The burden of disease (BoD) associated with ambient air pollution for the year 2016 is being estimated using methods developed by the Institute for Health Metrics and Evaluation (IHME) and expert groups for the Global Burden of Disease (GBD) project (1-4). This approach estimates the proportional reduction in specific diseases or causes of death that would occur if exposures were reduced to an alternative baseline level bearing a minimum risk (also referred to as theoretical minimum risk), while other conditions remain unchanged. For air pollution, it combines information regarding the population exposure distribution to ambient air pollution from particulate matter of a diameter equal or smaller than 2.5 μm (PM$_{2.5}$) and the exposure-response relationship (Figure 1).

![Diagram of burden of disease estimation](image)

Figure 1: Method for burden of disease estimation. DALYs: disease adjusted life years.

The population attributable fraction (PAF) was estimated by comparing current exposure distributions to a counterfactual distribution (see below), for each exposure level, sex and age group:

$$\text{(A) Population attributable fraction (PAF)} = \frac{\sum_{i=1}^{n} p_i (R_{Ri} - 1)}{\sum_{i=1}^{n} p_i (R_{Ri} - 1) + 1}$$

Where $p_i$ and $R_{Ri}$ are the proportion of the exposed population and the relative risk at exposure level $i$, respectively, and $n$ is the total number of exposure levels. Ambient air pollution attributable burden is obtained by calculating and applying the PAFs to each individual diseases (Figure 1).

**Source of the data**

**Demographic data**

Exposure data
Assessment of the global effects of air pollution requires a comprehensive set of estimates of exposure for all populations. Ground monitoring networks have provided the primary source of this information but, although coverage has increased, there remain regions in which there is no or very little monitoring. Ground measurement data therefore need to be supplemented with information from other sources, such as estimates from satellite retrievals of aerosol optical depth and from chemical transport models. The recently developed Data Integration Model for Air Quality (DIMAQ) incorporates data from multiple sources in order to provide estimates of exposures to PM$_{2.5}$ at high spatial resolution ($0.1^\circ \times 0.1^\circ$) globally (6). The model has been further developed to account for time in the calibration of satellite with ground measurements (7). Sources of data include: Ground measurements from more than 9000 monitoring locations in some 4300 cities around the world (8), satellite remote sensing; population estimates; topography; and information on local monitoring networks and measures of specific contributors of air pollution from chemical transport models (see (9) for a comprehensive list of references for the data sources).

The DIMAQ model calibrates data from these sources with ground measurements. The relationships between the various sources of data may be complex and will vary between regions due to differences in the composition of PM$_{2.5}$, and other factors. DIMAQ has a hierarchical structure within which calibration equations are produced for individual countries using, as a priority, data from that country where available. Where data within a country is insufficient to produce accurate estimates, it is supplemented with regional information.

When calibration equations have been established and tested, the model is used to estimate population exposures, together with associated measures of uncertainty across the globe. These high-resolution estimates can be used to produce air quality profiles for individual countries, regions and globally.

Health data
The total number of deaths and DALYs (disability-adjusted life years) for each country, by sex and age group for acute lower respiratory infections (ALRI), chronic obstructive pulmonary diseases (COPD), lung cancer, ischaemic heart diseases (IHD), and stroke have been compiled by the World Health Organization (10).

Exposure-risk relationships
To estimate the relative risk for a disease caused by air pollution exposure from PM2.5, an integrated exposure response function (IER) is used. The IER was originally developed for the Global Burden of Disease Study (2, 11) and has also been used by WHO (12,13). The IER combines the epidemiological evidence for outdoor air pollution, second-hand smoke, household air pollution and active smoking to estimate the level of disease risk (e.g. stroke) at different levels of PM2.5 concentrations (aka dose). In other words, the same mathematical relationship or measure is used to estimate the risk of heart disease from particulate matter originating from outdoor air pollution as that of second-hand smoke or household air pollution.

An updated version of the IER functions is used for ALRI, COPD, lung cancer, IHD and stroke, as in Cohen et al (4) and GBD 2016 (14,15).
Methods

Estimation of disease burden
The percentage of the population exposed to PM$_{2.5}$ was provided by country and by increment of 1 μg/m$^3$; relative risks were calculated for each PM$_{2.5}$ increment, based on the integrated exposure-response functions (IER). The counterfactual concentration for ambient air pollution was selected to be between 2.4 and 5.9 μg/m$^3$, as described in (4). The country population attributable fractions for ALRI, COPD, lung cancer, stroke and IHD were calculated according to formula (A) above. Currently, the IER is used to estimate the BoD (e.g. the number of deaths) for five causes:

- Acute lower respiratory infections (ALRI), in all ages
- Chronic obstructive pulmonary disease (COPD), in adults over 25 years
- Lung cancer, in adults over 25 years
- Ischaemic heart disease (IHD), in adults over 25 years
- Stroke, in adults over 25 years

DALYs are calculated by adding the YLDs and the YLLs. The relative risks (RRs) for YLDs were adjusted for IHD and stroke (14).

