Assessing the Recent Estimates of the Global Burden of Disease for Ambient Air Pollution: Methodological Changes and Implications for Low- and Middle-Income Countries

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**Abstract**

The Global Burden of Disease (GBD) is a comparative assessment of the health impact of the major and well-established risk factors, including ambient air pollution (AAP) assessed by concentrations of PM2.5 (particles less than 2.5 microns) and ozone. Over the last two decades, there has been considerable improvement in two important inputs in the methodology for estimating the impacts of PM2.5. The first is the assessment of global exposure to PM2.5 while the second is the development of integrated exposure risk models (IERs) that relate the entire range of exposures to PM2.5 (based on both air pollution and smoking studies) to cause-specific mortality risks. As a result, the estimated annual mortality attributed to AAP increased from less than 1 million in 2000 in the first round of estimates by the World Health Organization and World Bank, to roughly 3 million for GBD in years 2010 and 2013 to 4.2 million for GBD 2015. However, the magnitude of the change and uncertainty regarding the reasons for such a variation in the recent estimates have resulted, in some cases, in skepticism and reduced confidence in the overall estimates. To understand the underlying reasons for the change in mortality, we focused on the estimates for the years 2013 and 2015 for which a difference of one million deaths observed. We examined the quantitative implications of alternative model input assumptions. We calculated that the year 2013 estimates increased by 8% after applying the updated exposure data used in GBD 2015, and increased by 23% with the application of the updated IERs as used for the GBD 2015. The application of both upgraded methodologies together increased the GBD 2013 estimates by 35%, to almost 4.2 million deaths. We also found that 75% of the remaining difference of 200,000 deaths between 2013 and 2015 was due to demographics (i.e., population growth, aging and the disease mixture), with China and India contributing nearly half of this change. The remaining incremental burden was due to changes in population exposure. Improvements in the methods over time will continue to change the global estimates of air pollution-related deaths and a clear documentation of the changes in the methodology is necessary to maintain confidence in the overall process.

**Abbreviations**

AAP: Ambient air pollution

AOD: Aerosol optical depth

COPD: Chronic obstructive pulmonary disease

CRF: Concentration-response function

CTM: Chemical Transport Model

GBD: Global Burden of Disease

IER: Integrated Exposure Risk

IHD: Ischemic heart disease

IHME: Institute for Health Metrics and Evaluation

LMIC: Low- and Middle-Income Countries

LRI: Lower respiratory infections

PM2.5: Particles less than 2.5 microns

PM10: Particles less than 10 microns

RMSE: Root mean square error

WB: World Bank

WHO: World Health Organization

**Keywords:**

air pollution; health impacts; fine particles; PM2.5; Global Burden of Disease; mortality

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 **I. Introduction**

Efforts to quantify the worldwide burden of disease began in the early1990s, when the World Bank commissioned the original Global Burden of Disease (GBD) study resulting in the World Development Report in 1993 (World Bank, 1993). The World Health Organization (WHO) generated GBD estimates for several years with the first comprehensive evaluations for ambient air pollution (AAP) initiated for the year 2000 (Cohen et al., 2004) and then for the year 2004 (WHO 2009). Funded by the Bill & Melinda Gates Foundation in 2010, the scope of GBD was updated and included 291 diseases and injuries, 67 risk factors including AAP in 21 regions around the world. Ultimately, the Institute for Health Metric and Evaluation (IHME), housed at the University of Washington, became the main provider for a comprehensive set of GBD estimates which were provided for the years 2010, 2013, 2015, with technical support from WHO (Shaddick et al, 2017). AAP estimates were provided for mortality, years of life lost, years lived with disability, and disability-adjusted life years by country, age, and sex.

Over the last two decades, the GBD methodology for exposure assessment to AAP has made significant improvements and has become a useful instrument for health impact assessment. Exposure assessment, with some collaboration with WHO and other international agencies, is now based on several sources including ground-level monitors, chemical transport models, and remote sensing from multiple satellites, with each possessing unique advantages for certain types of terrain, altitude and geophysical characteristics (Brauer et al., 2012; Shaddick, 2017). In addition, the models that relate ambient concentrations to subsequent health risks have been updated integrating novel evidence provided by cohort studies of air pollution and smoking using advanced statistical techniques (Burnett et al, 2014). Unfortunately, as the initially reported burden estimates significantly changed over a short period of time (from around 3 million global deaths per year in 2010 and 2013 to 4.2 million in 2015, a 40% increase), the confidence in these estimates may be impacted. This may lead to differing assessments of the information by international institutions, national governments and environmental policy makers. The issue is likely to particularly acute for low- and middle-income countries where there is less expertise and resources available to provide their own country assessment estimates. Thus, it is important to describe and analyze the methodological changes in the GBD, document its inputs more transparently, and shed light on why the estimates have changed and what are the implications.

The review produced in this paper focused on PM2.5 since it dominates the overall mortality estimates and has been used most often to approximate the overall impact of air pollution. The scientific basis supporting the link between PM2.5 and adverse health outcomes is substantial. Dozens of studies of short-term exposure to PM2.5 and mortality have been published and include evidence from five continents. Several studies of long-term exposure form the basis for the concentration-response functions in GBD and the PM2.5 effect is the best documented and well supported by toxicological and human clinical studies. In addition, there is an extensive network of PM2.5 monitors around the world that can be used for calibration of global exposure models, although there are many low- and middle-income countries (LMIC) that have limited or no monitoring networks. All these factors set PM2.5 apart from all other air pollutants.

