared since, which modestly change the results.

Supplemental Material

Given the extent of the assessment, this article can only briefly describe each element, but more detail is found in the associated **Web Supplement**, including a map of the GBD-2010 regions (**Supplemental Figure 1**). (Follow the **Supplemental Material link** from the Annual Reviews home page at **http://www.annualreviews.org**.)

The CRA-2010 was the second global CRA, following the CRA-2000 published in 2004 (9). For brevity we do not repeat the CRA-2000's discussions on the toxicology of biomass smoke or other issues not directly needed to calculate the burden of disease, although these are relevant to determinations of causality, plausibility, and other issues (31).[1]

GBD: Global Burden of Disease

CRA: comparative risk assessment

HAP: household air pollution

Framing

Since the CRA-2000, we realized that its framing of the risk factor as "indoor air pollution from household use of solid fuel" was inadequate for a number of reasons:

[1]In the **Web Supplement**, we compare the results from the two CRAs and explain the differences.

- Much of the health-relevant air pollution exposure from cookfuel occurs in the near-household environment, not just indoors.
- Solid cookfuel is sufficiently polluting and widespread to appreciably affect widespread ambient (outdoor) air pollution levels and, thus, cause ill-health far from the source.
- The term indoor implies that an effective chimney or other venting would solve the problem entirely, when the basic problem is dirty combustion.
- In some parts of the world, incompletely combusted fuels are commonly used for space heating and/or lighting, as well as for cooking, thus confusing the attribution of risk and assessment of appropriate interventions unless it is specified which household uses are being considered.
- The short version "indoor air pollution" overlaps with much research on indoor pollution from sources of other types, for example from household furnishings and consumer products in the developed sector.

AAP: ambient air pollution

Thus, we have reframed the risk factor as household air pollution from solid cookfuels (HAP).

This reframing explicitly indicates that the assessment is of the total burden due to all exposures to this source of pollution and not to the exposure occurring in any one place in the household. It is more explicit that it refers only to cooking and to the pollution from the fuel, not the food. Because pollution exposures do occur from polluting combustion for space heating and lighting and nonsolid cookfuels, such as kerosene, future assessments will likely wish to add these sources as well. The currently available household survey databases, however, focus on cooking and contain insufficient information on space heating and lighting to enable global assessments.

One consequence of this reframing is that a portion of the burden determined by the ambient air pollution (AAP) CRA expert group is assigned also to HAP because in many areas household emissions form a significant portion of the total outdoor emissions (**Figure 1*c***). It is not removed from the AAP burden, however, because AAP is framed as pollution in a location and not pollution due to a particular source. Future burden estimates, however, may wish to further parse AAP into portions from transport, power plants, industry, etc., as well as households. Thus, the burdens from the two CRAs cannot be simply added to obtain total air pollution impacts because doing so would overestimate the burden by double counting. This is consistent with how attributable burdens from other risk factors operating on the same diseases, for example salt intake and smoking, are interpreted.

Counterfactuals: Theoretical Minimum Risk Exposure Distribution

In the CRA-2000, owing to data limitations, the counterfactual (lowest exposure level considered zero risk) was a loose grouping of the lower exposure categories of the available epidemiologic studies for HAP. This approach has several problems:

- Much mixed fuel use (i.e., solid fuels and cleaner fuels, such as liquefied petroleum gas or electricity) occurs, and thus the low end of exposures did not represent truly low or aspirational levels in most cases.
- The low, as well as high, end was not consistent across different populations and studies.
- The previous HAP CRA was inconsistent with the counterfactual used in the companion AAP CRA, which was an absolute exposure concentration.

Advances in the evidence now allow a more nuanced approach. Several counterfactuals were considered by the expert group (**Supplemental Table 1**), but the final choice was a narrow distribution around an ~7 $\mu g/m^3$ annual mean $PM_{2.5}$, the well-established best indicator of the health risk from combustion emissions. This is the theoretical minimum risk exposure distribution (TMRED) counterfactual chosen by the AAP CRA and represents roughly the cleanest cities in

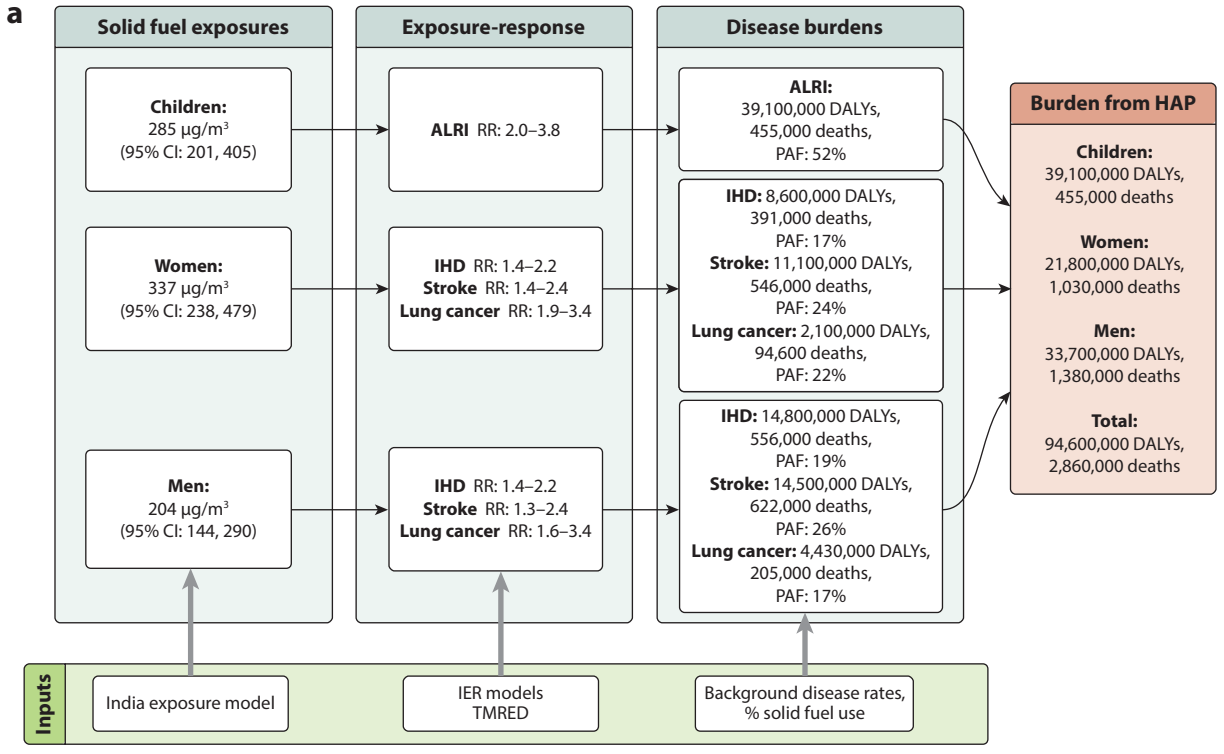

Figure 1

Summary of methods, models, and data sources used in the HAP CRA-2010. The total burden is a sum of the burdens found in panels *a–c*. (*a*) Integrated exposure-response (IER)-based outcomes with modeled uncertainty at the point of the IER estimate; (*b*) meta-analysis-based outcomes with the 95% confidence intervals (CI) shown; (*c*) proportion of the ambient air pollution (AAP) burden due to household air pollution (HAP). Deaths refer to premature deaths. Figures rounded to three significant digits. See **Figure 3** for totals. Other abbreviations: ALRI, acute lower respiratory infections; COPD, chronic obstructive pulmonary disease; CRA, comparative risk assessment; DALY, disability-adjusted life years; IHD, ischemic heart disease; PAF, population-attributable fraction; RR, relative risk; TMRED, theoretical minimum risk exposure distribution.

their database. It is roughly equivalent to what can be achieved by vented cooking with gas fuels. Because ~60% of the world already cooks with gas and/or electricity, it seems reasonable to assign it as a feasible if ambitious TMRED for the remaining ~40% using solid fuels.

