World Health Organization

REGIONAL OFFICE FOR Europe

# WHO Expert Meeting: Methods and tools for assessing the health risks of air pollution at local, national and international level

**Meeting report**
**Bonn, Germany, 12-13 May 2014**

# ABSTRACT

In May 2014, the WHO Regional Office for Europe organized a technical meeting to discuss the evidence for air pollution health effects and propose expert advice on the best options and methods to estimate health risks from air pollution and its sources. The workshop proposed an overview of available indoor and outdoor air pollution health risk assessment methods and tools and identified general principles as well as appropriate methods and tools for conducting air pollution health risk assessment for various scenarios and purposes. The meeting provided relevant advice to inform a variety of health risk assessment efforts at local, national and international scales.



## Keywords

AIR POLLUTION
ENVIRONMENTAL EXPOSURE
ENVIRONMENTAL HEALTH
HEALTH RISK APPRAISAL
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# Introduction: Scope and purpose

Air pollution is an important determinant of health and convincing evidence links air pollutants with the risk of disease, including premature death even at relatively low pollutant concentrations. Quantitative estimates of air pollution health impacts have become an increasingly critical input to policy decisions. Several large projects have recently estimated the burden of disease of exposure to air pollution in various populations and for a variety of policy scenarios of different spatial and temporal scales. For example, recently published figures from WHO show that ca. 3.7 million and 4.3 million premature deaths could be attributed to ambient (outdoor) air pollution and household (indoor) air pollution in 2012, respectively. In total, exposure to air pollution accounted for 7 million deaths worldwide. There is substantial regional variation in burden of disease estimates, with Western Pacific and South East regions bearing most of the burden.

An increasing number of health risk assessments (HRA) of air pollution are being developed for a variety of policy scenarios, using different methodologies, spatial and temporal scales. There is a need to: (a) consider available evidence in the fields of exposure quantification, risk characterization and methodologies for disease burden estimation which will contribute to a more comprehensive and consistent HRA of air pollution, and (b) identify general principles for applying HRA methods at a local, national and international level.

To this end, this WHO workshop convened 52 participants in Bonn, Germany on 12-13 May 2014 (list of participants is enclosed in Annex 1) to discuss the evidence for air pollution effects and propose expert advice on the best options and methods to estimate health risks from air pollution and its sources. This workshop provided relevant advice to inform a variety of HRA efforts at different scales, including but not limited to the Task Force on Health Aspects of Air Pollution (TFH) and the Task Force on Hemispheric Transport of Air Pollution (TF HTAP) of the UNECE Convention on Long Range Trans-boundary Air Pollution (LRTAP) as well as the Climate and Clean Air Coalition (CCAC). The programme of the meeting is presented as Annex 2. The presentations and discussions held during the meeting will be used as the basis for the development of a WHO publication, which will highlight general principles for the proper conduct of HRA for various scenarios and purposes. The target audience of this publication is the community of policy makers and the health risk assessment practitioners at local, national and international level as well as end users from various sectors in international agencies, research and advocacy groups.

The two purposes of the proposed expert workshop were therefore to:

1. Propose an overview of available indoor and outdoor air pollution HRA methods and tools;
2. Identify general principles as well as appropriate methods and tools for conducting air pollution HRA for various scenarios and purposes.

The workshop addressed preceding steps in the health risk assessment chain, such as emissions quantification, only as they directly relate to health risk assessment methods and tools.

Financial support for the organization of the meeting from the Federal Office for the Environment, Switzerland, the Federal Ministry for the Environment, Nature Conservation, Building and Nuclear safety, Germany and the United States Environmental Protection Agency was acknowledged.

# Organization of the workshop

Background papers (see Annex 3) were developed in answer to a series of guiding questions presented in section 3 of this document. This set of papers provided the experts with a good background of recent reviews and current evidence.

The workshop was chaired by Ross Anderson. Denise Felber Dietrich and Terry Keating were appointed as rapporteurs.

Following the short presentations of the background papers and relevant plenary discussion, three small working groups were created to identify general principles, case studies and examples, limitations and gaps in knowledge, as well as future opportunities for methodological advancements of HRA. They discussed the following topics:

- Group 1: Policy questions, tools and population exposure,
- Group 2: Mortality impacts and baseline mortality rate,
- Group 3: Morbidity impacts.

These were followed by a general discussion in plenary. The small working groups were respectively chaired by Jason West (Group 1), Klea Katsouyanni (Group 2) and Erik Lebret (Group 3). Rapporteurs were Lidia Morawska (Group 1), Mathilde Pascal (Group 2) and Otto Hänninen (Group 3).

# Summary of the presentations

## Guiding question 1: Policy context

***"What policy questions is air pollution health risk assessment currently being asked to inform?"***

The presentation made by Michal Krzyzanowski provided a summary of the variety of policy questions, including both for the calculation of current burden of disease and impacts from changes in exposure. An increasing number of HRA of air pollution are being developed for a variety of policy scenarios, using different methodologies, spatial and temporal scales. In many countries, HRA is a formally required policy tool. It accompanies all new programmes, projects, regulations and policies. In many other countries, it is conducted as a part of assessment or research projects even though there is no legal requirement for its implementation. The most common questions asked are:

1. What is the public health burden associated with recent levels of air pollution?
2. What are the human health benefits associated with changing air quality policy or attaining a more stringent AQ standard?
3. What are the human health impacts of emissions from specific sources or selected economic sectors, and what are benefits of policies related to them?
4. What are the human health impacts of current policy or implemented action?
5. What are the policy implications of the uncertainties of the assessment?

The results of the HRA help to optimize the policies in respect to their health benefits and costs.

## Guiding question 2: Tools and models available

***"What tools/models are available to assess the health risks of air pollution at various scales (local, national, regional, global)?"***

Susan Anenberg provided a summary of existing tools that are currently available and categorized the tools according to key technical and operational characteristics for different assessment contexts, and identified information gaps that should be considered for future work. In particular, it included the following tools:

- AirCountsTM
- AirQ2.2
- APHEKOM Health Impact Assessment Tool
- Rapid Co-benefits Calculator (Co-benefits Calculator or RCC)
- EcoSense
- Environmental Benefits Mapping and Analysis Program – Community Edition (BenMAP-CE)
- Environmental Burden of Disease (EBD) Assessment tool for ambient air pollution
- Economic Valuation of Air pollution (EVA)
- GMAPS
- IOMLIFET
- SIM-air (Simple Interactive Models for better air quality)
- TM5-FASST

Key characteristics include spatial resolution, pollutants and health effect outcomes evaluated, and method for characterizing of population exposure, as well as tool format, accessibility, complexity, and degree of peer-review and application in policy contexts. The range of key characteristics among the tools demonstrates that there is an important trade-off between technical refinement and accessibility for a broad range of applications.

Guidance should be developed to help analysts identify the tool most appropriate for the purpose of the assessment and to assist users in interpreting and communicating results. Future work should also strive to better account for multiple sources of uncertainty and to integrate ambient outdoor air pollution health impact assessment tools with those addressing household air pollution and other health factors, such as vehicle accidents and physical activity.

## Guiding question 3: HRA Methods

***"How have the scientific drivers of air pollution HRA changed since the 2000 WHO report (WHO, 2000)? Would any of these developments change the recommendations made in that report?"***

This session was divided in 5 presentations providing a summary of the evidence on various methodological aspects of HRA conduct relevant for ambient and/or indoor air pollution. For each guiding question below (3.a to 3.e), the following general issues were covered:

- How does this element of air pollution HRA relate to current policy questions?
- What is the current state of the science?
- What are the current limitations in available methods?
- What short and long-term opportunities exist for methodological advancements?

## *Guiding question 3.a: Population exposure*

*"What are the different methods available for estimating population exposure to air pollution for HRA at different scales and temporal trends (for both calculations of current burden and future scenario analysis)?"*

Gerard Hoek presented a summary of discussions held at a recent WHO consultation on "Developing a Global Platform on Air Quality and Health" in order to improve global estimates of exposure to outdoor air pollution for better assessments of related health impacts (WHO, 2014). In addition, he provided an overview of various approaches to refine exposure estimates to incorporate factors that are known to modify exposures based upon ambient concentrations such as fine-scale spatial variability within urban areas, population mobility and infiltration of outdoor air pollution into the indoor environment.

A core component of health risk assessment for air pollution is the assessment of exposure. While measurements of ambient air pollutants are the foundation for air pollution epidemiology, the applicability of measurements to health risk assessment is often limited by their temporal and spatial coverage. Very few measurements are available in some highly-polluted regions of the world. Further, measurements are typically only available in urban areas, despite the fact that approximately 50% of the global population resides in rural areas. In addition, measurements conducted in different locations often follow different procedures and use different technologies, making it difficult to harmonize data. Recent progress in methods based on remote sensing and (global) chemical transport and local land use regression models and other estimation approaches, combined with existing surface monitoring, has lead to an increase in availability of information on key air pollutants, including the most highly-polluted and data-poor regions. These approaches allow for improvement of air pollution health risk assessment.

## *Guiding question 3.b: Mortality impacts*

*"What dose-response, exposure-response, and concentration-response functions are available for estimating mortality impacts of concentration or emission changes?"*

Francesco Forastiere, Haidong Kan and Aaron Cohen presented a summary of recent reviews and available evidence in response to the question. Epidemiologic evidence currently provides the most reliable basis for air pollution risk assessment. This evidence is summarized in the form of concentration-response functions (CRF) that quantify the increase in the rates or risks of mortality related to exposure to different levels of ambient air pollution.

Two recent WHO documents from the REVIHAAP (WHO, 2013a) and HRAPIE (WHO, 2013b) projects have provided rationale and recommendations for CRFs in order to perform HRA of air pollution in Europe. The presentation briefly reviewed the CRFs available on the relationship between both $PM_{2.5}$ and $NO_2$ and long term mortality and provided updates on the basis of the recently published studies, including the results of the European ESCAPE project. New meta-analytical CRFs are provided for $PM_{2.5}$ and long-term all-cause, cardiovascular, respiratory mortality and for lung cancer. The long-term impact of $NO_2$ has been extensively discussed in REVIHAAP and HRAPIE and an update was provided based on recent publications. When estimating the impacts of both $PM_{2.5}$ and $NO_2$ some double counting may occur. Evidence suggests that the likely overlap can be up to 33%. Emerging literature on the long-term effects of PM components is premature to provide a convincing risk function.

In the absence of direct epidemiologic evidence on mortality risk from long-term exposure to $PM_{2.5}$ in the world's most polluted regions, the GBD 2010 project developed integrated exposure-response functions (IER) that combined evidence from studies of ambient air pollution, second-hand smoke, household air pollution and active smoking to estimate risk for ambient air pollution over the entire global range of exposure (Lim et al., 2012). The presentation highlighted that the IER provides the best approach currently available to estimate mortality attributable to $PM_{2.5}$ over the entire global range of exposure to $PM_{2.5}$, and was recently used by WHO to estimate the burden of disease in 2012 attributable to ambient air pollution in 2012. However, the IER depends on assumptions that require further evaluation.

Many public health and policy decisions require that the mortality attributable to ambient air pollution be considered in the context of mortality due to other major health risk factors. Comparative Risk Assessment (CRA) provides a way to provide comparable estimates for the various risk factors, but requires that consistent methods be used to estimate risks for each. Current estimates assume that air pollution-attributable mortality is independent of other risk factors and more research is needed to address this issue.

### *Guiding question 3.c: Datasets for baseline mortality rate*

*"What population and baseline mortality rate datasets are available for assessing the health risks of present-day concentrations and future changes in emissions?"*

Annette Pruess-Ustun provided a summary of the key available datasets and their main characteristics for population data, comparable mortality estimates, and future projections. Underlying population and disease burden data, whether historical or projections, is an integral component of any health risk assessment. The sources, methods and applications of different health and population datasets are important to consider when selecting such input data.