In sSection II, we briefly review the GBD model assumptions from 2010 to 2015 indicating how they have changed over time along with the resultant mortality estimates. In Section III, we provide a quantitative analysis of the impacts that changes in the model inputs have had on the country-specific and global estimates. This is followed by summary (IV), conclusions (V) and recommendations (VI) for future GBD estimates.

**II. Inputs and Enhancements of GBD for 2010, 2013 and 2015**

**II.1 Inputs**

There are five major inputs for the quantification process and different assumptions about them can generate significant differences in the outcome: 1) air pollution levels, 2) counterfactual selection; 3) population exposure; 4) death rates and 5) concentration-response function (CRF). Many of these components have changed with each successive GBD estimate of air pollution effects. These include the following:

1. An assessment of the annual concentration levels of an index pollutant, traditionally PM2.5, based on either ground-level monitors, remote sensing satellites, land use regression models, chemical transport models or some combination of the above. From the concentration levels population-weighted exposures are estimated (see input 3).

2. An alternative or minimum concentration of PM2.5, called a counterfactual, which could be either a background level, a target level such as a WHO guideline, a theoretical threshold or a no-effects level.

3. A determination of the size of the population group being exposed to the given concentration is essential to estimate population-weighted exposure For GBD, age-specific, population-weighted exposures are generated for every country .

4. The occurrence of the health effect being estimated such as the underlying cause-specific mortality rate in terms of annual deaths per 100,000, for example.

5. The concentration-response functions (CRFs) from the epidemiological literature that quantitatively relate ambient levels of PM2.5 to the risk of the health effect. For GBD, Integrated Exposure Response functions (IERs, see below) estimated for five disease categories (ischemic heart diseases, stroke, COPD, lung cancer and acute respiratory infections), quantitatively relate population-weighed exposure to PM2.5 to the risk of the health effect.

**II.2. GBD Enhancements and Limitations**

There have been two major enhancements to the GBD estimates of 2010, 2013 and 2015 compared to earlier estimates. First, the more recent estimates are based on exposures generated from models integrating multiple sources including remote sensing from satellites, chemical transport models (CTM) and ground-level monitors (Brauer et al., 2012; van Donkelaar et al., 2016; Shaddick et al. 2017). This is a significant improvement over earlier studies, such as for example the estimates of PM10 (particles less than 10 microns) for GBD 2000 (Pandey et al. 2000). However, each of these inputs used to estimate PM2.5 has some limitations.

For example, satellite observations are very limited during periods of significant cloudiness, such as during wintertime and at nighttime (van Donkelaar et al. 2015). CTM depend on the availability and quality of the emissions inventories. This may be particularly important in LMIC with potential limited information but going through a rapid economic transformation. Finally, there are also issues with the existing network of ground-level monitors. There are many countries where there is no monitoring of PM2.5, so the satellite and CTM estimates cannot be calibrated. In addition, measurement protocols and quality controls are not standardized around the world, as seen in the air quality data regularly compiled by WHO (WHO, 2016) Some of the general uncertainties created by these limitations are reduced through the combination of methods and the use of advanced statistical techniques that improve estimation accuracy and incorporate uncertainty. However, the need for carefully calibrated ground-level monitors with proper quality control is imperative for many LMIC.

The second major enhancement is the improvement in developing the CRF*.* For GBD 2010, IERs were developed that combine evidence from studies of ambient air pollution, second-hand smoke, household air pollution and active smoking to estimate air pollution risks over the entire global range of particulate matter exposure(Burnett et al., 2014). The studies of second hand and active smoke are particularly important since their equivalent PM2.5 concentrations are much higher than those that were associated with ambient air pollution in cohort studies. Therefore, these studies play an important role in determining the shape of the IER at higher concentrations. This non-linear function was necessitated because the naïve assumption of a linear CRF function up to highest observed concentrations would ultimately result in implausible and biologically inconsistent results (Cohen et al, 2004, Ostro 2004). In this approach risks of AAP on mortality from ischemic heart disease (IHD), stroke, chronic obstructive pulmonary disease (COPD), lung cancer and lower respiratory infections (LRI), were estimated rather than the more aggregated categories of all-cause or total cardiovascular or respiratory mortality as in the past. The studies selected for all four combustion sources of PM2.5 exposure were continuously updated (see WHO (2017), Table 4).

There are two critical assumptions about these IERs: first that PM2.5 is an appropriate indicator of the risk associated with a mixture of pollutants from these four sources; and second, that the health effects of PM2.5 measured in studies primarily in the western industrialized countries can be extrapolated to the effects of the mixture of PM2.5 constituents found in other parts of the world. The shape of the IER can have a significant impact on the ultimate mortality estimates (see below and for example for India, Chowdhury and Dey, 2016)

**III. Inputs and Results for** **GBD for 2010, 2013 and 2015**

Below and in Table 1 we have attempted to specify the assumptions for each of the inputs for the GBD estimates from 2010, 2013 and 2015. It is important to acknowledge that the documentation of the inputs, methodology, and data for the earlier GBD estimates were sometimes difficult to locate. This reflects both the significant, and varied data and efforts by GBD contributors that were necessary to develop these very complex GBD estimates for ambient pollution. Table 1 summarizes the main inputs in the GBD estimates.