Evidence Classes

Supplemental Material

As we elaborate in the **Web Supplement**, investigators divided the available evidence for the association of particular disease end points and HAP into three categories. Only those ranked Class I [multiple epidemiologic studies of good quality in less-developed-country household settings sufficient for meta-analysis, with consistent results as well as significant and positive summary estimates, and with supporting epidemiologic studies from particle exposures both at higher and at lower exposures (Class Ia) or exposure-response data available from several particle exposure settings (Class Ib)] were included in the burden-of-disease calculations because they met the criteria shown in **Supplemental Table 2**.

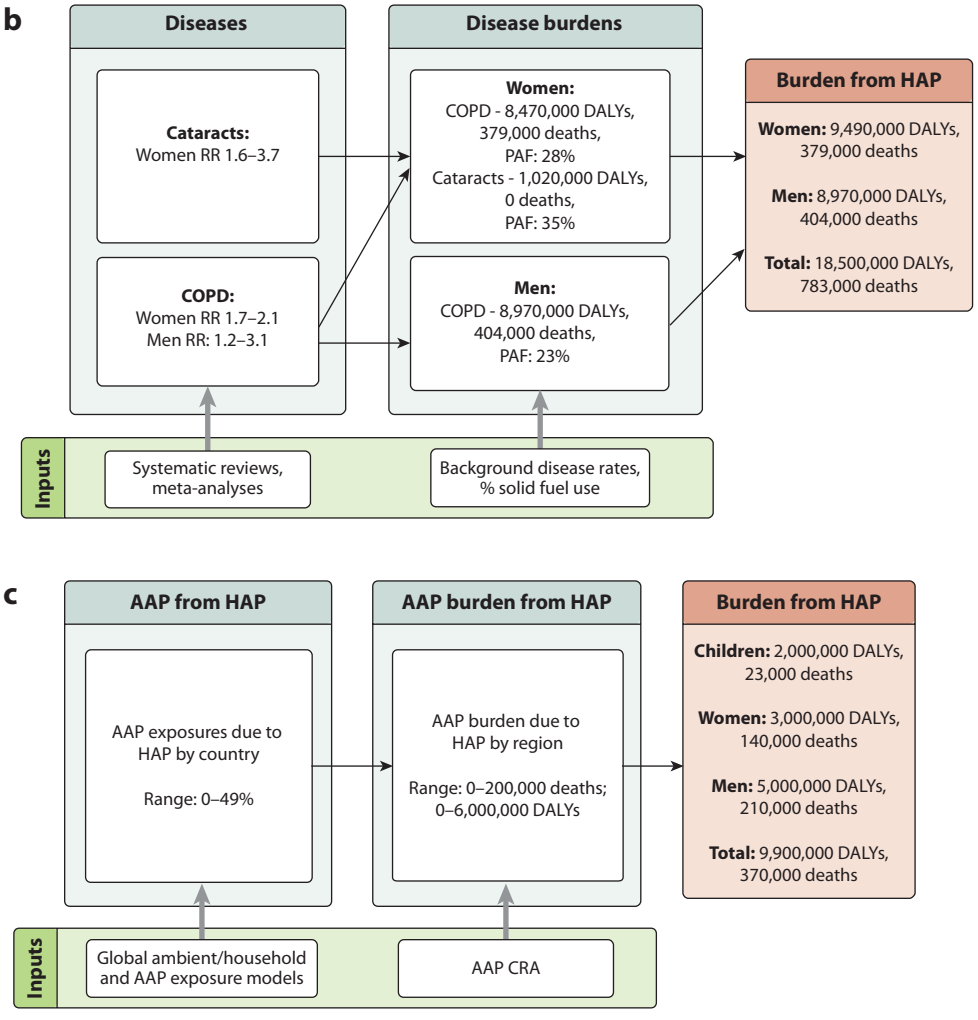

Figure 1

(*Continued*)

Consistency Across Combustion Particle Exposures

We sought consistency in risk estimates across the four combustion particle categories—AAP, secondhand tobacco smoke (SHS), active tobacco smoking (ATS), and HAP—by developing jointly with the AAP CRA group integrated exposure-response (IER) functions incorporating evidence from all four categories of exposure for ischemic heart disease, stroke, lung cancer, and child acute lower respiratory infections (ALRI) (see **Figure 1*a***). The traditional approach using meta-analyses was taken for chronic obstructive pulmonary disease (COPD) and cataracts (**Figure 1*b***). Thus two different counterfactual types are applied within one risk factor but should not exaggerate the overall burden because the second type produces a more conservative estimate than if exposure-response data were available and the aspirational counterfactual applied.

Application of the IERs is only possible, however, because there are now model results that give estimates of absolute exposures to $PM_{2.5}$ households using solid cookfuels in India, the country

SHS: secondhand tobacco smoke

ATS: active tobacco smoking

IER: integrated exposure-response

ALRI: acute lower respiratory infections

COPD: chronic obstructive pulmonary disease

where the most HAP studies have been done. We apply the results of this model worldwide, which seems reasonable given the consistency of measurements in other countries and given that India contains one-quarter of global households cooking with solid fuel.

EXPOSURE ASSESSMENT

This section describes the three components of the exposure assessment for the CRA for HAP:[2]

- a global solid fuel use (SFU) model showing the number of households and percentage of population in each country that cook primarily with solid fuels;
- an Indian model estimating average concentrations of $PM_{2.5}$ for urban and rural households cooking with solid fuels, values which were used as a basis for estimating average $PM_{2.5}$ exposures for children, women, and men residing in these households; and
- a global model estimating the contribution of household combustion of solid fuels to ambient $PM_{2.5}$ levels at the national level.

Global Solid Cookfuel Use Model

National SFU has served as a useful surrogate for exposure to HAP in many epidemiologic studies and in previous risk assessments because this information is easy to collect and frequently reported (21, 31). As a key step toward quantifying the number of households or the fraction of the population exposed to HAP, a nonparametric multilevel model was developed using national survey data to derive annual SFU estimates for countries between 1980 and 2010 (5).

The primary data source for the modeling was the World Health Organization (WHO) household energy database (36). This database is a systematic compilation of nationally representative surveys and censuses that provides estimates of the percentage of households cooking primarily with solid fuels (coal, wood, charcoal, dung, and crop residues), liquid fuels (kerosene), gaseous fuels (liquefied petroleum gas, natural gas, biogas), and electricity. At the time of the CRA, it housed results of 566 nationally representative household energy surveys covering 1975 to 2010 and 155 countries, including 97% of all lower- and middle-income countries (LMICs). Investigators used a multilevel model to estimate the percentage of households relying primarily on solid fuels for cooking for 150 LMICs with at least one survey data point. Regional estimates were used instead of model estimates for seven LMICs without survey data.

The absolute number of people using mainly solid fuel for cooking has remained stable over the past three decades at ~2.8 billion. The proportion of the world's households relying mainly on solid fuels for cooking, however, has declined from 53% [95% confidence interval (CI): 49, 56] in 1990 to 46% (95% CI: 42, 49) in 2005 and 41% (95% CI: 37, 44) in 2010 (5). There is large regional variation and sub-Saharan Africa and South Asia show the most widespread SFU. See **Supplemental Figure 2** for details.

Supplemental Material

Indian Model of Household Concentrations and Personal Exposures to HAP

As noted in the introduction, a set of IER functions was developed as part of the CRA-2010 to link HAP exposure with relevant health outcomes. Population-level exposure estimates are required to use these curves to estimate the disease burden attributable to HAP. Drawing on HAP measurements in rural households of multiple Indian states and nationally representative Indian

[2]A more detailed description of each component can be found in the **Web Supplement**.

data on cooking-related variables, researchers developed a model to estimate average household $PM_{2.5}$ concentrations (3). Average $PM_{2.5}$ exposures for different household members were derived from ratios of household concentrations to personal exposures reported in a global database of studies (2). These estimates for India were applied to all countries.

Studies measuring 24-h kitchen and living area $PM_{2.5}$ concentrations were conducted across 617 rural households drawn from 24 villages across four Indian states. A log-linear multiple regression model related measured $PM_{2.5}$ concentrations to different cooking-related household-level variables. Fuel type, kitchen type, ventilation, geographical location, and cooking duration were all significant predictors of $PM_{2.5}$ concentrations in the household-level model. Coefficients from these models were used with information on the same variables from the Indian National Family Health Survey (NFHS) 2005 to estimate household concentrations at state and national levels. Finally, median ratios between daily average personal exposures and kitchen concentration from available published studies (0.742 for women, 0.628 for young children, 0.450 for men) were applied to estimate exposures for different household members (2).