### *Guiding question 3.d: Morbidity impacts*

*"What is the state of the science for including morbidity impacts in air pollution health risk assessment at various scales?"*

Laura Perez's presentation summarized the state of the science for including morbidity impacts in air pollution HRA. It summarized what pollutants, sources and exposure times are currently considered or recommended in morbidity HRA, limitations with current approaches, and what opportunities for new methodological developments exist. The presentation was not based on an exhaustive review of the literature but built on information and recommendations proposed in the recent WHO review projects REVIHAAP and HRAPIE as well as other recent reviews.

A main objective of air pollution HRA is to help optimize policies with respect to their health benefits and costs. All monetary valuations of air pollution impact assessment show that the impact of morbidity outcomes is small relative to mortality. However the quantification of morbidity estimates at local, national and international level remains very important information for policy-making and for public health. Within the European context, methodological approaches have recently been reviewed and a set of pollutants, morbidity outcomes, and related CRFs to be used in morbidity HRA, been proposed (WHO, 2013b). A number of principles, however, need to be further refined to overcome limitations of current methodology and to respond policy needs at different scales.

### *Guiding question 3.e: Presentation of uncertainty*

*"How should health risk assessments quantify and express the uncertainty of their estimates, balancing the complexity of information and tools used in concert and the desire to produce simple results for non-technical decision-makers?"*

Greg Freedman addressed how to consider and combine different sources of uncertainty (e.g. from CRFs, simulated concentrations, projected demographic changes, etc.). Despite great improvements in the science behind HRA for outdoor air pollution, we still cannot know with complete certainty the effects of air pollution on health. However, policy makers look to experts in order to give recommendations on weighing the negative effects of outdoor air pollution against the economic benefits. Because of this, it is important to describe with as much accuracy as possible the uncertainty in estimates. This presentation attempted to describe the sources of uncertainty, as well as one way in which to carry all sources of uncertainty through an analysis to get estimates of the burden due to outdoor air pollution. The Global Burden of Disease 2010 (Lim et al., 2012) was provided as an example of the use of simulation methods to incorporate uncertainty from four sources (uncertainty in disease burden, the pollution exposure level, response to the pollution and the counterfactual level of air pollution).

## Summary of the working group discussions

The meeting discussions were first conducted in small working groups. All small working groups were asked to frame their discussions around the following issues: 1) general principles, 2) case studies and examples, 3) limitations and gaps in knowledge and 4) future opportunities for methodological advancements. Each group answered specific questions to further identify issues related to these points. All groups also discussed how to conduct proper assessment of uncertainty of health risk assessment and how to communicate effectively on health risks and on uncertainty of health risk assessment. These points were further discussed in a plenary session. The overall results of the discussions are presented in the following sections. The issues raised during discussion will be considered in preparation of the WHO publication on proper conduct of HRA.

## Policy questions, tools and population exposure

*a) General issues*

- The general principles of HRA are shared among groups and tools, and rooted in the underlying epidemiological studies.
- The tools differ mainly in their approaches to representing exposure or concentrations (whether modeled or using actual ground measurements).
- Atmospheric modeling is required for the assessment of the benefits of actions or future scenarios.
- It is important to better assess health impacts in developing countries, focusing on a range in annual concentration of 50-100 $\mu g/m^3$ $PM_{2.5}$.
- Long-term population exposure (annual concentrations) to air pollutants should be used in HRA when quantifying chronic health impacts.

- It is possible to study the effectiveness of interventions implemented in developing countries.
- Global reduced-form tools (such as co-benefits calculator and FASST) should be used for developing national applications (a broad scale), but there is a need to improve capabilities for assessment. Nevertheless, it is better to move ahead with tools and understanding currently available.
- HRA often comes at the end of a process; nevertheless it is important to allow sufficient time for the proper conduct and consideration of the health benefits.

*b) Critical mapping of tools being used to assess risk from air pollution, and recommendation about what tool(s) should be used for different policy contexts. Can the tools and methods be harmonized?*

- There is a variety of scales, pollutants, health effects, and tools available.
- It is important to first define the policy question to be answered, and the audiences to be informed, and identify the relevant pollutants and geographical scale, before choosing the proper tool that will satisfy.
- It is also important to consider who is asking the question versus who will take action based on the results of the HRA.
- A decision tree can be a useful way to provide guidance to address the choices and tradeoffs in selecting methods, tools, and data sets with considerations for different geographic scales and policy contexts, and the selection of endpoints.
    - The important characteristics of the tools and data should be provided.
    - Case studies can be used as illustrative examples of the tools.
    - It was recommended that a small group of experts continue to scope the effort and propose a way to best present the information.
- A web-based resource or information portal could be created in order to make the tools and methods more accessible to the HRA community. A range of possible approaches was discussed, including a simple webpage of links, a metadata catalog, a database or repository, as well as a user's forum.

*c) Availability of data on air pollution sources and sectors and potential use in health risk assessment*

- There is a long-term goal of increasing understanding of air pollution through local monitoring, emissions inventories, and modeling, to better understand air pollution sources.
- Models, ground monitoring, and satellite information all have their respective strengths.
- Products for $PM_{2.5}$, derived from combining the three sources, provide global coverage at 10 km resolution. Improvements should be encouraged, using more monitors and multiple models. This allows population-weighted $PM_{2.5}$ to be calculated for each country as an indicator.
- There is a need to relate the meaning of indicators to health. Air quality indicators that combine multiple air pollutants are discouraged for HRA.

- The contribution of sources and sectors requires extra modeling work that isn't always done. Receptor-based PM source apportionment studies can also be used.

*d) Appropriateness of use of air quality data with different spatial resolution from the exposure assessment used in the original epidemiological studies*

- Appropriate population exposure information is essential for the proper conduct of HRA.
- The spatial resolution used for exposure assessment for HRAs should be consistent with what is used in epidemiological studies.
- At a global scale, spatial resolution of ~12 km is appropriate for most applications; however, ambient measurements are not available for many regions and outside of urban areas for large parts of the world.Coarse resolution global models are likely to have a bias (generally underestimate the population-weighted concentration for $PM_{2.5}$).
- There is a need for finer spatial resolution:
    - To account for inequalities and socio-economic/distributional effects e.g. within urban areas.
    - To represent population exposure at finer resolution (~1 km). Current regulatory monitoring networks could be enhanced with additional measurements, e.g. using low-cost/personal monitoring approaches, for improved spatial representativeness.
    - To better estimate exposures for some pollutants for which the distribution is not homogenous in space and time (BC, UFP, $NO_x$). Concentrations at a finer spatial or temporal resolution (e.g. at residential address) should be estimated.
    - Land-use regression (LUR) and atmospheric dispersion models can help go to finer resolution, e.g. for urban scale assessments.
    - Research needs include the development of appropriate population characteristics and land use data sets, the consideration of multi-pollutant exposures and effects (for better estimation of total exposure), and matching scales of epidemiology, assessment, and observations.

## Mortality impacts and baseline mortality rate

*a) General issues*

- The global, regional, and urban scales are all needed.
- There is a need to study the interactions between air pollution effects and other behavioral/life style factors, in particular environmental factors and other major risk factors for CVD
- Up-to-date health data (e.g. baseline incidence) and projections (including climate change and air pollution emissions explicitly) are needed
- The following case studies, examples and resources were provided:
    - At global, regional and national scales: GBD 2010 (GBD 2013 provides Chinese estimates at the provincial level and Indian estimates by urban and rural location as well)

- At country scale: UK (COMEAP), Mexico, Germany (Homber et al., 2013 ) (Kallweit et al., 2013)
- At urban scale: French cities; London before and after the introduction of low emission zones (LEZ), Hong Kong.

*b) Appropriateness of the use of dose response curves at high levels of air pollution: policy implications and methods to estimate the health benefits of interventions at various air pollution levels*

- The composition, and potentially the toxicity, of the PM mixture are different in different areas of the globe.
- The underlying population and burden data also differs across the globe. For example, the CRFs in Europe are mainly driven by effects on the elderly, which may not be the case elsewhere.
- In the absence of direct epidemiologic evidence on mortality risk from long-term exposure to $PM_{2.5}$ in the world's most polluted regions, the GBD 2010 project developed integrated concentration-response functions (IER) that combined evidence from available studies of ambient air pollution, second-hand smoke, household air pollution and active smoking to estimate risk for ambient air pollution over the entire global range of exposure (Burnett et al., 2014).
- The IER provides the best approach currently available for application in global settings to estimate mortality attributable to $PM_{2.5}$ over the entire range of exposure to $PM_{2.5}$, but it depends on assumptions that require further testing.
- Alternatives to the IER, including linear extrapolation from available ambient air quality studies, should be included as sensitivity analyses.
- Epidemiologic studies of long-term exposure and mortality/morbidity from chronic diseases in the most highly polluted regions are lacking and are urgently needed. Studies are also needed at the low end of the exposure range for which not enough evidence exists.

*c) Considerations for estimation of impacts of correlated pollutants (use of CRFs from single- or multi-pollutant models, accumulation of the estimated impacts etc.)*

- A larger data base exists from single pollutant models
- Consideration of the use of single- or multi-pollutant models depends on the question being asked. The question should first be clearly defined, and then the model can be chosen.
- If there is potential confounding, it is important to assess if and how the pollutants are correlated.
- Available evidence suggests that both $NO_2$ and $PM_{2.5}$ have long-term mortality impacts, with a possible reduction of the effect estimate for $NO_2$ on adjustment of up to 33%. This evidence was considered under recent project HRAPIE of the WHO Regional Office for Europe, where expert recommendations were made in the context of cost-effectiveness and cost-benefit analysis for the revision of the air policy of the European Union. However, there was a lack of agreement regarding the extent to which the $NO_2$ exposure data available for this exercise properly reflected exposure of the population, and therefore the health impacts

from $NO_2$ exposure were not quantified. Further work is needed to characterize the link between estimated $NO_2$ exposure and the recommendations provided in the HRAPIE report.

- Whether $PM_{2.5}$ and/or $NO_2$ should be addressed in HRA depends upon the question being addressed. The context should be considered in deciding whether to include $PM_{2.5}$ alone, $NO_2$ alone, or $PM_{2.5}$ and $NO_2$ (taking into account the overlap).

*d) Special considerations for the estimation of mortality impacts in a comparative risk assessment context*

- CRA exercises are a useful tool to communication of risks from air pollutants in comparison to other risk factors and causes of disease.
- WHO could undertake such an effort.
- The concept is related to avoidable risks, and should not be translated to an "individual base".
- It is difficult to explain that attributable risks add up to >100%
- There is a need for CRA frameworks.

## Morbidity impacts

*a) General issues*

- Morbidity HRA may be more difficult to conduct than mortality HRA. Reasons for this include:
  - The limited number of air pollution epidemiology studies quantifying the morbidity risks associated with air pollution exposure, particularly in areas outside of North America and Europe;
  - Incomplete data regarding the baseline number of hospital, emergency department visits, asthma prevalence, and other morbidity outcomes.
- Approaches for characterizing the baseline incidence rate for morbidity impacts in countries where these data are not available include: (1) transferring rates from countries/regions in which they are available to locations in which they are not; (2) interpolating these rates using techniques including Bayesian disease mapping and Gradient Boosted Regression Trees. The development of surveillance and monitoring systems should be further encouraged, particularly in low and middle income countries.
- Morbidity impacts may have more appeal to lay audience, as some impacts are common and widespread. This is particularly the case when the population affected is vulnerable to air pollution, such as children.
- In cost or disability weighting one should consider effect on family, social network, immaterial costs to patient and surrounding.
- Better use should be made of primary healthcare data.
- For some endpoints, data and CRF are old and limited (e.g. restricted activity days).