Uncertainty analysis
The uncertainty in the estimates of the number of deaths attributable to ambient air pollution will arise from uncertainties in both the estimates of annual average exposures to PM2.5 from the exposure model (DIMAQ) and in the risks associated with different levels of exposure (i.e. uncertainty in the IER). The uncertainty intervals are constructed to acknowledge both of these sources of uncertainty. This is achieved by taking random samples from the (distributions of) exposures at each location which are matched with random samples from the (distribution) of the IER for a particular cause. The burden of disease calculations are repeated for each exposure-risk pair, resulting in a distribution of estimates for each cause with the limits of the uncertainty intervals (for each cause) being the 2.5% and 97.5% quantiles of these distributions. Uncertainty for baseline mortality was not taken into account.

Limitations and outlook

Exposure
- Exposure assessment for ambient air pollution is a concern given the complexity of the assessment (e.g. in situ measurements versus satellite or a combination), and especially in regions where there is little air quality monitoring. Regional and national exposure assessments of ambient air pollution from particulate matter may differ in their methodology and data inputs.
- Urban/rural data: while the data quality available for urban/rural population is generally good for high-income countries, it can be relatively poor for some low- and middle income areas. Furthermore, the definition of urban/rural may greatly vary by country.
- Grid-size: The grid size is 0.1° x 0.1° (10 x 10 km close to the equator, but smaller towards the poles). This resolution may cause limitations when considering local situations. Finer resolutions are planned for future studies.
- Model calibration in data-poor areas: The model produces a calibration equation for each country using country level data as a priority, with regional data being used to supplement local information for countries without ground monitoring data. It is acknowledged that the estimates
for data-poor countries may be relatively imprecise and this imprecision can result in apparently abrupt changes in air pollution levels at borders with data-poor countries. For enhanced accuracy of modelled data it is important that countries continue and/or improve their ground measurements.

- WHO’s current methodology for exposure assessment – the same as the one used by the GBD project – is under constant improvement within the framework of a global collaboration with worldwide experts and the World Meteorological Organization (WMO).
- Sand and desert dust is included in the current assessment. Further refinement of the methods will allow to assess the share of desert dust.

**Exposure-risk relationship**

- Although the Integrated exposure response (IER) functions present clear improvements in terms of coherence and comprehensiveness compared to other methods, allowing to derive risks at high level of PM$_{2.5}$, they contained several important assumptions, including that the toxicity of PM$_{2.5}$ from ambient air pollution, household air pollution, second-hand smoke and active smoking is roughly the same.
- The IER functions have been developed for the GBD project and used in the GBD 2010 (2,11) and have been updated twice, for GBD 2013 (3) and GBD 2015/2016 (4, 14). Methodological developments of the IERs over time and various applications have resulted in different estimates of the burden of disease due to ambient air pollution, which created some misunderstandings (16).
- WHO has convened a consultation meeting in January 2017 to discuss the issues and challenges of these functions and one of the recommendations was that as the evidence base increases over time it is imperative that a consented approach of adaptation and improvement of the exposure-response functions over time is performed (17). This work is currently ongoing.

**Cause-specific versus all-cause mortality (except injuries)**

There are two main approaches for assessment of health impacts from ambient air pollution at global, national and local levels and they vary with regards to the scope (burden of diseases or scenario analysis), the exposure-response functions (ERFs) applied the estimation of current exposure and the counterfactual (cut-off) values below which the health impact is not predicted.

1. linear or log-linear functions relating particulate matter of a diameter less than 2.5 µm (PM$_{2.5}$) to natural (all causes of death excluding violent deaths and suicides), cardiovascular and respiratory disease mortality based on outdoor air pollution studies over a range of concentrations occurring in North America and Europe (18), and

2. the IERs, as explained above, developed for and used in the Global Burden of Disease (GBD) project as well as by WHO, combining evidence from studies of ambient air pollution, second-hand smoke, household air pollution and active smoking to estimate risk for air pollution over the entire global range of particulate matter exposure.

All approaches depend on the underlying assumptions and have strengths and limitations that require appreciations and evaluations of the potential consequences. There is certainly the need to
assess the full range of air pollution concentrations around the globe and to provide a method to
be applicable in all countries. The use of IERs is currently the only valid approach for worldwide
assessments, as well as comparisons across countries and risk factors, as it covers the relevant
exposure ranges on a global scale, deals with specific causes of death (important in countries where
all-cause mortality includes a relatively large fraction of infectious diseases, malnutrition etc), and
allows direct comparisons to the burden of other risk factors for a disease. However, as soon as
new epidemiologic studies will become available for exposure ranges above those seen in Europe
and North America, there will be an interest in using only information from cohort studies of
outdoor air pollution rather than integrating relative risk estimates from several types of exposure,
like the IERs.

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