The measured mean daily $PM_{2.5}$ concentrations in rural solid fuel–using households ranged from 163 $\mu g/m^3$ in the living area to 609 $\mu g/m^3$ in the kitchen area (confidence intervals and other details in the **Web Supplement**). A fair degree of correlation ($r = 0.56$) between modeled and measured values was found in k-fold cross validation. Although not high enough to confidently predict levels in individual households, this result was judged sufficient to estimate population-wide levels.

Extrapolation of the household-level model to all solid cookfuel–using households in India, covered by NFHS 2005, resulted in a modeled estimate of 450 $\mu g/m^3$ and 113 $\mu g/m^3$, for a national average of 24-h $PM_{2.5}$ concentrations in the kitchen and living areas, respectively. Assuming similar kitchen to living area distributions for rural and urban solid fuel–using households, investigators estimated average national personal exposures to be 285 $\mu g/m^3$ (95% CI: 201, 405) for children, 337 $\mu g/m^3$ (95% CI: 238, 479) for women and 204 $\mu g/m^3$ (95% CI: 144, 290) for men. See **Supplemental Figure 3**.

Global Model of HAP Contribution to Ambient Air Pollution

Not only does household combustion of solid fuels subject cooks and their families to harmful pollution indoors, but—with pollutants exiting through windows, chimneys, or gaps in walls and roofs—it also contributes to AAP (28). This is particularly concerning for areas where most households cook with solid fuels, such as villages in many LMICs, where ambient $PM_{2.5}$ concentrations are often, but not always, lower than in most cities but nevertheless high enough to be of concern (6). Drawing on two existing global models, investigators calculated the proportion of ambient $PM_{2.5}$ attributable to household combustion of solid fuels; subsequently, this estimate was applied to derive the AAP-attributable burden due to HAP.

For this analysis, it was important to distinguish households from other emissions sources, such as industrial processes, electricity and heat generation, agriculture, and ground transport. To do so, we used the Fast Scenario Screening Tool for Global Air Quality and Instantaneous Radiative Forcing (TM5-FASST) (34), hosted by the European Union Joint Research Center. It was also important to separate household cooking emissions from those related to household space heating. For this, investigators used the emission inventory developed for the Greenhouse Gas and Air Pollution Interactions and Synergies (GAINS) model, hosted by the International Institute for Applied Systems Analysis (13). Emission estimates of household combustion of solid fuels as a percent of total ambient $PM_{2.5}$ were then calculated for 170 countries.

SRMA: systematic reviews and meta-analyses

Supplemental Material

In 2010, the fraction of outdoor combustion-derived $PM_{2.5}$ pollution attributable to household cooking with solid fuels varied from 0% (five regions) to 10% (East Asia, the region housing China), 26% (South Asia, the region housing India), and 37% (in southern sub-Saharan Africa), with a global average of 12%. Global averages for the years 1990 (13%) and 2005 (11%) are largely similar, but marked changes have been observed in many regions, for example in East Asia (1990: 23%; 2005: 14%) and South Asia (1990: 15%; 2005: 30%); in all four sub-Saharan African regions (Central, Eastern, Southern, and Western) the proportions of household combustion-derived $PM_{2.5}$ have more than doubled between 1990 and 2010. As shown in **Supplemental Table 4** for the year 2010, these data imply that 373,000 deaths and 9.9 million DALYs caused by exposure to AAP are attributable to household cooking with solid fuels (Z. Chafe, M. Brauer, Z. Klimont, R. Van Dingenen, S. Mehta, S. Rao, K. Riahi, F. Dentener, K.R. Smith, in review). Nearly 90% of this toll occurred in East and South Asia.

EVIDENCE BASE FOR PRIMARY HEALTH OUTCOMES

Two requirements for outcomes included in the CRA are (*a*) evidence of a causal association with HAP and (*b*) an estimate of risk derived from studies with sufficient adjustment for confounding, and free of serious bias. All outcomes considered by the expert group were systematically reviewed, but only Class I outcomes are summarized here. Reviews for Class II and III outcomes are summarized in the **Web Supplement**. All systematic reviews and meta-analyses (SRMA) of primary outcomes used similar methods, which are described in the **Web Supplement**, along with discussion of consistency with other recently published SRMAs. See **Supplemental Table 2**.

Child Acute Lower Respiratory Infections

Systematic review and meta-analysis. Child ALRI remain the single most important cause of global mortality under age five. This review, which has been published, identified 24 eligible studies (8). Only three studies included direct measurement of exposure; the remainder used proxies (fuel type, etc.). Outcome definitions varied from parental recall of signs to X-ray confirmation and included severe and fatal outcomes; included studies had to distinguish upper from lower respiratory infections. There was significant publication bias (Egger's: $p = 0.016$), which subsequent, stratified analysis suggests may be explained by smaller studies of severe/fatal outcomes having higher risk estimates. The pooled odds ratio (OR) was 1.78 (1.45, 2.18), with substantial heterogeneity ($I^2 = 74\%$). Sensitivity analysis of methodological factors had little impact; separate male and female values were available from only one study. There is a strong case for causation, with supporting intervention and exposure-response evidence reported below.

RESPIRE RCT and exposure-response studies. Only one RCT on HAP and child ALRI has been completed (30), involving 534 Guatemalan children aged ≤18 months randomized to use of a chimney wood stove or a traditional three-stone fire. The primary outcome was physician diagnosis, with pulse oximetry to define severity. Exposure was assessed for all children using repeated CO measurements, together with colocated kitchen CO and $PM_{2.5}$ measurements in a subsample to define the CO-$PM_{2.5}$ relationship.

In the intention-to-treat analysis, child exposure was reduced by 50% and was associated with a relative risk (RR) of 0.78 (0.59–1.06) for all physician-diagnosed pneumonia and of 0.67 (0.45, 0.98) for severe pneumonia (low oxygen saturation). Adjusted exposure-response analysis found significant relationships for both all and severe pneumonia (**Figure 2**). These findings support causal inference and show that the greatest risk reduction occurs at lower exposure levels.

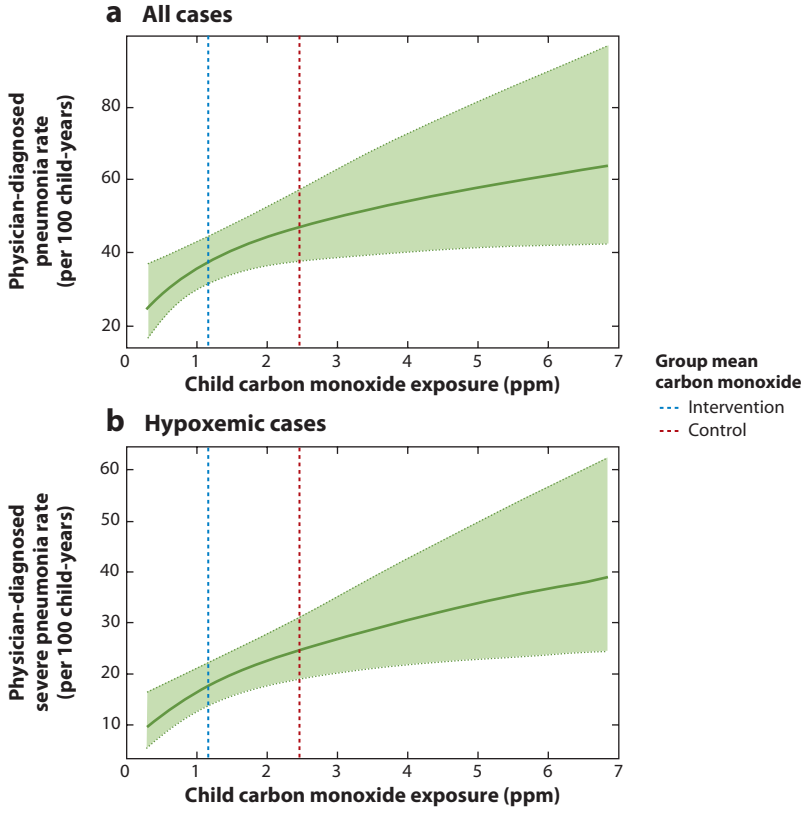

Figure 2

Relationships between long-term carbon monoxide (CO) exposure in children and pneumonia incidence (*upper curve*) and severe pneumonia (*lower curve*), from the RESPIRE study. The dashed (*red*) and (*blue*) lines represent the mean exposure levels in the control and intervention groups, respectively. The CO levels were converted to PM based on local studies to derive the PM/ALRI relationships for the integrated exposure response functions used in the CRA (6a). Based on data in Smith et al. 2011 (30).