- Maybe general determinants of frailty and vulnerability are more important than single pollutants; more thinking into multi-causal pathways is needed.
- More information is needed on interactions with other health risks, susceptibility and age dependence.
- WHO recommendations are needed and would be useful for conducting HRA at national/regional/local levels. Specifically, recommendations are needed about what important health endpoints to include, which may vary by country and/or region.
- It would be useful to develop more qualitative information about multi-causal pathways and frailty/vulnerability in relation to morbidity, to inform HRA. A conceptual diagram could be developed, describing how acute and chronic exposure to air pollution is related to the risk of premature death, and how air pollution particularly affects individuals already in a frail state, which makes them more susceptible to death from air pollutants and other causes.
- Journals should require that studies report necessary inputs for use in meta-analyses. Experts recommend that WHO stimulates journal editors to require that studies report necessary inputs for use in meta-analyses. Examples of necessary information for use in meta-analyses are included in Fann et al. (2011).

*b) Considerations for estimation of impacts of correlated pollutants (use of CRFs from single- or multi-pollutant models, accumulation of the estimated impacts etc.)*

- Most evidence still comes from single pollutant models. Availability of multi-pollutant models with more than 2 pollutants is limited.
- Previous experience has shown that interpretation of multi-pollutant models poses challenges.
- Knowledge on the sources of air pollutants could be used to inform on some of the issues related to correlation of pollutants, especially when pollutants originate from common sources.
- The application of new technologies e.g. big data & data-mining, biomarkers, (epi-)genomics may inform understanding/reasoning about morbidity in the future.

*c) Special considerations for the estimation of morbidity impacts in a comparative risk assessment context*

- CRA is important, but an ambitious enterprise which requires substantial resources.
- The context determines the relevant comparisons: about diseases or risk factors, but also between countries, population groups, geographical areas, or between policy measures.
- Morbidity incidence and prevalence are less comparable between countries across different diseases as mortality counts or lost life-years.
- Differences in baselines and handling of parallel risk factors need more consideration also in study design phase.
- For morbidity impacts, a broad set of outcomes with different metrics can be used, including: restricted activity days, loss of working days, hospitalisation days, medication use, costs.

## Suggestions for proper communication

### *General principles*

No matter whether communication deals with uncertainties or health risks, some general principles do apply. Good communication depends first on the target audience which could be policy makers, the general public, the media, public health and clinical care professionals or other stakeholders such as insurance companies, employers and NGOs. As an example, for politicians, economic indicators appeared more important than health indicators, whereas for the general public, discussions of lifestyle and quality of life may be more important. Also, the important impact of air pollution on non-communicable diseases should be emphasized. In any case, communication strategies, messages and terminologies should be tested against the target audience. Terminology and expressions used need to be considered carefully and reviewed on regular basis. Finally, it is strongly recommended to involve communication experts for more efficiency.

### *Assessment and communication of uncertainty of health risks assessment*

- The uncertainty analysis is an instrumental part of any scientific analysis. Such analysis is usually limited to uncertainty components which are already identified ("known unknowns").
- Uncertainties derive mainly from our understanding of concentration-response functions and from exposure representation. There are probably uncertainty components which we aren't aware of yet.
- However, certainty i.e. what we know based on the current evidence, is equally important and should also be communicated.
- Each study should clearly define its methodology and limits. It was also recommended that assumptions in models be transparent, that models be open sources and available for use.
- HRA should be accompanied by uncertainties intervals and errors should be weighted accordingly.
- The context is crucial when reporting uncertainties. A structured approach tied to the context has to be established indeed. The IPCS tiered uncertainty analysis framework (IPCS, 2008) or NUSAP method for uncertainty assessment (PBL, 2013) appeared useful. It was suggested to refer to documentation from WHO Regional Office for Europe developed in the context of the Fourth Ministerial Conference on Environment and Health (WHO, 2004) and to look at examples of frameworks such as those from the International Agency for Research on Cancer (IARC, 2006), the GRADE working group (Guyatt et al., 2008), the Intergovernmental Panel on Climate Change (IPCC, 2010), US EPA (Rooney at al., 2014) or the UK Food and Environment Research Agency (2010).

### *Communication of health risks*

- Participants found it easier to communicate on mortality than on morbidity metrics. For better communication, it was suggested to emphasize co-benefits (e.g. physical activity from reducing car use) and to compare numbers against other health effects, across nations and time trends.
- The concept of DALYs appears to be problematic in some audiences but the terminology 'disease burden' seems easier to comprehend. Healthy life expectancy is a newer concept that

incorporates morbidity losses. Participants wondered whether premature deaths should be used and whether the risk should be individualized.

- Another highlighted aspect of risk communication was the short versus long-term effects. Until now, we communicate on short-term effects when there is no evidence for long-term effects. Participants discussed whether these effects are "independent" along with their impact importance.
- For communication to public health experts, experts recommended that WHO organize regional workshops to illustrate and raise awareness of what HRA can deliver and how to adopt it within countries.
- As well, experts suggested that WHO should take a lead in harmonizing and promoting air pollution communication strategies, e.g. by pooling experience into good practices/training materials for communication of HRA results.

## Discussion on plan for the development of a publication on proper conduct of HRA

In addition to more general issues on proper communication of the results of HRA and related uncertainties, the participants discussed the following issues related to the structure and the content of the publication stemming from the background papers and discussions held at the meeting:

- Participants thought it useful to make the meeting report and background papers available on the internet only and develop a separate, short WHO publication that could be available electronically and in print.
- The publication should include a summary for policy makers and a glossary of technical terms.
- It is important to define the audience in order to scope the contents of the publication:
    - National decision makers need to understand why HRA is important, why it needs to be improved, and what resources and institutions are needed for HRA.
    - Experts conducting HRA need to understand how to properly do it.
    - Researchers need to know what data are available and needed and where to find them.
- The use of examples, figures and other schematic representations to illustrate various aspects of HRA chain was deemed helpful.

## Follow-up actions

1. A small group of experts will continue to scope the effort and propose a way to present the information (in the form of a decision tree or other) on how to select methods, tools, and data sets for proper conduct of HRA.
2. Based on the meeting discussions and efforts of the small group of experts established under 1), WHO will develop a publication highlighting general principles for the proper conduct of HRA for various scenarios and purposes. The outline as well as draft publication will be

circulated to all meeting participants for input and comments. This work will be ongoing through 2014.

3. Once finalized, the meeting report and background papers will be made available on WHO website.
4. WHO will explore possible approaches for wider dissemination of information on the tools and methods to the broader HRA community through a web-based resource or information portal.

## REFERENCES

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# Annex 1: Final programme

**Monday, 12 May 2014**

| | |
|---|---|
| 8:30 | Registration open |
| 9:00 | Opening of the meeting (*E. Paunovic; C. Dora*) |
| 9:10 | Objectives of the meeting (*M.E. Héroux*) |
| 9:30 | Introduction of participants, appointment of chairpersons and rapporteur, |
| 9:50 | Adoption of agenda and programme |
| 10:00 | Presentation of background papers (introduction) |
| 10:05 | Guiding question 1: Policy questions that air pollution health risk assessment (HRA) is currently being asked to inform (*M. Krzyzanowski*) |
| 10:30 | Guiding question 2: Tools/models available to assess the health risks of air pollution at various scales (*S. Anenberg*) |
| 10:55 | Coffee break |
| 11:20 | Guiding question 3a: Methods available for estimating population exposure to air pollution for HRA at different scales and temporal trends (*G. Hoek*) |
| 11:45 | Guiding question 3b: Dose-response, exposure-response, and concentration-response functions available for estimating mortality impacts (*F. Forastiere, H. Kan, A. Cohen*) |
| 12:15 | Guiding question 3c: Population and baseline mortality rate datasets available for assessing the health risks (*A. Pruess-Ustun*) |
| 12:35 | Lunch break |
| 13:30 | Guiding question 3d: State of the science for including morbidity impacts in air pollution HRA (*L. Perez*) |
| 13:55 | Guiding question 3e: Quantification and expression of uncertainty of estimates (*G. Freedman*) |
| 14:20 | Instructions for discussion in small working groups |
| 14:30 | Coffee break |

15:00 Discussion in 3 small working groups on:
- Identification of general principles and recommendations about methods/data to use
- Limitations and gaps in knowledge, including uncertainties
- Future opportunities for methodological advancements
- Case studies and examples

Group 1: Policy questions, tools and population exposure
Group 2: Mortality impacts and baseline mortality rates
Group 3: Morbidity impacts

17:30 End of day 1 discussion

19:00 *Informal dinner (optional)*

**Tuesday, 13 May 2014**

9:00 Recap from previous day's meeting

9:30 Reporting from Group 1: Policy questions, tools and population exposure

10:00 Reporting from Group 2: Mortality impacts and baseline mortality rates

10:30 Coffee break

11:00 Reporting from Group 3: Morbidity impacts

11:30 Group discussion on cross-cutting issues

12:30 Lunch break

13:30 Group discussion on cross-cutting issues (continued)

15:00 Follow up actions and plan for development of publication

16:00 Closure of the meeting

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# Annex 3: Background papers

## Background paper 1: Policy context of health risk assessment of outdoor air pollution

*Guiding question 1: "What policy questions is air pollution health risk assessment currently being asked to inform?"*

*Michal Krzyzanowski*

### Summary

In many countries, health risk assessment (HRA) is a formally required policy tool. It accompanies all new programmes, projects, regulations and policies. In many other countries, it is conducted as a part of assessment or research projects even though there is no legal requirement for its implementation. The most common questions asked are:

- What is the public health burden associated with recent levels of air pollution?
- What are the human health benefits associated with changing air quality policy or attaining a more stringent AQ standard?
- What are the human health impacts of emissions from specific sources or selected economic sectors, and what are benefits of policies related to them?
- What are the human health impacts of current policy or implemented action?
- What are the policy implications of the uncertainties of the assessment?

The results of the HRA help to optimize the policies in respect to their health benefits and costs.

### *Introduction*

The main purpose of health risk assessment (HRA) is to inform policies about the magnitude of the current impacts of a risk factor or of their changes resulting from planned policies or other modifications of environmental conditions. In many countries, the HRA is required by specific regulatory acts, many of them formulating questions to HRA. This chapter summarizes information on the policy framework for HRA of air pollution in various countries and presents questions addressed by HRA. The sources used in this chapter include information received from 23 parties to the Convention on Long Range Transboundary Air Pollution (22 countries and EC) supplied to WHO in response to a short questionnaire sent to all Task Force on Health focal points in March 2014. The overview of the responses is presented in Table 1.

It should be emphasized that this chapter does not aim at systematic review of the countries´ approaches to HRA. This would be not possible both due to the limited scope of the material collected from the countries and due to the resources and time limitations of the current project. The material has been used to illustrate the diversity of the frameworks for the HRA (even among the limited number of countries) as well as the range of questions asked by the HRA.

**Table 1. Formal requirements for HRA and availability of the assessments in the countries – parties to the CLRTAP: responses to WHO questions.**

| Party of the CLRTAP | Formal requirement for HRA | HRA conducted in practice | HRA overview available |
|---|---|---|---|
| Albania | N | N | N |
| Armenia | Y (2014) | N | N |
| Austria | N | Y | N |
| Azerbaijan | N | N | N |
| Belgium | N | Y | Y |
| Bosnia & Hercegovina | Y | Y | N |
| Canada | Y | Y | Y |
| Croatia | N | Y ** | N |
| EC | Y | Y | N |
| Germany | N | Y | Y |
| Ireland | N | Y | N |
| Kyrgyzstan | N* | Y ** | N |
| Norway | N | Y | N |
| Poland | N | Y | N |
| Republic of Moldova | Y (Dec 2013) | N | N |
| Serbia | Y*** | N | N |
| Sweden | N | Y | N |
| Switzerland | Y | Y | Y |
| TFYROM | Y | Y | Y |
| Turkey | N | N | N |
| Ukraine | Y | Y | N |
| UK | Y | Y | Y |
| USA | Y | Y | Y |

* Response indicates that the air quality assessment is required, but not the health risk assessment

** Methods do not correspond to WHO methodology

*** MoH expects the HRA to be performed by the state PH network but this is not reflected in legal acts.

## *Policy framework of HRA at national and international level*

Formal requirements or legal instruments requiring the conduct of health risk assessment of air pollution for research or governmental policy exist in 10 out of the 22 countries responding (and also in EC). However, the level of details specified by the regulations and circumstances of the required assessment vary considerably between the countries.