**III.1 GBD 2010**

Exposure estimates for GBD2010 as described in Brauer et al (2012) used 2005 data from remote sensing satellites and the CTM TM5 which is a nested 3-dimensional global atmospheric chemistry transport model, which simulates aerosol components at 1° × 1° resolution (approximately 11 km at the equator). Two different NASA satellite instruments (MODIS and MISR) were used to obtain Aerosol Optical Depth (AOD), a measure of light extinction by aerosols in a column near earth which has been shown to be fairly highly correlated with PM2.5. The CTM was also used to simulate the AOD over a wide spatial range. Available data indicated fairly similar results from satellites and the CTM so the authors chose to use an average of the two in each grid.

Ultimately a regression model was estimated to determine a quantitative relationship between spatially-resolved AOD and ground-level measurements of PM2.5 from monitors. This empirical model was then applied to all of the global grids. The 2010 analysis showed that the addition of CTM and satellite data increased the accuracy of the estimates of exposure over methods used in the GBD 2000 (Pandey et al., 2000). The concentrations were merged with population for each grid.

 As indicated above, the CRF was developed using an approach that combined the risks derived from studies of air pollution, second hand smoke and active smoking into one joint integrated function (Burnett et al., 2014). Eight cohort studies examining long-term exposure to PM2.5 and mortality were included to estimate the risks for IHD, stroke, COPD and lung cancer: Krewski et al ( 2009), Laden et al. (2006), Lipsett et al. (2011), Abbey et al. (1999), Chen et al. (2005), Beelen et al. (2008), Puett et al. (2008), and Miller et al. (2007). This equation was estimated by assuming a power function and then using non-linear least squares to fit the model across the full range of exposure from the different sources of PM2.5. The risk from each data point from the studies was weighted by its uncertainty in the estimation process. Three additional studies were used to estimate LRI for those under age 5. There were many studies of second hand smoke that contributed to the shape of the function including 8 for IHD, 10 for stroke, 43 for lung cancer, and 23 for LRI.

Ultimately, based on these inputs, the analysis indicated 3.2 million deaths per year worldwide from PM2.5 with an uncertainty interval (UI) of 2.8 to 3.6 million (Lim et al., 2012). Ozone, which was the only other pollutant added to the AAP estimates for GBD generated another 150,000 deaths.

**III.2. GBD 2013**

The data and methodology for 2013 were generally similar to those used in 2010. However, there was an increase in the number of ground-level monitors used to develop estimates of global PM2.5 incorporating data compiled by WH) in 2011(WHO 2016, Brauer et al., 2016) A new data series was created from instruments on three different satellites (MODIS, MISR and SeaWiFS) along with an improved estimation algorithm that incorporates uncertainty into the estimates. Each of the satellites and algorithms has a distinct advantage, such as collecting data at smaller grid size, better assessment over bright surfaces such as deserts or different geographic coverage (van Donkelaar et al., 2016).

Similar to GBD 2010, the AOD data from the satellites were combined with the CTM estimates and used in a regression model to predict ground-level PM2.5 measurements (Forouzanfar et al., 2015) with additional covariates added as explanatory variables. The results of the linear regression model were then applied to all global grid cells.

Brauer et al., (2016, supplement) reported the fit between the predicted concentrations and the available PM concentrations from ground-level monitors. For four of the seven super regions i.e., high income countries, North America, Latin America and the Caribbean, South Asia and South East Asia, the models performed reasonably well. However, the model under predicted concentrations for the following super regions: North Africa; the Middle East; Central and Eastern Europe, Central Asia; and Sub-Saharan Africa. The reduced accuracy in these regions was very likely due to the prevalence of dust and the lack of ground-level monitors which are used to calibrate the satellite data.

The IERs for GBD 2013 were conceptually similar to that of GBD 2010 but new risk models were developed using additional studies of long-term exposure and mortality published after 2010. In the IERs for the air pollution risks related to long-term exposure, 11 cohort studies were used for IHD mortality, eight for stroke, five for COPD and eight for lung cancer. These studies included Krewski et al. (2009), Lepeule et al. (2012), Lipsett et al. (2011), Puett et al. (2009), Miller et al. (2007), Chen et al. (2005), Puett et al. (2011) and Beelen et al. (2008). Furthermore, exposure estimated for second hand smoke was updated compared to GBD 2010. Age-specific risks were also provided for IHD and stroke, but not for lung cancer and COPD, since data were limited for these endpoints. In addition, LRI for adults was added to the calculation of mortality, whereas in the previous version LRI were restricted to children under 5 years.

 Ultimately, total mortality from PM2.55 AAP was estimated by IHME to be 2.9 (UI = 2.8, 3.1) million. Exposure to ozone added another 217,000 deaths.