Chronic Obstructive Pulmonary Disease

COPD is of growing importance, projected to be the third leading cause of global mortality and morbidity by 2020, and HAP may be the most important cause in nonsmoking populations. This review identified 24 studies, all observational (17 cross-sectional). Exposure measures were proxies and differed greatly; no study directly measured HAP. Outcome definitions variously used clinical diagnosis, spirometry, and chronic symptom recall. There was strong evidence of publication bias (Egger's test: $p = 0.007$); the pooled OR was 1.94 (1.62, 2.33) with substantial heterogeneity ($I^2 = 85\%$). Sensitivity analysis identified influences of study design, smoking, age, and type of fuel (wood versus coal) and indicated a significant trend by duration of use (not all adjusted). Separate estimates by sex were 2.30 (1.73, 2.06) for women and 1.90 (1.15, 3.13) for men.[3] Causal

[3]The RR values used in Reference 16 were 2.70 (1.95–3.75) and 1.90 (1.56–2.32), respectively, for women and men, based on an earlier version of this review. Subsequent reanalysis produced the RR estimates reported here, which resulted in an approximate 15% lower burden in women for COPD globally or ~67,000 premature deaths. No change was noted for men.

inference is supported by these findings, consistency (almost all studies reported increased risk, though not all significant), positive intervention-based findings (7), exposure-duration evidence, analogous evidence from smoking, and biological plausibility.

Lung Cancer

The International Agency for Research on Cancer (IARC) has concluded that emissions from household use of coal are a Group 1 carcinogen, whereas those from biomass are Group 2(a), a probable carcinogen, with more limited epidemiologic evidence (12). Consequently, although the review of coal updated the effect estimate, the review for biomass also focused on whether recent epidemiologic evidence would support causal inference.[4]

Coal and lung cancer. The SRMA for coal, which have been published (11), identified 25 case-control studies investigating household coal use, 7 of which provided cooking-specific estimates. Exposure was assessed by fuel type, and lung cancer was confirmed by pathology for most cases, otherwise by X-ray. No significant publication bias was noted (Begg's test: $p = 0.15$). For cooking, the OR was 1.81 (1.19, 2.76), and when restricted to China and Taiwan (to reduce heterogeneity), and compared with clean cooking fuel, the 2 remaining studies (women only) had an OR of 1.98 (1.16, 3.36). No equivalent analysis was available for men; an estimated OR of 1.31 (1.05, 1.76) was obtained by applying the F:M ratio for biomass (see below).

Biomass and lung cancer. This review identified 14 eligible studies of cooking and/or heating with biomass, including reanalysis of one European study (17) by IARC to obtain sex-specific estimates and examine exposure-response evidence. Exposure was determined by fuel type, and no study directly measured HAP. As with coal, most cases of lung cancer were confirmed pathologically. There was no evidence of publication bias (Egger's test: $p = 0.61$). The overall OR was 1.18 (1.03, 1.35) with moderate heterogeneity ($I^2 = 40\%$). For men, restricting analysis to studies of cooking, adequate adjustment, and clean fuel comparison, the OR ($n = 2$ studies) was 1.26 (1.04, 1.52), $I^2 = 0\%$. The equivalent OR for women ($n = 5$ studies) was 1.81 (1.07, 3.06), $I^2 = 61\%$. These findings, combined with evidence of exposure-response relationships in the reanalysis of the study by Lissowska (significant for men only) and the previously reviewed animal and mechanistic evidence (12), support causal inference.

Cataract

Cataract is a leading cause of blindness, including high rates in countries with high solid fuel use. Evidence of increased risk with smoking suggests that a link with HAP is plausible. This review identified eight eligible studies, most case-control designs and all from India or Nepal. No strong evidence of publication bias was noted. The pooled OR was 2.46 (1.74, 3.50) with substantial heterogeneity ($I^2 = 62\%$). Sensitivity analysis found no important effects resulting from smoking or UV (ultraviolet) exposure. Adjustment for or exclusion of diabetes found conflicting results, possibly explained by recent evidence linking solid fuel use and diabetes (14). The OR of 2.47 (1.61, 3.73) for women from studies adjusting for smoking, or excluding smokers, appears to be the most reliable estimate, but evidence for men was judged to be insufficient to

[4]The results of the assessments of lung cancer from both household biomass and coal smoke were used in creating the IER for lung cancer, which was the basis of both the HAP and AAP CRAs.

propose this as a Class I outcome.[5] These findings, the risks from smoking, consistency (albeit all in South Asia), toxicology, and some exposure-response evidence support causal inference (23).

EXPOSURE-RESPONSE ACROSS COMBUSTION PARTICLE SOURCES: IERs

During the development of the CRA methodology, two papers were published (24, 25) that model cardiovascular and lung cancer mortality risks across the three orders of magnitude in range of fine particulate exposures associated with three major sources of combustion pollution: AAP, SHS, and ATS. These papers used the nominal (inhaled) daily dose of combustion particles as the exposure metric, which had been used previously to compare health risks across these sources of exposure (27).

This approach has been expanded and elaborated to develop effect estimates for the AAP and HAP CRAs in IER for several major categories of disease. Where possible, evidence from HAP epidemiologic studies, as well as that from epidemiologic studies of AAP, SHS, and ATS, has been included.

The use of IERs is a major innovation of the CRA-2010. It overcomes some difficulties in the methods used in the CRA-2000 by allowing estimation of

- the risks for diseases for which there is AAP evidence at lower exposure levels but no evidence at the higher levels typical in many parts of the world—to do this, the ATS results anchor the upper end of the relationship for most diseases and, in the case of child ALRI, HAP results anchor the upper end;
- HAP risk for diseases known to be caused by ATS, SHS, and AAP, but for which there are no or minimal HAP studies by interpolating between ATS results at higher exposures and SHS/AAP results at lower exposures; and
- the total risk range for burden calculations by HAP and AAP using the same TMRED (counterfactual).

Here we briefly summarize the IER results by disease, focusing on the implications for the HAP CRA (for details, see 6a).

CVD in Adults

Although we have supporting evidence of various kinds, including studies showing effects of HAP on blood pressure (4, 20) and cardiac ST-segment (18), there seem to be few studies done yet on cardiovascular disease (CVD) itself. [In 2012 (32), a special issue of *Global Heart* reviewed the existing literature on epidemiology and mechanisms.] On the other hand, the massive evidence of CVD effects at higher exposures (ATS) and lower exposures (SHS and AAP) argues strongly that HAP exposure levels likely produce effects. In this CRA, HAP by definition consists of smoke from coal and/or biomass combustion. Tobacco is biomass, and much of AAP comes from biomass combustion as well as, of course, burning of fossil fuels, dominated by coal globally. Although the literature reports some differences, all major reviews of combustion particle health impacts indicate that there is insufficient evidence to treat the various combustion particles differently (e.g., 35, 37). From this evidence, investigators drew two conclusions for this CRA:

- Although there is little direct evidence, it is reasonable to expect CVD risks in the particle exposure region between ATS and SHS/AAP that are also intermediate. This conclusion

[5]This is slightly less precise than the estimate used in Lim et al. (2012) (16) 2.47 (2.04, 3.15), a difference that does not affect the central estimate.

relies on interpolation within existing evidence, an operation with much more acceptance in scientific work than extrapolation beyond the range of the evidence.

- Because we do not have sufficient evidence to treat HAP particles differently from those in the other categories (AAP, SHS, ATS), it is reasonable to use nominal inhaled dose as the linking exposure metric because it works reasonably well in models linking risks from particle exposures from the other source categories.