In some countries (UK, USA, as well as EC), the assessment of benefits and costs (including health) must accompany all (or defined according to the expected cost) proposed programs, projects, regulations and policies. The assessments are also conducted to evaluate the effectiveness of already introduced policies in respect to their objectives. In some countries, HRA is a part of the Environmental Impact Assessment (EIA) procedure. In Switzerland and Ukraine, EIA of all new or modified installations is required. The data on health outcomes and subsequent costs attributable to air pollution in general and to traffic generated air pollution in

particular, are analysed and published regularly in the framework of the analysis of the external costs of traffic in Switzerland. In several other countries, HRA is included in the (sometimes quite recently introduced) public health laws without specification of the scope of the required assessments.

In the USA, the HRA is a part of a broader regulatory analysis, defined in the Office of Management and Budget circular (1) as follows: "*Regulatory analysis is a tool regulatory agencies use to anticipate and evaluate the likely consequences of rules. It provides a formal way of organizing the evidence on the key effects, good and bad, of the various alternatives that should be considered in developing regulations. The motivation is to (a) learn if the benefits of an action are likely to justify the costs or (b) discover which of various possible alternatives would be the most cost-effective…. Since agencies often design health and safety regulation to reduce risks to life, evaluation of these benefits can be the key part of the analysis*."

Also in the EC, the HRA belongs to a broader impact assessment process, defined as a set of logical steps to be followed when a policy proposal is prepared. Impact Assessment Guidelines document (2) defines those steps, and its Annex 9 describes elements of the HRA (3).

Institutional arrangements vary as well. In the USA, HRA is one of the tasks of the Environmental Protection Agency. In several other countries (Armenia, Bosnia and Herzegovina, Moldova, TFYROM) HRA is the task of the public health institutes or services. Also in Canada, HRA is conducted within the department of health, though such task is not assigned by regulations. In Switzerland and UK, special expert groups are created by the governments to advice on the scientific and methodological questions of the assessments (Federal Commission for Air Hygiene in Switzerland and Interdepartmental Group on Costs and Benefits (Air) with Committee on the Medical Effects of Air Pollutants in UK).

The methodology of the assessment is strictly defined in UK (4, 5) and USA (1). The impact assessments made in connection to policy initiatives by the EC are scrutinised by an internal board to secure that common standards are met. In some other countries, the HRA methodology is open to interpretation of the implementing agencies. Some examples provided by the responding countries show that HRA is interpreted there as an analysis of associations between local pollution levels and morbidity indicators or as a comparison of the pollution levels with certain reference (or standard) values.

## *Questions asked in local and national projects*

Health risk assessment has been conducted in 18 out of the 23 parties responding to the WHO questions. It means that it has been conducted also without formal requirement for it. Besides fulfilling formal requirements, HRA has been conducted in the framework of research projects implemented by governmental institutions or academic groups. The results of many of those assessments have been published in reports available on web sites of the agencies ordering or conducting the projects, and in scientific journals.

### *"What is the public health burden associated with recent levels of air pollution?"*

The most commonly reported objective of the HRA projects is evaluation of the magnitude of the impacts of air pollution on health and their spatial distribution in a country or region. Such analysis was conducted to assess the distribution of impacts of population exposure to PM in Austria both for all country (6) and for selected region (Steiermark) (7), or in selected cities of

Estonia (8) and Lithuania (9). In Poland, the impacts of PM were assessed for selected metropolitan areas with data on PM concentration collected by air quality monitoring networks (10). Similar analysis, covering all country and separating impacts of regional and local pollution, was conducted in Sweden (11). In UK, the impacts of PM exposure, presented as fraction of mortality attributable to long-term exposure to anthropogenic ambient particulate air pollution at a local authority level, are included in the set of indicators in the Public Health Outcomes Framework (PHOF) for England (12). The indicator has been included in the PHOF to allow Directors of Public Health in local authorities to appropriately prioritise action on air quality in their local area and to help in reducing the health burden due to air pollution.

The regional differentiation, pointing to the cities or regions of the world with the greatest need for pollution abatement has been an important aspect of the international projects estimating the burden of disease attributed to ambient air pollution such as APHEIS (13), Global Burden of Disease collaboration (14), or of WHO BoD estimates prepared in the framework of the Global Health Observatory (15, 16).

In each of these analyses, the impacts were calculated in relation to certain counterfactual level, defined as the national standard (Poland), WHO AQG level (APHEIS), background (natural) level of pollution (Sweden, UK, Estonia, Lithuania) or the lowest level observed in epidemiological studies (Austria, GBD, WHO).

*Comparison of impacts* on health of recently observed air pollution with health burden of other risk factors is also contributing to the answer to the question on the magnitude of the impacts. Comparative risk assessment has been one of the tasks of the Global Burden of Disease study (14), in an international project comparing burden of disease due to nine environmental risk factors in six European countries (17) as well as of an analysis conducted in Germany (18) and UK (19). Such analyses help to select the priorities in disease prevention or in addressing various environmental risks.

***"What are the human health benefits associated with changing air quality policy or attaining a more stringent AQ standard?"***

More prospective intentions have health risks assessments conducted to evaluate *impacts of various policy scenarios*. It was the core of the benefit analysis conducted by the EC revising its air quality policy and focussing on effective pollution source control and emission reductions until 2030 (20). Four options for strategic impact reduction targets were examined in terms of a 25%, 50%, 75% or 100% closing of the gap between the current legislation "baseline" scenario and the maximum technically feasible emission reduction scenario. A further option to meet the WHO guideline values was assessed but considered not within reach before 2030. The preferred option sets the next strategic objectives at the level where marginal costs and benefits are optimized (i.e. at 75% of the maximum reduction). A fully implemented baseline will reduce impacts in 2020 by 36% for $PM_{2.5}$ and 23% for ozone, compared with 2005. The preferred option for 2025-30 will reduce impacts by 50% for $PM_{2.5}$, 33% for ozone (relative to 2005) – i.e. an extra third of the reduction in health burden delivered by the baseline.

Besides estimating current mortality burden attributable to air pollution, COMEAP's 2010 report (21) also included an estimate of the health benefit (based on reduction of mortality) that would result from decrease in air particulate pollution (both a 1 $\mu g/m^3$ decrease in population-weighted annual average $PM_{2.5}$ and removal of all anthropogenic $PM_{2.5}$). Also the UK government's Air Quality Strategy of 2007 was underpinned by a detailed economic analysis of the benefits to

health that would result from reductions in air pollutants achieved by the various policy options considered (22).

The US EPA Quantitative HRA for PM (23) provides estimates of the potential magnitude of effects on premature mortality and/or on selected morbidity associated with recent ambient levels of PM as well as with just meeting the current and alternative suites of PM standards considered in selected urban study areas. It also includes, where data are available, consideration of impacts on susceptible populations. Also the introduction of the more stringent national air quality standards for fine particulate matter in 2013 was preceded by regulatory analysis including assessment of expected health benefits resulting from reduction of pollution levels to those proposed by the new standards (24). The value of the health benefits exceed expected costs of attainment by 12 to 171 times. Similar assessments were conducted earlier before the national AQ standards for ground-level ozone and lead were updated.

The global concern due to climate change and the impact of anthropogenic emission of air pollutants on climate implies the highest priority for climate-related policies. The synergy between some of the policies addressing climate change is a topic of the UNEP integrated assessment of black carbon and ozone (25). Health risk analysis conducted in the framework of this assessment demonstrates the collateral benefits to health which can be derived from practical measures to reduce short-lived climate pollutants: black carbon as well as the gases which contribute to the formation of tropospheric ozone, especially methane. UK analysis of the national policy on climate change indicated that selecting options maximizing air pollution reduction brings substantial additional health and economic benefits of combined policies (26). The report indicates which actions would bring such co-benefits (promotion of ultra-low-carbon vehicles, renewable sources of electricity which do not involve combustion, energy efficiency measures, and reducing agricultural demand for nitrogen) and gives examples of actions which tackle climate change but damage air quality (such as biomass combustion for domestic heat generation).

Similar prospective approach has the analysis of air pollution impacts under changing climate presented by a Polish study (27). Though it does not address a specific policy, it indicates what health impacts the currently considered climate scenario and current pollution emission patterns would have in the future.

***"What are the human health impacts of emissions from specific sources or selected economic sectors, and what are benefits of policies related to them?"***

Examples of such projects include the assessment of impacts of current pollution from various industries conducted in a region of Ukraine (28) and an analysis of external costs of transport in Switzerland (29). In the Swiss analysis, the impacts of air pollution on health (and their costs) are assessed along with the impacts of traffic accidents and noise on health as well as the impacts of transport on climate or other aspects of the environment. Calculated costs include those due to traffic congestion. Analysis is conducted for various modes of transport, allowing for comparison of their impacts.

Reduction of the impacts of the air pollution on health through emission reductions from the main pollution sources (including household combustion of solid fuels) was also analysed by a World Bank project in Ulaanbaatar, Mongolia (30). Benefits and costs of eight different options for pollution abatement were analysed, with five of the options resulting in economic benefits significantly exceeding costs of the actions.

USEPA conducted impact analysis of residential wood heaters (31) and stationary compression ignition (CI) engines (32), including the assessment of health benefits of the introduction of more efficient heaters or CI engines with reduced emissions. Health benefits associated with these proposed regulations are valued to be much greater than the cost to install cleaner, lower emitting appliances or engines.
Also the comparison of health impacts of air pollution from the local (national) sources compared with those of trans-boundary air pollution belongs to this category. A study assessing the impacts on health in Poland of air pollution originating in various European countries and the impacts of air pollution emitted in Poland on health in other countries illustrates the significance of international policies in risk reduction (33).

***"What are the human health impacts of current policy or implemented action?"***

A series of assessment of the benefits and costs of the Clean Air Act in the USA provides good example of such assessment, including both retrospective and prospective analysis (34). These studies ask: *"How do the overall health, welfare, ecological, and economic benefits of Clean Air Act programs compare to the costs of these programs?"*. The 2nd Prospective Study, 1990-2020, published in 2011, demonstrates that the benefits of the programs and standards required by the Clean Air Act significantly exceed costs of this implementation.

There are relatively few studies conducting retrospective analysis of health benefits of specific policies of actions implemented to reduce air pollution. Their recent review, conducted in the framework of APHEIS study, analyses results of 28 such interventions (35). This review concludes that there is consistent evidence in the published studies that most of the interventions were associated with health benefits. For five of the interventions, data on mortality over the intervention period were available demonstrating that observed decrement in mortality was greater than expected in the HRA models.

***"What are the policy implications of the uncertainties of the assessment?"***

The uncertainties of the health risk assessments and their implications for the policy decisions are often included in debates on the policies supported by those assessments. Therefore the uncertainty analysis is an integral part of most of the health risk assessments and is reflected both in the textual description and in numerical results of the outcomes of the analysis. Though the communication on the impacts highlights individual numbers ("3.7 million deaths due to ambient air pollution" (15)), the results of analysis are usually presented as ranges, giving a sense of the (in-) precision of the estimates. Not less important is discussion of the assumptions made in the analysis, which may have bigger impact on the estimates than statistical parameters used in impacts quantification. The Swiss assessment of external costs of transport (36) is an example of such uncertainty analysis using Monte Carlo methods. In the EC assessments (37), a sensitivity analysis, demonstrating the influence of various assumptions on the estimated impacts (and costs) provides information about the uncertainty of the assessment.