**III.3. GBD 2015**

Updates have been made for all five inputs for GBD 2015 (see below and Table 1). There was a significant upgrade to the exposure assessment due to an increase in the number of satellite products (each with distinct advantages), an increasing number of ground-level monitors and methodological improvement. . Exposure estimates used a CTM similar to that used in GBD 2013. Aerosol optical depth estimates for 2014 were obtained from multiple satellite products (MISR, MODIS Dark Target, MODIS and SeaWiFS Deep Blue, and MODIS MAIAC), each with a distinct advantage. Global AOD was then created through simulations of the CTM so that it could be used in a regression model to develop an empirical relationship with ground-based PM2.5 (van Donkelaar et al. 2016). A map of the 6003 ground level PM2.5 monitors in 2972 metropolitan areas compiled by WHO is provided in Figure 1, and a list of the number of monitors in each country is provided in Appendix A.

Van Donkelaar et al. (2016) extended the approach used in GBD 2013 by adding covariates such as such as land use and PM2.5 chemical composition to the regression model predicting PM2.5 concentrations. The exposure estimation was further enhanced by Shaddick et al. (2017) who utilized a Bayesian hierarchical model to combine the data more efficiently and better incorporate uncertainty. In addition to including the data from the satellites and CTM, the regression model for estimating PM2.5 also included covariates such as population, the type of ground-level PM2.5 monitor used; whether ground-level PM2.5 was estimated from PM10; the concentrations of sulfate, nitrate, organic carbon and ammonium, and land use elevation (See Shaddick et al. 2017 and Forouzanfar et al. 2015 for additional details). These covariates facilitated a region-specific predictive model rather than a single predictive model for the entire globe. The predictive power (measured as root mean square error or RMSE) was significantly enhanced by adding these explanatory values cited above.

The fits of the models by Super Region are displayed in Figure 2. The results indicate that moving from Model A to B which entails adding local population data to the regression model, significantly improved the model fit with the R2 improving from 0.54 to 0.90. Adding additional covariates (e.g., estimates of dust, sulfates and nitrates and monitor elevation) in Model C slightly improved the fit.

The general fit of the data relating the AOD estimates (from CTM and satellites) to the ground-level PM2.5 was greatly improved over previous GBDs, notably in High Income; Central Europe, Eastern Europe, Central Asia; Latin America and Caribbean; and Southeast Asia. However, the figure also indicates significantly greater uncertainty in Northern Africa and the Middle East, Sub-Saharan Africa and South Asia with the RMSE tripling relative to the high income countries. This reduction in accuracy is a result of the higher concentrations experienced in these areas and the lack of ground-level monitoring data.

 For the IER, additional air pollution cohort studies not previously available were added to the CRF procedure which now involves 24 studies. The studies include additional cohorts from the U.S. as well as from Canada, the UK, Japan, Italy, Norway and the ESCAPE study which contributed results from smaller cohorts from 14 European nations (see Appendix B for a list of all the included papers). Additional information about each of these studies is available in Cohen et al. 2017). In addition, the estimation of PM2.5 exposure from second-hand smoke was updated and improved. Four studies including adults were used in the estimates of LRI. As in the past, through use of simulations the IER procedure was able to incorporate uncertainty in the estimates of population, exposure and the counterfactual. Current and past GBD estimates of both exposure and health outcomes using the assumptions from GBD 2015 can be found at https://www.stateofglobalair.org/data.

The global estimate for 2015 was 4.24 (UI = 3.7, 4.8) million and consists of IHD (1.52 M), stroke (0.90 M), COPD (0.86 M), lung cancer (0.28 M) and LRI (0.675 M) (GBD 2015 Risk Factors Collaborators, 2016). Exposure to ozone added another 254,000 deaths. Recently, GBD estimates for 2016 were published using inputs very similar to those for 2015, with a resulting global mortality estimate of 4.1 million (GBD collaborators, 2017).

**IV. Analyzing the Quantitative Impact of Changes from GBD 2013 to GBD 2015**

As indicated above, the original GBD AAP mortality estimates increased significantly from both 2010 (3.2 million) and 2013 (2.9 million) to 2015 (4.2 million). Therefore, it is important to understand how the assumptions about the exposures and IERs quantitatively impacted the original estimates of the GBD for AAP. Below, we have provided several analyses of the impacts of these updated methodologies. For the comparison with 2015, most of our focus is on the year 2013 since this estimate is similar to that of 2010 and the reason for changes between it and 2015 estimates will be the same as those for 2010. To examine the impacts of the inputs, we first had to reconstruct the global estimates for those two years. To do so, we applied the IER functions that were reported by Burnett et al. (2014) for year 2010 and for years 2013 and 2015 (see Appendix C) using information provided by Burnett (personal communication). The shapes and differences in the respective IERs are discussed below (Section IV.1).

Next, we used population-weighted exposure information at the country scale for GBD 2013 based on Brauer et al. (2016, supplement) and for 2015 based on data from the World Bank (2017). With these inputs and data on country-specific population, we re-calculated the global estimates of mortality. Our mortality estimates differ slightly from GBD results because the latter are based on the IER applied to grid cell calculations (0.1 by 0.1° resolution, 11 km at the equator) for population and exposure. Our estimates are based on the application of the IERs to the aggregated country-specific estimates of population-weighted PM2.5 concentrations but are within a few percent of the official GBD estimates. Our results are presented in Section VI.2, which also shows the separate quantitative impacts of both the existing and updated (i.e., using the methodology for GBD 2015) exposure and IER inputs. In Section VI.3 we detail the quantitative impact of alternative input assumptions on GBD 2013, while Section VI.4 details the country-specific changes in the 2013 estimates as a result of the updated methodology. Finally, Section VI.5 shows the impacts on country- and disease-specific changes due to the updated GBD 2013.