There are additional assumptions inherent in this approach, of course, among which is that the pattern of exposures during the day and over the life course does not affect the results substantially. Even without considering these, the uncertainty intervals in IER modeling are substantial; see **Supplemental Figure 9** (6a).

Supplemental Material

Lung Cancer

Unlike with CVD, evidence from HAP studies of the risks from lung cancer is plentiful (see Section 3.3), which thus informs the modeling of the IER (**Supplemental Figure 10**). For the purposes of the CRA, however, no distinction was made between biomass and coal smoke, even though some evidence indicates that the latter is more carcinogenic (12).

ALRI in Children

Unlike CVD outcomes, there is an exposure-response study for ALRI for HAP as well as many binary-exposure-category studies, as discussed above. In parallel to what was done for CVD outcomes, therefore, the IER for ALRI was informed by AAP, SHS, and HAP studies (6a). Unlike CVD, of course, there are no studies from ATS because young children do not smoke. This work was informed by

- an SRMA of studies conducted in areas with average annual ambient concentrations ranging from 12.1 to 25 $\mu g/m^3$ (22);
- estimates of ALRI risk due to SHS exposure from either parent, at an estimated $PM_{2.5}$ exposure of 50 $\mu g/m^3$ from the US Surgeon General's Report (33); and
- information on the incidence rates of ALRI from the RESPIRE study observed at deciles of average personal exposure to $PM_{2.5}$ ranging from ~40–400 $\mu g/m^3$ estimated from personal monitoring of carbon monoxide (19, 30).

The result is shown in **Supplemental Figure 11** and indicates that the risk of ALRI from child exposures to HAP at Indian levels (285 $\mu g/m^3$) would range from 2.0 to 3.8. This is consistent with what was found for the ALRI SRMA for RESPIRE, considering that those studies had a lower exposure category far above the 7 $\mu g/m^3$ that is being applied here. The AAP studies indicate that there is considerable additional risk at those levels, i.e., below ~40 $\mu g/m^3$.

COPD

Although the AAP CRA utilized the IER derived for COPD, the HAP group decided to use the results of the meta-analysis presented above because the HAP results lay far from the model fit to the results for AAP and ATS in the IER (6a). This result may be due to differences in the life course of exposures across the risk factors, including the age at which exposures begin.

RESULTS

Many metrics are available for comparing results from the CRAs for different risk factors, which is one of the strengths of the GBD projects. Given the space limitations here, however, we focus

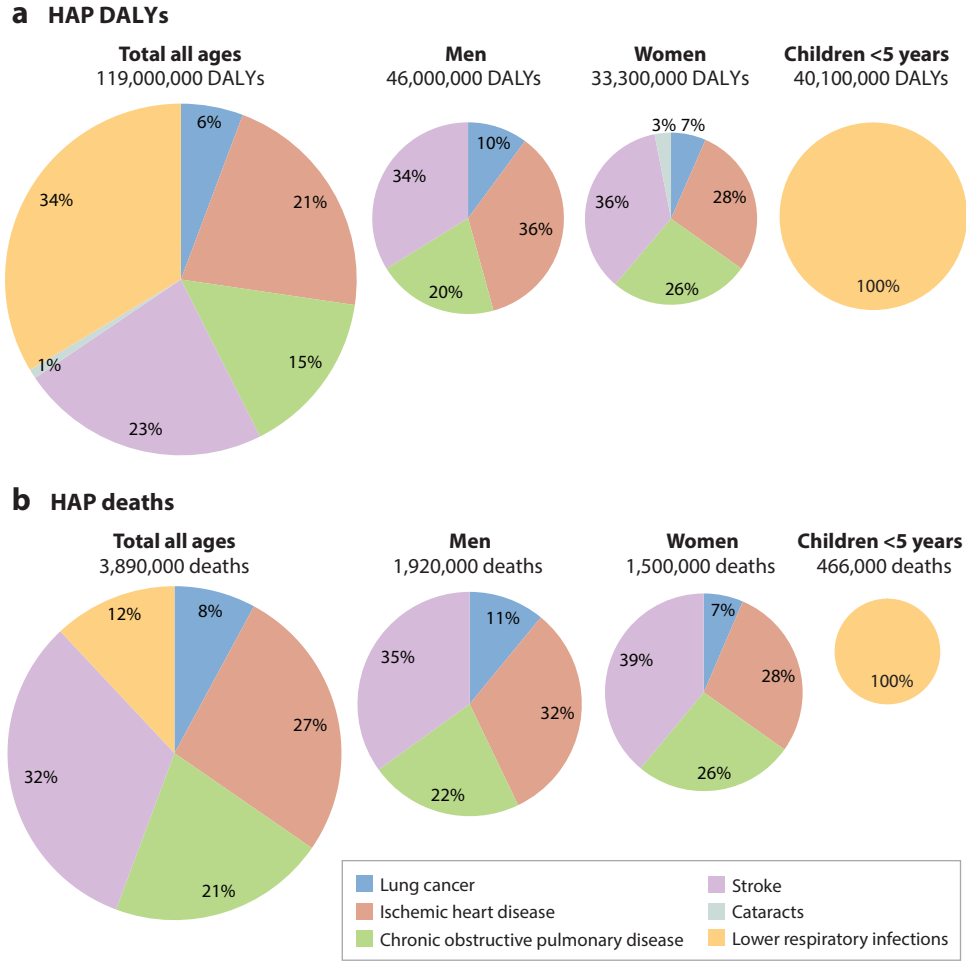

Figure 3

Adjusted total household air pollution (HAP) burden-of-disease results for 2010. The results of **Figure 1*c*** were adjusted by the overlap in population-attributable fractions (PAFs) found for India for HAP and AAP as shown in **Figure 5** before being added to the results from **Figures 1*a*** and **1*b***. Disability-adjusted life years (DALYs) and premature deaths.

on disability-adjusted life years (DALYs) and premature mortality just for 2010.[6] The adjusted total DALY burden from HAP globally is 119 million or 4.8% of the GBD and accounts for ~3.9 million premature deaths.[7] See **Figure 3**.

As discussed above, investigators attempted to bring the assessments of four of the five combustion particle source categories into some coherence through the IER functions. Because

[6]Readers are encouraged to investigate the interactive graphical presentation options at the Institute for Health Metrics and Evaluation (IHME) website for displaying GBD and CRA information (**http://www.healthmetricsandevaluation.org/tools/data-visualizations**).

[7]The total in **Figure 1*c*** from the AAP due to HAP has been adjusted for the overlap in population-attributable fractions (PAFs) found in India for adult and child air-pollution-related diseases. See **Figure 5**.

Supplemental Material

occupational particle exposures tend to affect relatively healthy working populations and include a wide range of particle types, no attempt was made to include these exposures, although this might well be done in future. **Supplemental Figure 17** shows the disease categories used in each of the four PM CRAs. Note that owing to much higher exposures, easier-to-identify exposed populations, and perhaps larger research funding over longer periods, many more disease categories have been identified for ATS than for any other category. Although there is general coherence in that more end points are found for higher exposure categories, there are some discrepancies. Cataracts were identified as an end point for HAP in the CRA-2010 but not for ATS, for example, and otitis media was identified for SHS but not for HAP. That ALRI and otitis media in children were not listed for ATS is consistent, however, because young children do not smoke but are exposed to all three other categories. Owing to differences in risk factor prevalence and different regional burdens of disease, there are also some differences in the extent to which end points and populations were addressed across risk factors and geographies. For example, there is a much smaller evidence base on risk factors for COPD among nonsmoking populations in developed countries, where smokers bear the largest burden, and little direct evidence of ALRI mortality in AAP studies done in developed countries with better health care and in prospective studies anywhere owing to ethical requirements to provide treatment. Although some 60 risk factors were examined in the CRA-2010, we focus on environmental risk factors, including both ATS and SHS (**Supplemental Table 9**). **Figure 4** shows the 2010 comparisons across environmental risk factors globally and by five major regions for both DALYs and deaths, normalized to population.[8] The regions are ranked by Human Development Index and show trends for the major risk factors that are roughly commensurate with the Environmental Risk Transition framework; i.e., household risks decline with development and community-level risks first rise and then fall with development (29).