## *Limitations imposed by policy context of HRA*

Though the practical application of the assessment conducted to support certain policy development process emphasizes its significance to public health, strict deadlines and (often) limited resources of such assessments play a role in determining the scope of the analysis. As a rule, it is based on existing, routinely collected input data and existing models allowing estimation of the current exposure or its changes under various policy scenarios. This limits the

range of the air quality indicators considered in the assessment: an example is the omission of $NO_2$ from cost-benefit analysis conducted in support of the 2013 revision of the EU policies (38). The CRFs are based on accumulated research, imposing a selective approach to the estimation of risks and its focus on the best studied pollutants and health outcomes. The update of CRFs requires dedicated evidence review, which is often not conducted due to restricted resources, or is not complete at the time of HRA publication due to constant expansion of the evidence base. The background health data are often missing or are insufficiently precise to allow estimation of full range of health effects of the exposure. Therefore, the quantification of the risks is often incomplete and is more likely to under- than to over-estimate the impacts of pollution. Full presentation of the assumptions made and discussion of HRA limitations is an essential part of the analysis. Improvement of the HRA supporting policies requires systematic investment in relevant studies, data collection systems and modelling tools, as well as development of institutional capacities for systematic evaluation of evidence and regulatory analysis. Experience of several countries demonstrates that such investment in resources results in better policies, achieving cleaner air and better health at lower cost.

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# Background paper 2: Methods and tools for assessing the health risks of air pollution at local, national, and international levels

*Guiding question 2: "What tools/models are available to assess the health risks of air pollution at various scales (local, national, regional, global)?"*

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## Abstract

Analysts quantify the health impacts of air pollution to estimate the total public health burden of ambient air pollution and the potential health benefits of reducing air pollution levels. Risk assessors and policy analysts now employ several tools to automate air pollution health impact assessments. This paper reviews 12 air pollution health impact assessment tools that are currently available, categorizes the tools according to key technical and operational characteristics for different assessment contexts, and identifies information gaps that should be considered for future work. Key characteristics include spatial resolution, pollutants and health effect outcomes evaluated, and method for characterizing of population exposure, as well as tool format, accessibility, complexity, and degree of peer-review and application in policy contexts. The range of key characteristics among the tools demonstrates that there is an important trade-off between technical refinement and accessibility for a broad range of applications. Guidance should be developed to help analysts identify the tool most appropriate for the purpose of the assessment and to assist users in interpreting and communicating results. Future work should also strive to better account for multiple sources of uncertainty and to integrate ambient outdoor air pollution health impact assessment tools with those addressing household air pollution and other health factors, such as vehicle accidents and physical activity.

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## *Introduction*

Analysts estimate the health impacts of air pollution to answer one or both of the following questions: (1) what is the total public health burden of air pollution levels; and (2) what are the health benefits of reducing air pollution levels? In addition, there are a number of variants to these two questions—for example, analysts may wish to understand the historical trend in the human health burden of air pollution among a specific sub-population such as children. Over the last decade, governmental, intergovernmental, and non-governmental entities have invested in tools that are better able to meet the growing demand for more specific and timely information regarding health impacts associated with exposure to air pollutants. For example, the U.S. Environmental Protection Agency developed the Environmental Benefits Mapping and Analysis Program (BenMAP-CE) in part to help fulfill requirements by the Office of Management and Budget and the Clean Air Act to characterize the benefits and costs of U.S. air pollution regulations. Other countries and intergovernmental organizations such as the World Health Organization and World Bank have invested in similar tools to quantify air pollution-related health impacts for a variety of purposes.

Health impact and health burden assessments depend strongly on the evidence available from air pollution epidemiology and exposure science. Recent advances in these two disciplines have enabled health impact assessments to combine findings from atmospheric science and epidemiology in novel ways, allowing analysts to quantify an increasing number of health outcomes in far greater detail than previously possible. Quantitative air pollution health impact assessments can now be performed at various scales and resolutions for many air pollutants, including fine particles ($PM_{2.5}$), ground-level ozone ($O_3$), oxides of nitrogen ($NO_x$), and oxides of sulfur ($SO_x$). Results of these assessments are often reported in numbers of attributable deaths and disease cases, years of life years lost (YLL), disability-adjusted life years (DALYs), or change in life expectancy attributable to total air pollution exposure or a change in air pollution exposure.

Using computer programs to automate the procedure for calculating the incidence of air pollution-related health impacts offers several advantages: simplicity (lowering the barrier of entry for new analysts to conduct assessments), consistency, comparability among assessments, and quality assurance. Many of these studies use the attributable fraction approach to quantifying health impacts, wherein epidemiology-derived concentration-response functions and population-level exposure estimates are used to determine the portion of cases of a particular health effect that may be attributable to air pollution. This method requires information about air pollution concentration levels, the relationship between concentrations and health outcomes, and the characteristics of the populations exposed which generally include their baseline health status, age, and location (Figure 1). Automated tools are typically pre-loaded with health and demographic data and health impact functions, and some allow for user-specified inputs. Some automated tools also have built-in air pollution exposure information connecting emissions to the exposure metric, requiring only information about emission changes from the user, while others read in user-specified exposure estimates.

This paper reviews 12 air pollution health impact assessment tools that are currently available, categorizes the tools according to key technical and operational characteristics for different assessment contexts, and identifies information gaps that should be considered for future work. These tools, often designed for a particular type of assessment context, vary in methodological approach, technical complexity, geographical scope, resolution, and other aspects. Tools that apply to a single country as currently configured are summarized in Appendix B but are not

synthesized in this paper due to their limited geographical scope. This paper does not address methods to assign an economic value to health outcomes, though many of the tools reviewed include that capability. In addition, these tools reviewed here focus on ambient air pollution, as methods and tools for quantifying household air pollution health impacts are in an earlier stage of development (e.g. the Household Air Pollution Impacts Tool).

## *Classifying tools and key factors to consider when selecting tools*

While analysts may consider a host of factors when selecting a health impact assessment tool—technical complexity, pre-loaded data, etc.—among the most common is the geographic scope. Geographic scope is the spatial coverage or extent of the tool as currently configured, which is distinct from spatial resolution (described below). For example, a tool with global scope may have a national resolution (i.e. including all countries for the world) or city resolution (i.e. including cities all over the world).

The 12 tools are categorized according to geographical scope as pre-configured in Table 1 and summarized in Appendix A. Nine of the tools have global scope, encompassing countries and/or cities around the world (Tables 2 and 3). Three of these tools are designed to be flexible in scope and can be used for analyses ranging from the local to global resolutions (AirQ2.2, BenMAP-CE, IOMLIFET). The three remaining tools apply to a specific region of the world encompassing several countries (Tables 4 and 5). Additional tools are available for some individual countries but are not reviewed here due to their limited geographical scope. Five national scope tools are summarized in Appendix B and include the Air Quality Benefits Assessment Tool (AQBAT) and the Illness Cost of Air Pollution tool (ICAP) for Canada, the Integrated Transport and Health Impact Modeling Tool (ITHIM) for the United Kingdom, and the Co-benefits Risk Assessment Screening Model (COBRA) and AP2 (formerly APEEP) model for the United States.

After having selected a tool based on its pre-defined geographic scope, the analyst would next consider: how spatially resolved the impact estimates are (region/nation/administrative boundary), which pollutants and health effect outcomes the tool is pre-configured to assess, and the method for characterizing population exposure (Sections 2.1 and 2.2). Additional operational factors may also be important: format, accessibility, complexity, and degree of peer-review and application in policy contexts (Section 2.3). This section describes each of these key characteristics.

*Key technical factors to consider: Pollutants and health effect outcomes*

The tools reviewed here differ in terms of pollutants addressed and health outcomes quantified. All tools reviewed in this paper except one (GMAPS) are pre-configured to assess fine particulate matter ($PM_{2.5}$) impacts, though two (AirCounts$^{TM}$ and EcoSense) include only primary $PM_{2.5}$ (excluding secondarily formed sulfate, nitrate, and secondary organic aerosols). Most tools are readily able to estimate coarse particulate matter ($PM_{10}$) and ozone impacts, and some include $NO_x$, $SO_x$, and CO. A few tools also include other pollutants such as heavy metals and black smoke.

Similarly, all the tools reviewed here calculate impacts of air pollution on premature mortality in terms of the number of excess or avoided deaths. Many tools can also quantify YLLs, DALYs, and morbidity cases (e.g. cases of chronic obstructive pulmonary disorder). Most tools such as BenMAP-CE and the Co-benefits Calculator estimate impacts attributable to air quality changes

in a single year, though these impacts may lag over a multi-year period. The IOMLIFET model can characterize the change in the risk of premature death among a cohort of individuals over the course of their lifetime.

Quantifying air pollution-related morbidity impacts around the world is made difficult by the lack of high quality baseline morbidity rates in many countries. These types of administrative records are generally more challenging to collect than death records. In addition, extrapolating concentration-response functions for morbidity outcomes like hospitalizations and asthma attacks from one population to another is difficult because health care access and systems differ widely around the world and both diagnoses and coding of diagnoses can be inconsistent. Therefore, while several of the tools with global scope have the capability to quantify morbidity impacts, the capability may be limited to certain contexts and applications where high quality baseline morbidity rates are available.

*Key technical factors to consider: Resolution and exposure characterization*

A key difference among the tools reviewed here is their approach to characterizing population exposure to air pollution, changes in exposure resulting from emission or concentration changes and whether ambient pollutant data are available in the tool or whether users must specify these data from an external source (Table 6). Methods for characterizing exposure often determine the spatial resolution at which air pollution-related health impacts are calculated and results reported. Some tools assign air quality values to a grid, wherein the geographical scope is divided into cells (either uniform or variable in shape) and population exposure and health impacts are quantified separately for each cell. Other tools assign air quality data to geopolitical boundaries, such as countries, regions of countries, and cities. Ideally, the spatial resolution of the tool would be matched with the spatial resolution of the assessment context (e.g. using a tool with city-level or finer resolution to assess air pollution impacts in cities).

All tools except for two (Aphekom and GMAPS) use some form of air quality modeling to simulate concentrations or exposure estimates. Compared with monitoring, the advantages of using models to simulate air pollutant concentrations for health impact assessment include that they have broader spatial coverage than *in situ* ground-based monitoring (though this may not be the case for satellite-based observations) and that they allow for evaluating different future scenarios of emission changes. By contrast, monitoring data reflects actual ambient levels in a specific location for a discrete period in time. Certain tools (e.g. Aphekom, BenMAP-CE) allow users to adjust these monitoring data to reflect hypothetical air quality policies (i.e. a monitor "rollback").

Some of the tools reviewed here can be used to estimate air pollution-related health impacts at gridded resolution (e.g. BenMAP-CE, EcoSense). These tools are generally considered the most rigorous for health benefits assessment because they use full air quality modeling—which in turn accounts for the complex atmospheric chemistry and transport governing air pollution and also simulates the influence of emission controls on air pollution levels. However, these tools may be prohibitive in some assessment contexts because full-scale air quality modeling is generally resource intensive and operating the tool requires significant technical expertise (though web-based and classroom training is often available). Gridded assessments can typically be aggregated to geopolitical boundaries such as cities (though depending on the grid resolution, there may only be one or two grid cells for each city), countries, and regions.

When air quality modeling is unavailable, "reduced-form" tools can generate broad-scale estimates of air pollution impacts from built-in relationships between emissions and the exposure metric (often concentration) derived from externally conducted air quality model simulations. For example, the Co-benefits Calculator relies on influence coefficients generated by the global chemical transport model GEOS-Chem Adjoint that link gridded emissions to impacts at the national level. Another example is the TM5-FASST tool, which is driven by a region-to-region source-receptor matrix (i.e. the quantified influence of emissions in one region on health impacts in another) that was developed from TM5 global chemical transport model simulations. However, the results may be less able to account for atmospheric chemistry and transport than those based on full-form modeling (i.e. taking the difference between separate model simulations of a base case and a control case), and thus may be of limited interpretability in certain contexts (e.g. estimating the health benefits of reducing $SO_2$ emissions after $NO_x$ emission reductions are in place).