**IV.1. IER functions used for 2010, 2013 and 2015 GBD.**

The shape of the functions for IHD, Stroke, COPD, Lung Cancer, for the 2010, 2013 and 2015 GBD are shown in Figure 3. For IHD and stroke, the functions and subsequent risk calculations are age-specific so we display the functions for ages 75 to 79 which is among the highest risk group. Figure 3 also indicates the change in the counterfactural or minimum risk exposure level as reported in Table 1. These changes also influenced the shape of the curve.

**IV.2.** **Decomposing Global Changes from GBD 2013 to GBD 2015**.

In this section we quantify the mortality impacts of input changes from 2013 to 2015. We begin with mortality estimates based on the GBD 2013 methodology and then quantify the changes in 2013 mortality after separately applying the 2015 exposure and IER methodologies. In this way, we can better understand the factors that led to the significant increase from the original 2013 estimates to those published in 2015. Figure 4 provides our estimates for GBD 2013 and GBD 2015 under different assumptions. Column 1 is our result for the GBD 2013 IERs and exposures (the latter from Brauer et al. 2016) which generated a total of 3.06 million deaths for the year 2013. This compares with the original GBD estimate for 2013 of 2.92 million. The second column holds everything constant including the 2013 IERs but updates the 2013 population exposure using the same exposure methodology used in GBD 2015. This resulted in an 8% increase over the original 2013 estimate to 3.31 million deaths. Column 3 keeps the original 2013 exposures but applies the IERs used for GBD 2015 to the 2013 data. This generated an increase over GBD 2013 by 23% to 3.75 million deaths, indicating that the 2015 IERs added about 710,000 deaths to the original 2013 GBD estimate. Next, column 4 combines the IERs from GBD 2015 and the updated exposures (using GBD 2015 methodology) for GBD 2013 which together generated a 35% increase over 2013 to 4.12 million. The difference between the 4.12 and 3.06 million deaths (column 4 minus column 1) reflects the changes in both the exposure assessment and IER methodology.

Finally, in column 5 we used both the IERs and exposures from GBD 2015 which generates a total mortality of 4.31 million in the year 2015, a 41% increase over the original GBD 2013 estimates for the year 2013. Our calculation is about 1.6% more than that of the official GBD 2015 estimate of 4.24 million. Overall, our analysis indicates that the change in IERs from 2013 to 2015 generated most of the increase in the GBD estimate over this time period, but exposures played some role in certain countries (see Tables 2 and 3). Using the updated IERs and exposure estimates for 2013, there is an estimated increase of 190,000 deaths moving to GBD 2015 (i.e., the difference between column 5 and 4). This is in contrast to the difference between the original estimates of GBD 2013 and GBD 2015 of about 1.3 million. The updated difference of 190,000 deaths is related primarily to demographic changes including population growth, changes in disease prevalence and aging which added 145,000 deaths in 2015. Over half of these demographic-related changes occurred in China and India. The remaining increment in mortality of around 45,000 additional deaths is due to changes in exposures.

**We also examined the impact of changes in the counterfactual from 2013 to 2015. Recall that the simulations of the mortality impact assumed a uniform distribution from 5.8 to 8.7 µg/m3 for GBD 2013 and from 2.3 to 5.9 for GBD 2015. 'Since the IERs are constrained to reach a risk of 1.0 at the lower bound, the shape of the IER will be impacted as the counterfactual changes. As a result, we found that the counterfactual change itself adds about 175,000 deaths globally to GBD 2013, a 6% increase. The country level impact varies significantly with about 75% of the change occurring in countries with a population-weighted exposure less than 30 µg/m3**

**VI.3**. **Disaggregation by disease**

Figure 5 shows the breakdown by disease for each of these estimates that were generated and displayed in Figure 4. While 2013 IHD increased in absolute number from the first column (2013 IER and 2013 exposure: 1,183,782 deaths) to the third column (2015 IER and 2013 exposure: 1,463,059 deaths), it slightly decreased as a share of the total from 39% to 36%. Stroke mortality also decreased as a percent of the total. The proportion of respiratory deaths (COPD plus LRI) increased from about 17% of the total in GBD 2013 to about 36% in GBD 2015, and lung cancer deaths decreased from 13% in GBD 2013 to under 7% in GBD 2015.