The difference in the ranking when comparing results by DALYs instead of deaths comes from two factors. Some important outcomes cause few if any deaths but are associated with many years lived with disability (YLDs in the DALY). This is particularly evident in the occupational category where low back pain and noise account for 40% of global DALYs (a bit more than all injuries) but no deaths.[9] In addition, those categories that increase mortality among younger populations will be represented more heavily in DALY terms than in mortality because the YLL term in the DALYs (years of lost life compared with the world's best life expectancy, 86 years) will be much higher than for adult deaths. For example, ALRI in children account for less than 13% of deaths from HAP globally but account for nearly 35% of DALYs.

It is tempting to add the separate results of the CRA from each risk factor to obtain an estimate of the total impact of environmental risk factors. This process must be done with caution, however, because there are sometimes overlaps, correlations, and other nonlinear interactions. Where the disease outcomes are entirely different, for example radon and unimproved water, no serious error is created by adding them. Or where the populations are separate, for example ATS and SHS, they can be added. In a few situations in which synergistic interactions have been documented, for example smoking and radon, the impact of the two together is greater than the sum of the two independently (15). The level of interaction among air pollution exposure categories is not well understood, which is why no aggregate total was shown in the CRA-2010 for air pollution.[10]

[8]The table from which **Figure 3** was prepared is found in the **Web Supplement**.

[9]Another factor is that fairly high disability weights were determined for low back pain. See Reference 26.

[10]The error of simply adding CRA results without considering overlaps and interactions was made in the original CRA-2010 paper. The difficult-to-interpret result is that in some regions the sum of burdens due to the examined risk factors impossibly add to more than 100% of all DALYs (see Ref. 16, figure 6).

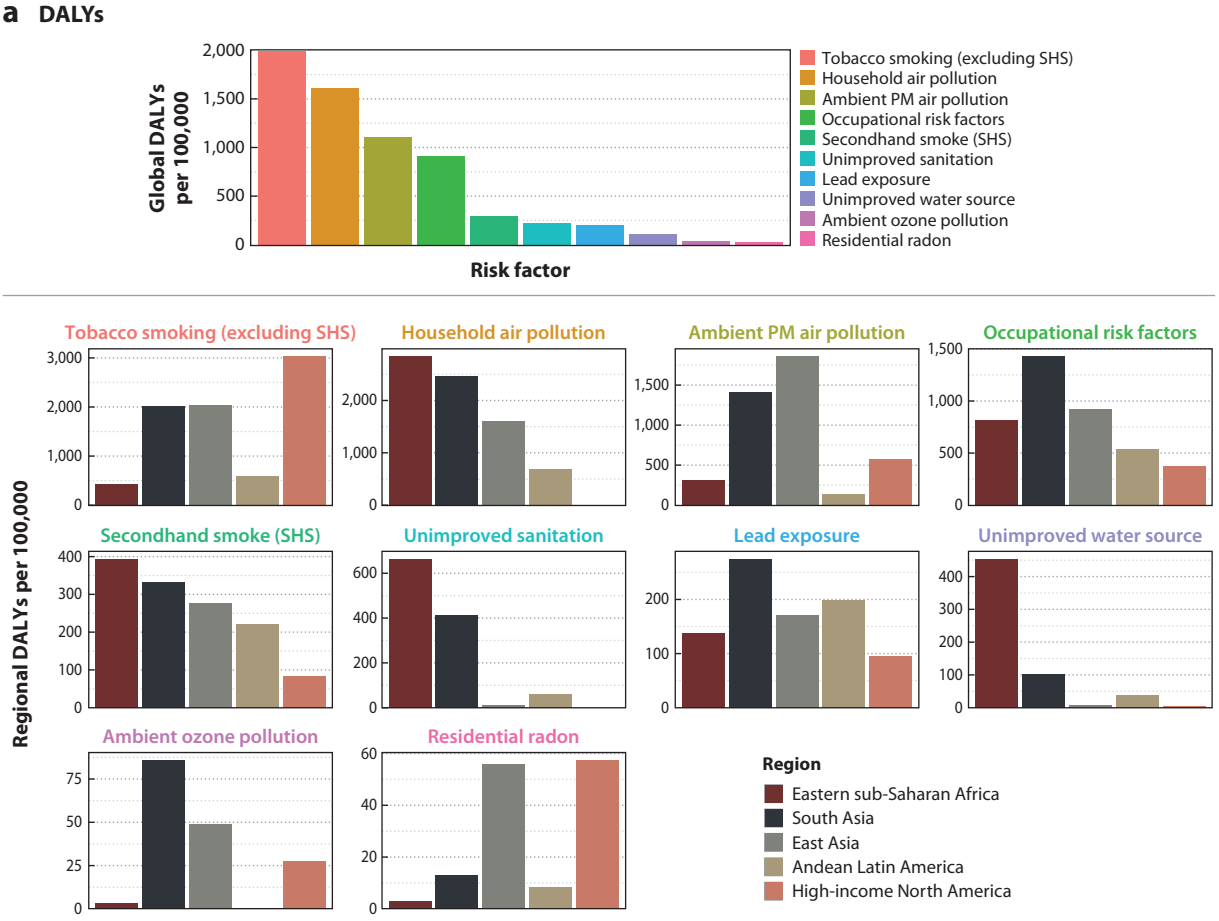

Figure 4

Comparison of environmental risks across regions and globally per 100,000 population. (*a*) Disability-adjusted life years (DALYs); (*b*) premature deaths. Representative regions are ranked by Human Development Index (HDI) from lowest to highest—left to right. Abbreviation: PM, particulate matter.

By assuming independence and little correlation between risk factors with impacts on the same diseases, however, the total impact can be calculated to be less than the sum on the basis of a straightforward calculation using the associated population-attributable fractions (PAFs) (10). **Figure 5** shows the results of such a first-level calculation for the overlap of the four PM exposure groups in the CRA-2010 for heart disease in men and women separately and for child ALRI in India.

As is true globally, in India men smoke more than women, which results in a larger overlap with other risk factors for men, as shown in **Figure 5**. The figure also reflects the apparently counterintuitive result in the HAP CRA shown in **Figure 3** that, although the risk from HAP is greater in women because they have higher exposures, the burden is higher in men because they have greater background rates of the major smoke-related diseases—ischemic heart disease (IHD), COPD, stroke, and lung cancer—because they are more likely to smoke. With a somewhat different counterfactual, however, stated as "how much burden would be associated with HAP if there was