Using air quality models for health impact assessment also has several disadvantages, including that simulated concentrations may not be accurate and the resolution of the air quality model may not match actual exposure patterns (e.g. near-roadway exposures, high urban concentrations). Similarly, modeled concentrations may not match the method or spatial resolution of the exposure characterization in the epidemiology studies from which concentration-response functions are drawn. Thus, while air quality models are necessary to address health benefits of alternative future scenarios across broad spatial scales, simulated concentrations should be evaluated against observations and care must be taken to match spatial resolutions among the assessment context, air quality model, and epidemiological inputs to the health impact function as closely as possible. Some tools use *in situ* ground-level monitors, finely resolved population information, or remote sensing (e.g. satellite observations) to improve the performance and resolution of current concentrations simulated by the model (e.g. Co-benefits Calculator, TM5-FASST). This type of data assimilation, however, is not possible for model simulations of future air quality or present-day counterfactuals, for which observed data are not available.

Three additional tools use other methods for characterizing exposure specifically in cities. AirCounts™ uses intake fraction calculations based on externally conducted air quality modeling to estimate population exposure to primary (directly emitted) $PM_{2.5}$ components. The Aphekom tool relies on *in situ* air quality monitoring. GMAPS uses a reduced-form econometric model to simulate $PM_{10}$ concentrations.

*Key operational characteristics*

The tools also range in format, affecting how accessible they are to less technical audiences. Some tools are client-based software programs, requiring users to download and install the software to use it. These tools include extensive datasets of health impact functions, population, and health data that users may modify, but are generally more complicated to use and may require users to invest time and resources in training themselves. Other tools run within Microsoft Excel, which is generally accessible to most users but may require them to purchase the Microsoft Office suite. Since many analysts are familiar with Microsoft Office, these tools may not require training materials. A few tools are web-based, enabling users to generate air pollution health impact estimates without downloading or installing a program. Web-based tools may be most accessible to non-technical users, particularly in countries that lack the resources to conduct full-scale, detailed, and very refined health impact assessments.

Users may also wish to consider the complexity of the tool (e.g. data inputs and resources required) and the extent to which it is pre-loaded with the data needed to perform an assessment. The range of tools described here reflect a range of technical complexity and accessibility. Users will want to consider balancing their tolerance for technical complexity with the level of specificity called for in the policy context. For example, the health benefits of U.S. air quality policies are generally estimated using the most refined tool for the U.S. (BenMAP-CE), detailed demographic datasets, and the difference between air quality model simulations of a base emissions scenario and a control emission scenario. In contrast, it may be time and cost-prohibitive to run air quality modeling for more data- and resource-limited countries; in the absence of more refined tools and datasets that are also accessible with limited resources, reduced-form tools (e.g. the Co-benefits Calculator) that do not require air quality modeling or detailed demographic datasets as inputs may be the only way to estimate health benefits of reducing emissions in those areas.

Analysts should also consider whether the tool has been peer-reviewed, the extent to which analysts have used it to inform policy, and whether it is open-source or proprietary. Some tools (e.g. BenMAP, the predecessor to BenMAP-CE) have received external peer review and have been "exercised" extensively in the course of supporting national air quality regulations (e.g. U.S. EPA National Ambient Air Quality Standards). A critical advantage of open-source tools over those that are proprietary is that they are fully transparent, allowing analysts to evaluate the underlying algorithms and datasets used to calculate impacts.

Finally, analysts must consider whether the tool is maintained as a "living" tool, or whether the included datasets and methods are fixed in place or obsolescent. The data inputs required to run air pollution health impact assessments must be updated over time to reflect changes in the science. For example, the size of the population exposed to air pollution is a major driver of air pollution health impacts, and datasets should be updated to capture growth, aging, and migration over time. Similarly, baseline mortality and disease rates should be updated over time to capture the "epidemiological transition" from infectious disease to chronic disease as economies develop. Air pollution exposure levels are also changing rapidly as economies develop and urbanization occurs, and exposure characterization methods should be updated with the latest emissions, meteorology, and atmospheric chemistry information. On a more operational level, some tools requiring software downloads (e.g. AirQ2.2) may not function on updated operating systems.

## *Challenges*

Despite significant advancements in quantifying the health impacts of ambient air pollution over the last decade, several uncertainties and information gaps remain. This section describes key uncertainties that propagate throughout the air pollution health impact assessment methodology (Section 3.1), the degree to which ambient air pollution health impact assessment tools have been integrated with other health risks (Section 3.2), and challenges in interpreting technical information generated by air pollution health impact assessments for use in policy decisions (Section 3.3).

### *Uncertainty and information gaps*

Air pollution health impact assessment combines information from different sources, including estimated pollutant exposure, demographics, and the relationship between ambient

concentrations and health outcomes. Each of these information sources carries with it some degree of uncertainty that influences the precision and confidence in the health impact results. Figure 2 illustrates how each input parameter is subject to uncertainty, and that this uncertainty propagates as the health impact assessment moves through each stage.

Many air pollution health impact assessments express the quantitative level of uncertainty by calculating a confidence interval using the standard error from the epidemiologically-derived concentration-response relationship.[2] However, additional uncertainties exist as to the shape of the concentration response curve at different concentration levels, the extent to which different air pollutant mixtures pose more or less risk, and the degree to which concentration-response relationships found in one population can be extrapolated to others with different lifestyles, age structures, and medical care (e.g. from a U.S. cohort to other countries). Some tools (e.g. BenMAP-CE) allow for simple pooling techniques (e.g. fixed effect and random effects) to combine concentration-response functions to create a new function that may better account for different populations and study methods.

Aside from the standard error from the epidemiologically-derived concentration-response relationship, other uncertainty sources are generally described qualitatively. For example, exposure estimates are subject to uncertainties in the magnitude and spatial distribution of emissions, chemical and physical processes influencing the impact of emissions on pollutant concentrations, and the spatial (horizontal) and altitudinal (vertical) resolution. For simulations of future air quality, uncertainties in socioeconomic assumptions such as economic growth and population health are also important. Though we are more confident in recent estimates of population size and spatial distribution, other demographic parameters including the baseline mortality and morbidity rates around the world are uncertain. Projecting future demographic changes are subject to uncertainties regarding population aging, migration, and the epidemiological transition from infectious disease to chronic diseases, which are more affected by air pollution exposure.

Fully accounting for all sources of uncertainty remains a significant challenge in air pollution health impact assessment and this limitation is reflected in the tools reviewed here. Future work should strive to better understand the scope and magnitude of these various sources of uncertainty so that they may be reflected in confidence intervals or sensitivity analyses.

*Integrating ambient air pollution health impacts with other health risks*

The tools reviewed here focus on ambient air pollution, but several new tools seek to quantify household air pollution health impacts and capture the interplay between air pollution and other health risks. Several tools under development compile information on household air pollution exposures in different countries (e.g. World Health Organization global database of household air pollution measurements[3]). Other tools are being developed to go beyond household air pollution exposure characterization to health impacts. For example, the Household Air Pollution Impacts Tool (HAPIT) developed by University of California-Berkeley aims to build a spreadsheet model for every country in which users can input reductions in exposure

[2] The 2010 Global Burden of Disease analysis (Lim et al. 2012) reported confidence intervals that reflected uncertainty from two input parameters: (1) the predicted air quality levels; (2) the effect coefficient from the epidemiological study.

[3] Available at http://www.who.int/indoorair/health_impacts/databases_iap/en/

concentrations to estimate premature deaths and DALYs avoided. The tool also includes the ability to compare benefits against mitigation costs to generate estimates of cost-effectiveness. Since household emissions can contribute significantly to outdoor air pollution in many places around the world, this type of tool could be integrated with ambient air pollution health impact tools to assess the total benefits of household air pollution mitigation due to exposure both indoors and outdoors, avoiding double counting.

Policies affecting air quality can also influence other sources of risk. For example, encouraging commuters to substitute bicycles for automobiles may reduce air pollution attributable risk, but increase risk of traffic accidents. To date, only a couple tools are capable of assessing air pollution health impacts and other population health factors (including vehicle accidents, noise, and physical activity) within the same framework. The International Futures project at the University of Denver[4] integrates household air pollution and ambient air pollution impacts into a much broader global model that includes economic, health, environmental, technological and other changes over time. The IOMLIFET model can incorporate mortality hazard rates for any risk factor, including air pollution and other health risks—provided that the end user can provide the appropriate risk parameters. Finally, the Integrated Transport and Health Impact Modeling Tool (ITHIM) for the United Kingdom integrates health impact assessment of transport through changes in physical activity, road traffic injury risk, and urban air pollution (see Appendix B).

Other tools can assess a variety of health risks within the same framework, but have not included the capability to assess air pollution health impacts. The Lives Saved Tool (LiST)[5], which allows users to estimate the global health benefits of public health interventions (e.g. Vitamin A supplementation and malaria treatments), may soon include the ability to estimate the benefits of household air pollution interventions (Bruce et al. 2013). The Health Economic Assessment Tool[6] includes the impact of increased walking and cycling on health, but does not currently include the capability to quantify air pollution health impacts. Future work should seek to expand the existing tools to quantify air pollution and other health risks in a rigorous and integrated way.

In addition, air pollution and climate are inter-related in several ways and tools should increasingly consider both health stressors together. In addition to air pollutants that contribute to climate change (e.g. black carbon, ozone) and the influence of climate change on air pollution (e.g. via changing emissions and meteorology), health-harmful air pollutants and long-lived greenhouse gases like $CO_2$ are often emitted by the same sources. Therefore, some mitigation measures will likely influence both simultaneously. Some evidence suggests that the health effects of air pollutants are modified by temperature, indicating synergistic health effects induced by climate change and air pollution exposure. The Co-benefits Calculator quantifies impacts of emission changes on human health, climate change, and agricultural yields. Given increasing policy interest in both climate change and air pollution around the world, tools that can quantify impacts to both can be informative for policy decisions.

[4] Available at http://pardee.du.edu/

[5] Available at http://www.jhsph.edu/departments/international-health/centers-and-institutes/institute-for-international-programs/list/index.html

[6] Available at available at http://www.heatwalkingcycling.org/

*Interpreting technical information for policy decisions*

Another challenge not fully accounted for in these tools is that end-users must interpret and report the results correctly. That is—end users carry the burden of interpreting and applying these analytical results in a way that both reflects the underlying uncertainties in the data and is also accessible for the decision-maker. While easily-applied tools are more accessible, they may enable misuse of or misinterpreted findings, potentially leading to poorly designed policies. In addition, the presentation of analysis results may range from complex (including formulas, descriptions, and multiple results with confidence intervals) to basic (a single numerical result). Some tools may make key assumptions visible with the tool output and encourage users to assess the impacts of the assumptions on results (e.g. by conducting sensitivity analysis). Guidance should be developed to assist users in interpreting numeric results from air pollution health impact assessment tools and communicating results to decision-makers. Where possible, this type of guidance should be incorporated into training materials for individual tools with specific application to the type of results (e.g. avoided mortality cases, life expectancy changes, percent reduction in air pollution mortality burden) produced by the tool.

## *Conclusion*

This paper reviewed 12 current and publicly available tools that combine air quality information, epidemiologically-derived concentration-response functions, and demographic datasets to estimate air pollution-related health impacts. Nine of the tools are capable of assessing air pollution health risks in cities, countries, regions around the world or on a gridded resolution at any geographical scope from local to global (we define these to be global in scope). Three of the tools encompass several countries (we define these to be regional in scope). The tools shared several common attributes. Nearly all could estimate $PM_{2.5}$ impacts, though two include only the directly emitted components of $PM_{2.5}$; consider mortality outcomes; and were open source. The tools also varied in important respects: some were focused on estimating local impacts while others were designed to quantify country-level or regional impacts, some incorporated modeled or monitored air quality data while others required users to specify these values, some were self-contained while others required that users either have access to the web or Microsoft Office, and some were explicitly designed to be simple to operate while others required users to possess some minimal technical training.