**IV.4.** **Global and** **Country-specific Mortality Impacts of updating GBD 2013**

Next, we examine the country-specific effects for GBD 2013 using the new methodology for the IERs and the updated exposures. Table 2 summarizes the alternative assumptions and subsequent mortality globally, and for 12 countries with high pollution-related mortality. Columns 2 and 3 show the original GBD 2013 PM2.5 concentrations and attributable deaths using GBD 2013 IERs. The mortality count for the 12 countries is 2.19 million with a global total of 3.06 million. Columns 4 and 5 show the PM2.5 concentrations and associated mortality if only exposures for GBD 2013 are updated using the GBD 2015 exposure methodology, with everything else (i.e., the GBD 2013 IERs) unchanged. This increases the 12 country mortality count to 2.3 million and the global count to 3.3 million. Next, columns 6 and 7 show mortality if both exposures and IERs (using GBD 2015 IER) are updated for the 2013 data. This raises the 12 country count to 2.9 million and the total global estimate to 4.1 million. Column 8 displays the increase in GBD 2013 mortality (column 7 minus column 3); that is, the combined impact of using the updated IER functions and exposure methodology from GBD 2015 on the 2013 data. The mortality increase due to the updated methods for the 12 countries is 755,000 or 72% of the global increase of 1.05 million (last row in table). This latter number represents the additional deaths added to the original GBD 2013 estimates as a result of the newer methodology used for exposure and IERs. Note, for example, the large impact of India where over 400,000 additional deaths are now calculated for 2013.

Next, Column 10 shows the GBD 2015 mortality estimates, and Column 11 indicates the global and country-specific differences between these estimates and the fully updated GBD 2013 estimates (i.e., using GBD 2015 methodology applied to 2013). . For the 12 countries, the change in annual mortality is 135,000 deaths. After using the updated methodology for 2013, the increase in mortality from 2013 to 2015 is 4.9% or 198,000 deaths. Again, the change is dominated by increases in India and China. In contrast, column 12 displays the differences between GBD 2015 and the original GBD 2013 amounting to 1.25 million deaths, globally.

**IV.5**. **Disease-Specific Changes Due to Updated GBD 2013**

Country- and disease-specific mortality estimates as a result of the changes in inputs are shown in Table 3 for the year 2013. The six countries in the table, which have the largest change in mortality due to the updated exposures and IERs, comprise about 66% of the change in mortality. The table indicates the changes in the five diseases that were estimated in the 2013 and 2015 GBDs: IHD, stroke, COPD, lung cancer and LRI. In order, the columns indicate the disease-specific counts for the following scenarios: (1) the original GBD 2013 estimates, (2) GBD 2013 with updated IERs but original exposures, and (3) the fully updated GBD 2013 estimates with IERs from GBD 2015 and 2015 updated exposure methodology.

The table indicates how the mortality mix has changed with the different inputs used for GBD 2013. For China, India and Pakistan most of the change in mortality can be attributed to the newer IERs, with the composition of diseases altered over the years. For China, the changes in the IER alone increased COPD mortality from 75,000 to 270,000 with the updated exposure methodology not adding much to the total. In contrast, lung cancer estimates for China decreased from 210,000 to 136,000. This clearly demonstrates the importance of the updated IER for 2015. For Bangladesh and Nigeria both the IER and exposure differences play an important role in the different mortality estimates, and for the Philippines, the change in the population exposure dominates the difference in mortality estimates.

**V. Discussion**

The GBD for ambient air pollution aims to quantify the global burden of disease. Compared to the global estimates, the uncertainty is greater for country-specific estimates, particularly for those countries without ground-based monitors. The latter are dominated by LMIC. The updating of the integrated exposure response functions for GBD 2015 was largely responsible for an increase of 1.25 million deaths from GBD 2013 to GBD 2015. The improvement in the assessment of exposure also played an important role and was sometimes equally or more significant for certain countries (e.g., Philippines).

As displayed in Figure 4, the GBD 2013 global mortality estimate (3.06 million) increased by 8% after the application of the improved exposure methodology used in GBD 2015. In contrast, the GBD 2013 estimates increased by 23% with the application of the GBD 2015 IERs. The application of both updated methodologies (i.e., 2015 IERs and application of 2015 methodology to 2013 exposures) led to an increase in the GBD 2013 mortality burden by 35% to 4.12 million deaths. Once the 2013 GBD estimates were updated using the 2015 IERs and the more accurate exposure methodology used in GBD 2015, the incremental mortality between year 2013 and year 2015 was under 200,000 (Table 2), primarily resulting from demographic changes including population growth and aging. China and India accounted for just over half of this difference.

Clearly, the GBD estimates have changed over time, but not because of accidental omissions, and will continue to change. These changes are expected and are due to multiple factors including: (1) increases in population and changes in demographics (since the health risks are age-specific); (2) real changes in exposure; (3) updated counterfactual assumptions based on additional cohort studies and exposure measurements; (4) updated IERs incorporating newer cohort studies of outdoor air pollution when available, and (5) updated exposure methods incorporating additional satellite data, updated CTM and updated statistical methods.

Over time, the sophistication of many of the inputs in the estimation of the GBD has increased. This is especially true for the exposure estimates and the IERs. The exposure assessment now incorporates multiple satellites with improved algorithms and sophisticated statistical methods that efficiently fuse the data and better incorporate uncertainty in the inputs. This has resulted in a significant improvement in the accuracy of estimating PM2.5 concentrations, as evidenced by the high correlation between predictions and ground-level monitors in GBD 2015. Likewise, the chemical transport models that are used incorporate the latest emissions inventories and methodology. There has been a significant increase in the number of global PM2.5 monitors although the spatial coverage of monitors varies widely by region, being much more complete in high income countries while measurements are sparse in low-income countries such as in Sub-Saharan Africa, for example. As indicated by Figure 2, there is significantly less accuracy for several of the regions with LMIC where ground level monitoring is limited or non-existent.