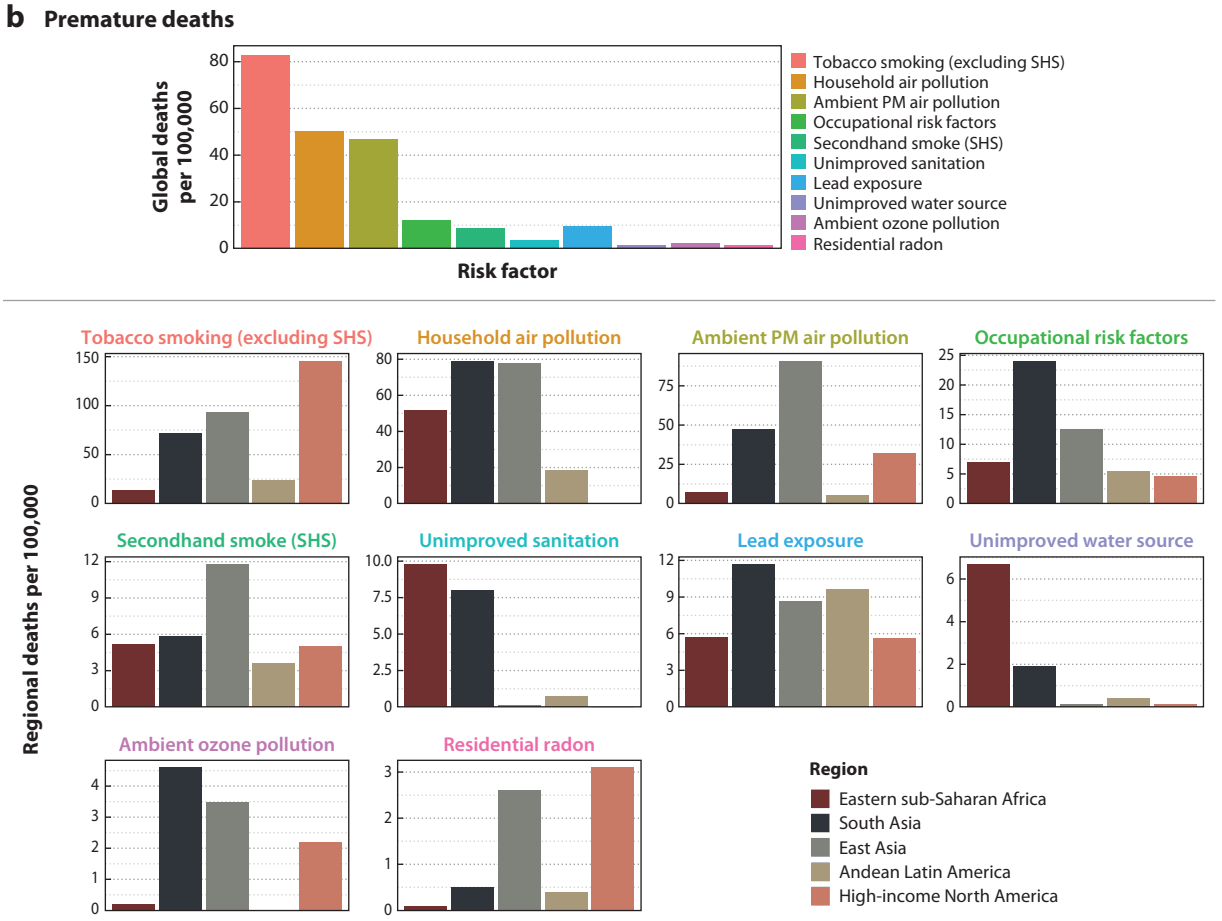

Figure 4

(*Continued*)

no smoking," the burden for women would be greater than that for men. Again perhaps counter-intuitively, the burden from smoking could be reduced by controlling HAP alone and vice versa.[11]

Figure 5 indicates that in India in 2010 all but 24% of IHD in men, 42% of IHD in women, and 33% of ALRI in children could have been eliminated had there been no exposures to ATS, SHS, HAP, and AAP. Alternatively, past control of HAP and AAP together would have reduced IHD in men, IHD in women, and ALRI in children by 55%, 52%, and 59%, respectively.

DISCUSSION

Several judgments were made in doing the HAP CRA, which reflect choices in addressing uncertainties and making cut-offs. The following are among the more important:

[11] For the same reason, men also have a higher burden from AAP than women do, even though their exposures are considered the same.

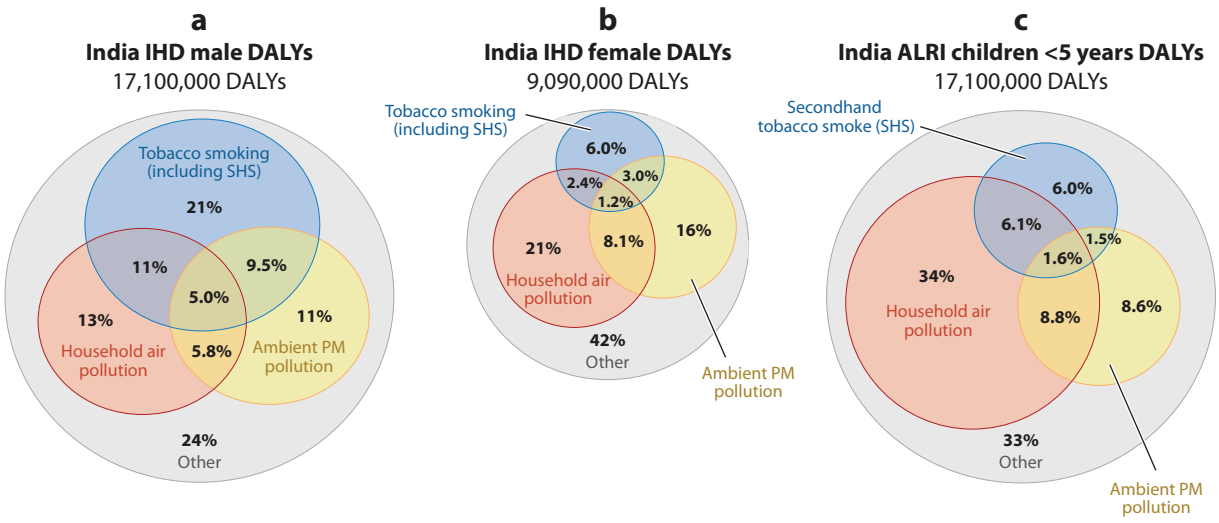

Figure 5

Population-attributable fraction (PAF) diagrams: overlaps in India of PAFs for the four main categories of exposure to combustion particles [active tobacco smoking, secondhand smoke (SHS), household air pollution, and ambient particulate matter (PM) pollution]. (*a*) Adult male ischemic heart disease (IHD); (*b*) adult female IHD; (*c*) child acute lower respiratory infections (ALRI). Abbreviation: DALY, disability-adjusted life years; n.b. total DALYs for male IHD and child ALRI in India are coincidentally similar.

- Investigators had to choose which disease outcomes to include. Exclusion of IHD and stroke because of the lack of any direct HAP evidence, for example, would have resulted in a major reduction in estimated burden but would have been inconsistent with the CRAs for ATS, SHS, and AAP. Inclusion of outcomes deemed Class II in terms of the available evidence (tuberculosis, for example) would have resulted in a major increase (see discussion in the **Web Supplement**).
- The use of the IER functions to calculate risks, particularly by interpolation, implies a range of similarities across particle exposure categories that have not yet been fully confirmed (see discussion in (6a).
- The use of a quite low TMRED (counterfactual) seems consistent with those used in other CRAs but does represent levels that cannot be achieved for HAP at present except by use of gas or electric cooking. Other counterfactuals could be considered, for example, WHO air-quality guideline levels.
- Investigators had to estimate annual exposure levels for use with the IERs with a model informed by less than 1,000 household measurements in India alone and apply it to the entire world. As noted above and in the **Web Supplement**, although the model does not have high predictive power, the purpose in the CRA, however, is not to assign a value to particular households, but to describe wide scale central values and distributions. It is valuable, nevertheless, to understand how sensitive the final burden figures are to the estimated exposures.

Supplemental Material

Figure 6 shows the results of a sensitivity analysis that varies the exposure estimates from the lower to the upper 95% confidence levels in the exposure model used in the HAP calculations for burden of disease in India (see **Web Supplement**). Perhaps surprisingly, the burden estimates are not highly sensitive (+/− ~10%) to such big changes (−30% to +40%) in exposure because of the highly nonlinear form of the IERs, as described above. The degree to which this happens,

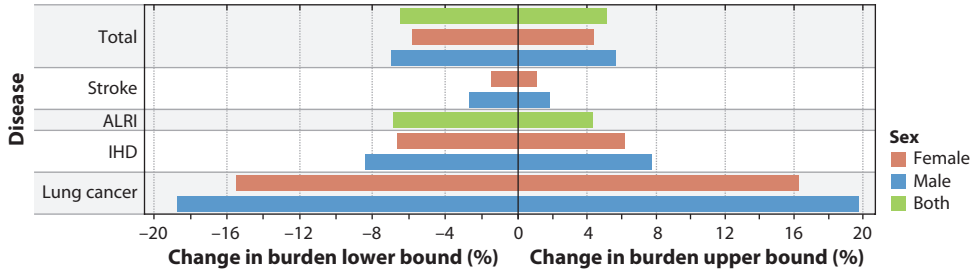

Figure 6

Sensitivity of the Comparative Risk Assessment (CRA) for HAP in India to uncertainty in exposure estimates. Percent change in burden at the lower bound and percent change in burden at the upper bound for each sex, broken down by disease. Change in child acute lower respiratory infection (ALRI) burden was calculated on the basis of exposure bounds for children <5 years. Note that even taking the upper and lower intervals of the exposure estimates (−30% to +40% of the central estimate) shifts the burden estimates by <10%. Abbreviation: IHD, ischemic heart disease.

however, varies by disease because they each have somewhat different forms; lung cancer being closest to linear (i.e., most affected), followed by IHD and ALRI, with stroke showing a nearly flat response over that range.