Different tools are appropriate for different assessment contexts, and analysts must consider the technical and operational specifications of the tool necessary to meet the needs of the assessment context. The range of key characteristics among the tools demonstrates that there is an important trade-off between technical refinement and accessibility for a broad range of applications. For some purposes, it may be sufficient to use a coarsely resolved global tool based on reduced-form air quality modeling given data and resource and time limitations. Even in geographical areas for which high quality data exist, reduced-form tools may be useful to screen many potential emission scenarios, identifying those that may benefit from more detailed evaluation. However, where possible, more finely resolved and sophisticated tools based on full air quality modeling should be used, particularly for regulatory analysis. Given the heterogeneity among technical and operational characteristics, analysts should consider which of the available tools provide the appropriate geographic scope, resolution, and maximum degree of technical rigor within the resources constraints.

Matching the abilities of individual tools with specific assessment contexts could highlight ways in which the currently available tools could be improved or whether new methods or tools are

needed to fill a specific need. Guidance should be developed to help analysts identify the tool most appropriate for different assessment contexts and to assist users in interpreting and communicating results. Future work should also strive to better account for multiple sources of uncertainty and to integrate ambient outdoor air pollution health impact assessment tools with those addressing household air pollution and other health factors, such as vehicle accidents and physical activity.

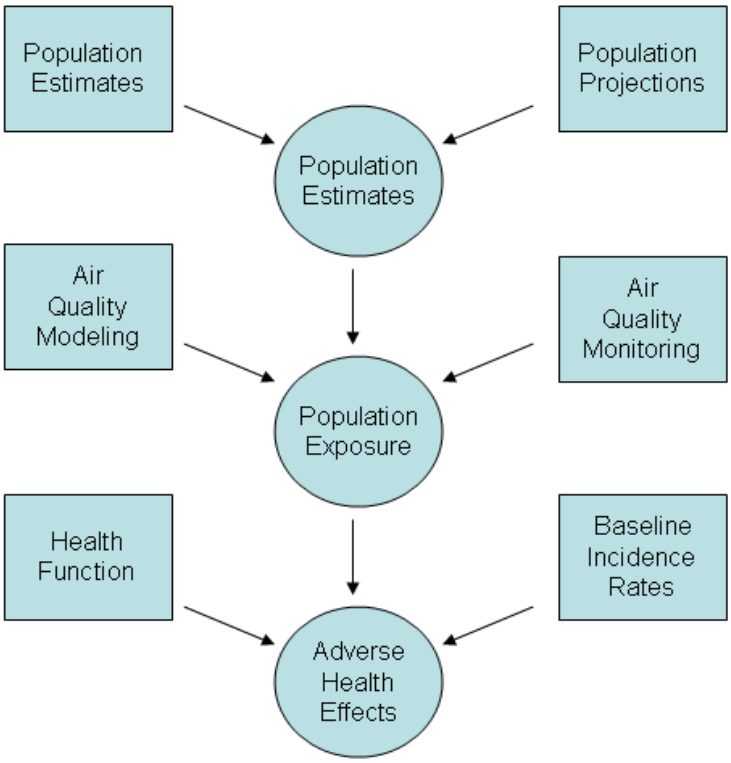


Figure 1. Diagram of air pollution health impact assessment method and typical data inputs.

Table 1. Mapping of existing tools (as now configured) according to geographical scope.

| Tool | Global | Regional |
|---|---|---|
| **AirCounts™** | x | |
| **AirQ2.2** | x | |
| **Co-benefits Calculator** | x | |
| **Environmental Burden of Disease (EBD) Assessment tool for ambient air pollution** | x | |
| **Environmental Benefits Mapping and Analysis Program – Community Edition (BenMAP-CE)** | x | |
| **GMAPS** | x | |
| **IOMLIFET** | x | |
| **SIM-Air** | x | |
| **TM5-FASST** | x | |
| **Aphekom** | | x |
| **EcoSense** | | x |
| **Economic Valuation of Air pollution (EVA)** | | x |

Table 2. Key technical characteristics of tools with global scope

| Characteristic | AirCounts[T] [M] | AIRQ2.2 | BenMAP-CE | Co-benefits Calculator | EBD | GMAPS | IOMLIFET | SIM-Air | TM5-FASST |
|---|---|---|---|---|---|---|---|---|---|
| **Spatial resolution:** | | | | | | | | | |
| **Regional** | | x | x | | x | | x | x | x |
| **National** | | x | x | x | x | x | x | | x |
| **City-level** | x | x | x | | | x | x | x | |
| **Any grid** | | x | x | | | | x | | |
| **Pollutants:** | | | | | | | | | |
| **$PM_{2.5}$** | x (primary) | x | x | x | x | | x | x[1] | x |
| **$PM_{10}$** | | x | | | x | x | x | x | |
| **Ozone** | | x | x | x | | | x | | x |
| **$NO_2$** | | x | x | | | | | | x |
| **$SO_2$** | | x | x | | | | | | x |
| **CO** | | | x | | | | | | |
| **Other** | | Black smoke | | | | | *Any affecting mortality* | | |
| | | | | | | | | | |
| **Health outcome:** | | | | | | | | | |
| **Mortality (cases)** | x | x | x | x | x | x | x | x | x |
| **Disability-adjusted life years (DALY) or years of life lost (YLL)** | | x | x | | x | x | x | | x |
| **Morbidity (cases)** | | x | x | | x | | x | x | |

[1] The SIM-air framework outputs all the criteria pollutants, with linkages for use of all the relevant pollutants in the regional/urban chemical transport models. Only in case of the health impacts, PM is considered as the target pollutant.

Table 3. Key operational characteristics of tools with global scope.

| Characteristic | AirCounts$^{TM}$ | AIRQ2.2 | BenMAP-CE | Co-benefits Calculator | EBD | GMAPS | IOMLIFET | SIM-Air | TM5-FASST |
|---|---|---|---|---|---|---|---|---|---|
| **Format:** | | | | | | | | | |
| **Software download** | | x | x | | | | | | |
| **Microsoft office program** | | | | x | x | x | x | x | x |
| **Web-based** | x | | | In prep | | | | | In prep |
| **Open-source** | | x | x | x | x | x | x | x | In prep |
| **Proprietary** | x | | | | | | | | x |
| | | | | | | | | | |
| **Peer reviewed/policy applications:** | | | | | | | | | |
| **Peer-reviewed** | In prep | Expert | x | In prep | x | In prep | x | x | In prep |
| **Used for policy applications** | | x | x | x | | x | x | x | X |

Table 4. Key technical characteristics of tools with regional (i.e. multi-country) scope

| Characteristic | Aphekom | EVA | EcoSense |
|---|---|---|---|
| **Region** | Europe | Northern Hemisphere | Europe |
| | | | |
| **National** | | x | x |
| **City-level** | x | x | x |
| **Grid** | | x | x |
| **Pollutants:** | | | |
| **$PM_{2.5}$** | x | x | x (primary) |
| **$PM_{10}$** | x | x | x |
| **Ozone** | x | x | x |
| **$NO_2$** | | x | x |
| **$SO_2$** | | x | x |
| **CO** | | x | |
| **Other** | | Dioxins, mercury, black carbon | Heavy metals |
| | | | |
| **Health outcome:** | | | |
| **Mortality (cases)** | x | x | x |
| **Disability-adjusted life years (DALY) or years of life lost (YLL)** | x | x | x |
| **Morbidity (cases)** | x | x | x |

Table 5. Key operational characteristics of tools with regional scope.

| Characteristic | Aphekom | EVA | EcoSense |
|---|---|---|---|
| **Format:** | | | |
| **Software download** | | x | |
| **Microsoft office program** | x | | |
| **Web-based** | | | x |
| **Open-source** | x | | |
| **Proprietary** | | x | x |
| | | | |
| **Peer reviewed/policy applications:** | | | |
| **Peer-reviewed** | x | x | |
| **Used for policy applications** | x | x | x |

Table 6. Source type and required user input (emissions, concentration, or intake fraction) for population exposure information for each tool according to the categories of geographical scope.

| Exposure information source | User Input | Global scope | Regional scope |
|---|---|---|---|
| **Any concentration input by user** | Concentration | BenMAP-CE[1]<br>AirQ2.2<br>IOMLIFET | EBD |
| ***In situ* monitor** | Concentration | | Aphekom |
| **Global chemical transport model (input by user)** | Concentration | | EVA |
| **Regional or urban atmospheric chemistry model (input by user)** | Emissions | SIM-Air | |
| **Reduced-form global chemical transport model** | Emissions | Co-benefits Calculator[2]<br>TM5-FASST[3] | EcoSense[3] |
| **Reduced-form econometric model** | Economic and climate indicators[4] | GMAPS | |
| **Intake fraction (primary $PM_{2.5}$ only)** [5] | Emissions | AirCounts™ | |

[1] Pre-loaded with monitor data for the U.S. and China.

[2] Emissions are translated to concentrations and impacts using gridded per unit emission influence coefficients.

[3] Emissions are translated to concentrations and impacts using a nationally-averaged source-receptor matrix.

[4] Inputs are: total primary energy consumption by type of energy, per capita gasoline and diesel consumption, country and city population, population density, suite of city specific climate variables, heating degree days, cooling days, gross national income per capita, gross domestic product, technical progress, historical PM and total suspended particulate (TSP) concentrations where available.

[5] The intake fractions used in AirCounts™ are limited to directly emitted $PM_{2.5}$ and cannot be used to estimate secondarily formed pollutants (e.g. ozone, secondarily formed $PM_{2.5}$ components such as sulfate and nitrate).