Finally, the development of the IERs now includes more cohort studies and in the future will include studies from outside the western industrialized nations. Highly developed statistical methods combine data into a non-linear function that is plausible over the entire range of observed air pollution concentrations as well as over the higher concentrations from other sources of particulate matter. As a result, it is clear that the accuracy of the health estimates has improved over time.

Each of the inputs into the estimates (i.e., exposure, CRF, counterfactual, health statistics) have limitations and the process can always be improved. In addition, to date it has been difficult to understand the specific quantitative impact that each change in the input makes in the subsequent GBD estimate. The burden estimates and associated journal papers and presentations would be enhanced if the inputs to the estimates were more clearly documented, and easier to find in the literature and on websites. The changes in model assumptions and inputs over time should be made more transparent. However, it is important to note that given the inherent uncertainties in estimated global mortality, the GBD methodology is able to quantitatively incorporate some of the uncertainty in the IER, the counterfactual and the exposure estimates through multiple simulations (Burnett et al. 2014).

There are other important uncertainties such as the issue of how well the IER incorporates differential toxicity of ambient PM2.5 versus active and passive smoking. There is also uncertainty regarding the extrapolation of the IER, based primarily on studies in North American and Europe, to the rest of the world where the mixture of PM2.5 is very different. Such extrapolation must assume that all of the components of PM2.5 are of equal toxicity. Recent evidence (Ostro et al., 2015, Thurston et al., 2016) suggests that long-term exposure to certain components and sources such as sulfate and elemental carbon may be more toxic than generic PM2.5 but more research is needed in this area. Related to this is the issue of the toxicity of dust, which is assumed to have toxicity equal to other fine particle components. The treatment of the toxicity of dust can have a major impact. For example, Lelieveld et al. (2015) attributed 90% of the air pollution-related mortality in Egypt to dust exposure and determined that globally, dust particles could increase overall mortality by 20%. Among epidemiologic studies of long-term exposure Ostro et al. (2011) and Vedal et al. (2013) found effects from silicon on cardiopulmonary mortality, and Thurston et al (2013) reported effects of soil on respiratory mortality. Furthermore, recent evidence indicates that fine particulate matter may impact not only cardiovascular diseases and lung diseases including lung cancer, but also metabolic diseases such as diabetes and neurodegenerative diseases (Thurston et al., 2017).

**VI. Recommendations**:

1. **There is an urgent need for high quality and reliable ambient PM2.5 ground-level monitors to be located in LMIC.** The placement of universally accepted ground-level monitors and AERONET monitors, including the measurement of both mass and components, in countries with limited or non-existing monitors would represent a significant enhancement to current knowledge. Not only would this information help identify the magnitude of the air pollution problem and the components that are most important to control, it would help in calibrating estimates from remote sensing satellites. This would enable LMIC to verify the accuracy of projections made from existing exposure models. Ideally these monitors would also maintain full quality assurance procedures to ensure accuracy. There is also a need to **review existing monitors in countries that have not had a long history of quality control and/or are not using U.S. or European federal reference method monitors.**

2. **There is a need for further development of the methods deriving the IERs, and of the methodology for reporting the results of the GBD estimates.** As science is progressing quickly and new studies will become available, more data will be available for deriving the IERs and alternative methodological approaches may be considered and developed, especially because the IER approach, which is currently based on only a few selected causes of death, may underestimate the overall burden of air pollution on all-cause, natural mortality. Ambient air pollution is suspected to exhibit an indirect impact on mortality by increasing morbidity and to interact with other risk factors such as diabetes and dyslipidemia, which may be an area of future method development. Furthermore, in the future, additional morbidity outcomes may be considered including for example adverse birth outcomes.

3. **There is a need for complete transparency in and full documentation of the GBD historical and current estimates and easy availability of the data sources.** As the GBD estimates change over time, the quantitative impact of each of the inputs should be very clear. Sensitivity analysis would be a useful way of illustrating this by, for example, holding all the inputs except one constant and demonstrating the impact of the single input. This would enhance the public’s understanding of the process and lend credibility to the estimates. The latest estimates from IHME include global burden calculations for the years 1990 – 2015 (generally at 5-year intervals) using the updated IERs and exposure methodology (see Figure 6). This may add some confusion since they are now different from the original GBD estimates. It is important to clearly indicate the input assumptions when past and future GBD estimates are presented. The IHME updated mortality estimate for 2010 is now 3.75 million, as opposed to the original estimate of 3.2 million. Finally, it would be useful to maintain a central site for both historic and current data and methods used in the GBD estimates.

4. **Additional epidemiologic research on the components of PM2.5, dust and coarse particles should be undertaken** along with **cohort studies of PM2.5 mass.** This research could help reduce some of these uncertainties, especially for low- and middle-income countries. Additional information on current exposures to and epidemiologic studies of the health impact of PM2.5 and its components, dust, and coarse particles at a refined spatial scale would be a major contribution. Conducting epidemiologic studies in these countries would not only fill important gaps in knowledge, it would also help to evaluate the GBD assumption of extrapolating existing concentration-response functions to other parts of the world. In addition, conducting new exposure and epidemiological studies will increase the local knowledge base by providing training and experience.