An unfortunate aspect of the CRA-2010 is that not all important risk factors were examined. This limitation is mentioned in the publications but often disregarded in summaries and the media. Although this is not an issue with HAP, per se, it has important implications for how the HAP results should be interpreted. For example, poor HIV control (e.g., lack of condom promotion), poor malaria control (e.g., lack of bed net promotion), lack of child vaccination, and lack of child health services were not included but are major risk factors in many poor regions. Here we illustrate by re-examining the CRA results for a country, Uganda, where HIV/AIDS and malaria together account for a very large portion of the national disease burden. Indeed, they were numbers one and two in terms of YLLs, accounting for five times more YLLs than the third disease, ALRI. In **Figure 7**, however, the solid bars show the major risk factors in the presentations from the CRA-2010; HAP is seen to be the second most important risk factor in the country, between alcohol and child malnutrition, and no risk factors are shown for HIV/AIDS and malaria.

In the spirit of a sensitivity analysis, we calculated simple CRA results for Uganda that compare what level of reduction it could have been achieved had it been able to achieve the HIV/AIDS and malaria rates of the best-performing sub-Saharan African countries: Senegal and Botswana, respectively. We also include the ethically required counterfactual of zero incidence (as with smoking) for the major vaccine-preventable child diseases—measles, whooping cough, and tetanus—which is nearly reached by Western Europe. These are shown as brown bars in **Figure 7** and shift not only the ranking of risk factors but the entire scale of impacts.

As the figure illustrates, reasonable counterfactuals for these three important outcomes would have put them among the top group of potential interventions for Uganda and, thus, brought them to the attention of policy makers and donors who might wish to use the CRA results to inform their actions and investments, even if they are not calculated in exactly the same way as the other risk factors.[12]

[12] Similarly, no risk factor was included in the CRA-2010 for road injury, which leaves it off the policy map for making decisions about interventions, even though it is a quite important outcome globally, particularly in middle-income countries (29).

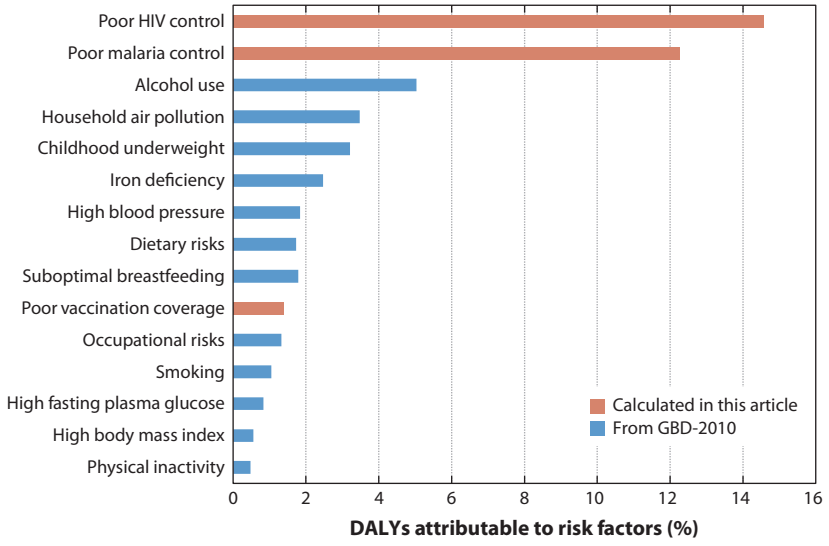

Figure 7

Percentage of total disability-adjusted life years (DALYs) due to the top risk factors in Uganda from the GBD-2010 plus additional risk factors based on the level of reduction that could have been achieved had Uganda been able to achieve the HIV/AIDS and malaria rates of the best-performing sub-Saharan African countries. For the major vaccine-preventable child diseases, the counterfactual was zero incidence. See text for further discussion. Abbreviation: GBD-2010, Global Burden of Disease project.

CONCLUSIONS

The sensitivity analysis in **Figure 6** implies that, at least for the purposes of the CRA, the results are not highly sensitive to the still-large uncertainties in PM exposure in solid cookfuel households across the world.[13] We are not implying, however, that more exposure assessment is not needed. Indeed, additional assessment is critical to pinning down the IERs more accurately, particularly for the disease end points (IHD and stroke) for which there is little direct HAP information to date. It may imply, however, that more attention needs to be paid to developing monitors and protocols to pin down exposures at the lower end, i.e., $<100\ \mu g/m^3$, as interventions are introduced to bring households into that range.

Because CRAs depend on PAF calculations, the burden of disease from the CRAs is dependent on background health conditions. The CRA-2010 relies on the national GBD-2010 results for this purpose, but HAP is not a universal risk in any country, being confined nearly entirely to lower-income populations and, to a lesser extent, rural areas. The levels of the major diseases associated with HAP in such populations generally differ from the national averages. ALRI and COPD, for example, are likely to be higher, whereas lung cancer, IHD, and stroke may not be. This variance is complicated by smoking patterns, which also are not uniform across countries by HAP status but greatly affect the background rates of the same diseases. Future elaborations of the CRA for individual countries may wish to differentiate background disease patterns according to rural versus urban or by income quintile to better reflect these differences.

[13] Although the GBD-2010 and associated CRAs devote considerable effort to systematically determine uncertainty bounds on the estimates, there is not space in this article to explore this issue further.

There is a natural urge to forget that the CRAs, at best, estimate "attributable" impacts and apply them directly to estimate what might be achieved by interventions today, i.e., "avoidable" impacts. The CRA estimates how much less ill-health there would have been in 2010 if no one had used poorly combusted solid fuels for cooking in the past, and the analysis intrinsically incorporates all past history of population distribution, health conditions, trends in fuel use, etc. Of more relevance to policy, of course, is how much impact could be avoided if changes were made now because there is no option to change the past. To answer this avoidable impact question, however, requires estimates of future changes in population, health, and solid fuel use that would occur without intervention and then compare to what would happen with it. This is a related but even more difficult exercise than a CRA.[14]

In addition, the CRAs assume more or less stable conditions; e.g., the COPD attributable burden today is the result of exposures to HAP over long periods in which HAP levels did not change precipitously. Interventions, however, are, by definition, changes that perturb a system that will then not reach equilibrium among the different factors for some years. An intervention will not actually result in a change in COPD rates for some years, for example, because there is already a future committed COPD burden due to past exposures. ALRI in infants, in contrast, can be expected to change fairly quickly after intervention. The result is that the benefits of intervention will be spread out over time; reductions in chronic diseases with long lag times will take much longer to accrue than will reductions in more acute conditions.

Perhaps the most striking aspect of the HAP CRA, as derived from the IERs shared with the AAP CRA, is the highly nonlinear character of the exposure-response at levels of $PM_{2.5}$ below $\sim$100 $\mu g/m^3$ annual mean. These exposure-response relationships derive from modeling across orders of magnitude of mean exposures with disparate temporal patterns using epidemiologic evidence from quite disparate populations. Although currently sufficiently compelling to be used in the CRAs, they need to be confirmed with more direct evidence in HAP settings for the major outcomes. The implications are clear, however: Interventions to reduce HAP exposures must lower exposures substantially in order to produce large health benefits. Such reductions will be difficult to achieve with current technologies using solid fuels, although there is much ongoing effort to do better. Beyond being more expensive, introduction of gaseous fuels and electricity also sometimes does not immediately achieve reductions as large as might be expected because households do not shift completely away from solid fuels immediately. Thus much remains to be learned about how to achieve these reductions, but avoiding millions of premature deaths annually in the world's most vulnerable populations provides a compelling a reason to do so.

DISCLOSURE STATEMENT

The authors are not aware of any affiliations, memberships, funding, or financial holdings that might be perceived as affecting the objectivity of this review.

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[14]Some risk factor groups in the CRA-2000 did attempt to calculate avoidable impacts (9), but this was not done for the CRA-2010.

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