5. **There should be a custodial agency, such as WHO or some other international institution, to ensure the existence of critical assessment and continuous improvement of the scientific quality of these estimates.**  In addition, such an agency would serve as a repository for past and current data and methods and full documentation.

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Tabel 1. Summary of Inputs for GBD 2010, GBD 2013 and GBD 2013

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| GBD Year | Countries include | Number of ground monitors | Population | Counter-factual#(µg/m3) | Cause of death | # of AAP Studies\* | EstimatedMortality (millions) |
| 2010 (Lim et al, 2012) | 187 | DP (475)North America and Western Europe provided 404 PM2.5 or PM10 (converted to PM2.5). Others were provided for Australia, Brazil, Chile, China, Colombia, Egypt, Ghana, Israel, Kuwait, Lebanon, Mexico, New Zealand, South Africa and 31 other Asian locations (not specified) compiled by the Clean Air Initiative Asia (Brauer 2012, supplement).The ratio of PM2.5 to PM10 was based on the closest local or country-specific monitor, with a default estimate of 0.5. | Gridded population data for 2005 comes from NASA’s Socioeconomic Data and Applications Center (http://sedac.ciesin.columbia.edu/data/collection/gpw-v3).  | 5.8 – 8.8 | Ischemic heart disease, stroke, chronic obstructive pulmonary diseases, lung cancer, acute respiratory infections (children) | 8 | 3.2 (2.8, 3.6) |
| 2013 (GBD 2013 risk factor collabora tors, 2015) | 188 | C (79)UL (3387)DP (4073)In total, 4073 data points from 3387 unique locations in 79 countries were obtained, of which 1854 data points were from direct measurements of PM2.5. | Same as for GBD 2010 | 5.9 – 8.7 | Ischemic heart disease, stroke, chronic obstructive pulmonary diseases, lung cancer, acute respiratory infections(children and adults) | 11 | 2.9 (2.8, 3.1) |
| 2015 (GBD 2015 risk factors collabora tors, 2016) | 195 c | C (104)UL (2972)DP (6033)Further details regarding the city location, the annual mean for PM2.5 and PM10, the year the type of monitor, the temporal coverage and the agency reporting the data can be found at WHO (2016b). Most of the measurements (46% or 2760 monitors) were based on data for 2014, given the lag in providing the data.  | Updated Version 4 from NASA based on censuses conducted between 2005 and 2014. Additional details are provided in Country-specific historical growth rates were applied to project populations to 2015. | 2.4 – 5.9 | Ischeamic heart disease, stroke, chronic obstructive pulmonary diseases, lung cancer, acute respiratory infections children and adults) | 24 | 4.2 (3.7, 4.8) |

# A uniform distribution of the range was used in the simulations; \*non-air pollution studies are summarized in WHO (2017); DP = Data points; C = Countries, UL = Unique locations.; AAP: Ambient Air Pollution

Table 2. Country-specific and Global Effects on GBD 2013 with Updated Inputs.



Table 3. Country- and Disease-specific Changes for GBD 2013 Due to Updated Methods for selected countries



Figure 1. Locations and Mean Concentrations of Ground-level Measurements Used in GBD 2015



Source: WHO (2016a)

Figure 2. Super Region-specific predictions of PM2.5 for alternative regression models

Comparison of root mean square error from three models by super-region. Dots denote the median of the distribution from 25 simulations and the vertical lines the range of values. Super-regions are 1: high income, 2: Central Europe, Eastern Europe, Central Asia, 3: Latin America and Caribbean, 4: Southeast Asia, East Asia and Oceania, 5: North Africa / Middle East, 6: Sub-Saharan Africa, 7: South Asia. Model A predicts concentration as a function of satellite and chemical transport data; Model B adds local population to the model and Model C also adds such as particle species and monitor elevation.

Source: Forouzanfar et al. (2015, supplement)

Figure 3. Integrated Exposure Risk functions for GBD 2010, 2013 and 2015.





Figure 4. Effect of Changes in Exposures and IERs on estimated mortality from 2013 to 2015.



 Note: The percent change in column 4 is greater than the sum of columns 2 and 3 due to the combination of the increase in exposure and risks. The scenarios are based on a counterfactual that varies between **4.9 to 5.9 µg/m3 for GBD 2013 and from 2.3 to 3.4 µg/m3 for** GBD 2015

Figure 5. Disease-specific Mortality for Alternative Assumptions in GBD 2013 and GBD 2015.

Figure 6. Time Series of GBD mortality based on IHME Software using GBD 2015 exposure and IER methodology



Appendix A. Number of Ground measurements from Each Country Used in GBD 2015 (Ambient Air Pollution Database, WHO, 2016b.)

**Appendix B. Studies used for GBD 2015 Integrated Exposure Risk Model** (studies with asterisk were used for LRI estimation; otherwise the studies were used for cause-specific cardiovascular and respiratory disease and lung cancer mortality). “Unpublished data” indicates results that were supplied by study author.

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