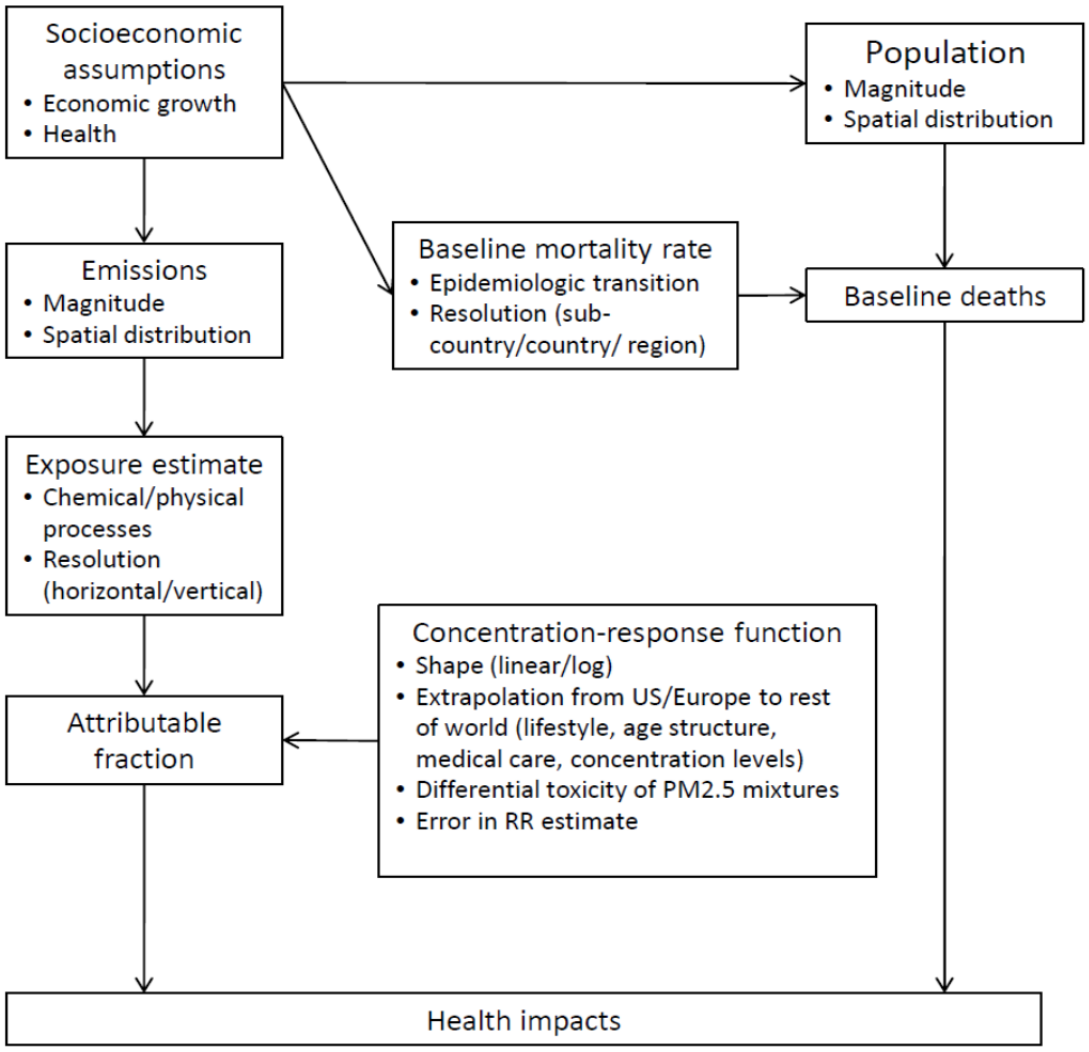


Figure 2. Sources of uncertainty affecting quantification of air pollution-related health impacts. RR=relative risk.

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## APPENDIX A:
## Summaries of available ambient air pollution health impact assessment tools

### AirCounts™

AirCounts™ can estimate the local benefits of transportation projects that reduce $PM_{2.5}$ in cities around the world. It reports benefits in terms of avoided mortality as well as monetized benefits. Several approximations are used in order to enable these calculations.

*Points of contact: AirCounts@abtassoc.com*
*How to obtain: Web-based tool at http://www.aircounts.com/*

### AirQ2.2

The software tool AirQ performs calculations that allow the quantification of the health effects of exposure to air pollution, including estimates of the life expectancy reduction. AirQ 2.2 estimates:
• the effects of short-term changes in air pollution (based on risk estimates from time-series studies);
• the effects of long-term exposures (using life-tables approach and based on risk estimates from cohort studies).
For each type of estimate, separate HELP files explain details of calculation and provide examples of the program application. Methodological principles of the procedure and scientific basis for the risk estimates are summarized in the WHO documents 'Quantification of health effects of exposure to air pollution' and 'Health aspects of air pollution with particulate matter, ozone and nitrogen dioxide'. It has been created in 2001, with some modifications made in 2003-2004, with the software running under Windows NT and XP, but not under later version of Windows (Vista, Windows 7 etc). Due to the availability of the newer tools and lack of WHO resources, the update of the software is not foreseen.

*Point of contact: Christian Gapp (World Health Organization, chg@ecehbonn.euro.who.int)*
*How to obtain: Free download from http://www.euro.who.int/en/health-topics/environment-and-health/air-quality/activities/tools-for-health-impact-assessment-of-air-quality-the-airq-2.2-software*

### APHEKOM Health Impact Assessment Tool

The tool include excel files and text guidelines (plus online tool) to perform short and long term HIA (life-expectancy, mortality and hospitalization) of urban air pollution under counterfactual scenarios. It can be adapted to alternative scenarios and CRF. The tool is available in English, Russian and French (with a more detailed guidance in French, see http://www.invs.sante.fr/surveillance/psas9/evaluation_impact.html#guide). It was designed to be easily used by people familiar with environmental health issues but not experts of air pollution, and was largely used as a training support.

*Points of contact: Magali Corso (French Institute of Public Health Surveillance, m.corso@invs.sante.fr), Mathilde Pascal (French Institute of Public Health Surveillance, m.pascal@invs.sante.fr), Sylvia Medina (French Institute of Public Health Surveillance, s.medina@invs.sante.fr)*

*How to obtain: Free download from www.aphekom.org/publications*

**Rapid Co-benefits Calculator (Co-benefits Calculator or RCC)**

The Co-benefits Calculator is a rapid assessment tool being developed under the Climate and Clean Air Coalition to Reduce Short-Lived Climate Pollutants (CCAC). This tool allows users to rapidly estimate air pollution-related health, climate, and agricultural impacts of reducing emissions. The tool is driven by sensitivity coefficients that link gridded emissions of air pollutants and precursors to health, climate, and agricultural impacts at the national level. These sensitivity coefficients generated by the chemical transport model GEOS-Chem Adjoint obviate the need for expensive and resource-intensive air quality modeling. The Co-benefits Calculator can thus be used by non-technical experts to achieve a general understanding of the benefits to their country associated with reduced air pollution emissions. The tool is currently Excel-based. Versions for all countries and a web-based interface are under development.

*Points of contact: Susan Anenberg (U.S. Environmental Protection Agency, Anenberg.susan@epa.gov), Harry Vallack (Stockholm Environment Institute, harry.vallack@york.ac.uk)*
*How to obtain: Contact the developers*

**EcoSense**

EcoSense is an integrated atmospheric dispersion and exposure assessment model which implements the Impact Pathway Approach developed within ExternE. It was designed for the analysis of single point sources (electricity and heat production) in Europe but it can also be used for analysis of multi emission sources in certain regions. The model was developed to support the assessment of priority impacts resulting from the exposure to airborne pollutants, namely impacts on human health, crops, building materials and ecosystems. The current version of EcoSenseWeb, covers the emission of 'classical' pollutants $SO_2$, $NO_x$, primary particulates, NMVOC, $NH_3$, as well as some of the most important heavy metals. It includes also damage assessment due to emission of greenhouse gases as well as the higher concentrations of $NO_2$ and PPM in urban areas due to urban emissions, the so called "Urban Increment".

*Point of contact: Joachim Roos (University of Stuttgart, Joachim.Roos@ier.uni-stuttgart.de)*
*How to obtain: EcoSenseWeb provides a web interface for single source calculations (http://ecosenseweb.ier.uni-stuttgart.de). It can be accessed for a small fee.*

**Environmental Benefits Mapping and Analysis Program – Community Edition (BenMAP-CE)**

BenMAP-CE is a Windows-based program that uses a Geographic Information System (GIS) to estimate the health and economic impacts associated with ambient air pollution changes. BenMAP was first developed by the U.S. Environmental Protection Agency in 2003, has been extensively used for a variety of applications – including for U.S. regulatory policy analysis, and has recently been redeveloped to be open source. BenMAP includes nearly all of the information users would need to start performing a benefits analysis; advanced and non-U.S. analyses can customize the program to address their policy question. Because BenMAP is based

on a GIS, the results can be mapped for ease of presentation. BenMAP is used frequently for regulatory purposes and is flexible enough to run analyses at any scale and resolution.

*Point of contact: Neal Fann (U.S. Environmental Protection Agency, fann.neal@epa.gov)*
*How to obtain: Free download from http://www.epa.gov/air/benmap/*

**Environmental Burden of Disease (EBD) Assessment tool for ambient air pollution**

Excel spreadsheet to estimate the health impacts from air pollution at city or country level. It is based on air pollution levels (annual mean $PM_{10}$ or $PM_{2.5}$) and disease data inserted by the user to estimate respiratory and cardiovascular health impacts. It is based on Comparative Risk Assessment methods as used in the Global Burden of Disease estimates. A previous version exists, and an updated tool is under development.

*Points of contact: EBDassessment@who.int*
*How to obtain: Contact EBDassessment@who.int*

**Economic Valuation of Air pollution (EVA)**

EVA is an integrated model system, based on the impact-pathway chain, to assess the health-related economic externalities of air pollution resulting from specific emission sources, sectors or geographical areas, which can be used to support policymaking with respect to emission control. Central for the system is a newly developed tagging method capable of calculating the contribution from a specific emission source or sector to the overall air pollution levels, taking into account the non-linear atmospheric chemistry.

*Points of contact: Prof. Jørgen Brandt (Aarhus Universtiy, jbr@dmu.dk)*
*How to obtain: Contact Prof. Jørgen Brandt (jbr@dmu.dk)*

**GMAPS**

GMAPS is an econometric model developed to predict ambient PM10 levels for world cities larger than 100,000. The key determinants are current energy consumption, energy mix, economic activity, population and population density together with city level geo-climatic data. It provides separate predictions for residential areas as well as for pollution hotspots.

*Points of contact: Kiran Dev Pandey (World Bank, kpandey@worldbank.org)*
*How to obtain: World Development Indicators database*

**IOMLIFET**

IOMLIFET is a set of spreadsheets for calculating time-based mortality impacts of changes in mortality hazard rates. It uses standard life-table methods but deals separately with different age cohorts. It is designed to be as flexible as possible in the patterns of changes it can handle, and can accommodate cause-specific inputs, and effects lagged following pollution changes.

*Point of contact: Dr. Brian Miller (Institute of Occupational Medicine, brian.miller@iom-world.org)*

*How to obtain: Free download from IOM website*

**SIM-air (Simple Interactive Models for better air quality)**

Every city has unique air quality challenges that require customized approaches to monitor and model pollution. Critical pollutants, sources, meteorology, geography, population distribution, history, institutions, and information base vary for every city. The SIM-air family of tools were developed to use the available information to support integrated air quality management. The modules are designed to estimate emissions and to simulate the interactions between emissions, pollution dispersion, impacts, and management options. All the databases, calculations, and interfaces (to GIS) are maintained in spread sheets for easy access. For the analysis of emissions inventory and health impacts, a database of emission factors and concentration-response functions are included in the tools, which can be adjusted with specific data from cities. All the tools and the documentation are distributed for free.

*Points of contact: Sarath Guttikunda (Urban Emissions, simair@urbanemissions.info)*
*How to obtain: Free download at http://www.urbanemissions.info*

**TM5-FASST**

TM5-FASST is an Excel based software which enables exploring in a interactive and user-friendly way impacts of air pollutant emissions (or emission changes) based on an extensive set of previously calculated TM5 simulations from which a library of source-receptor matrices for all relevant atmospheric pollutants has been compiled. TM5-FASST takes as input emission inventories of pollutant precursors for $O_3$ and PM (by economic sector, or aggregated over all sectors) in 56 source regions covering the globe + global international shipping and global aviation, and delivers $PM_{2.5}$ and $O_3$ concentrations with their associated impacts on human health and ecosystems. Further, the model calculates a series of climate-relevant parameters for short-lived species and methane ($CH_4$), like the global instantaneous radiative forcing, the equivalent $CO_2$ emission based on Global Warming Potential for various time horizons, annual deposition of black carbon to the Arctic region. A more sophisticated and elaborate (less user-friendly) version of TM5-FASST is available in Interactive Data Language (IDL) code, with region-to-grid source-receptor relations, which is able to produce global grid maps of the TM5-FASST output at a global1 degreex1 degree resolution. Output(s) : - Regional concentrations, column integrated amounts, and deposition of air pollutants - Impacts (e.g. health, vegetation) - Radiative forcing per sector/region - Gridded fields of above (IDL version) - Source apportionment (by emitting region and by sector) of pollutants in any custom-defined region

*Points of contact: Rita van Dingenen (European Commission Joint Research Centre, rita.van-dingenen@jrc.ec.europa.eu)*
*How to obtain: Contact the developer*

## APPENDIX B:
## Ambient air pollution health impact assessment tools with national scope

This appendix summarizes five ambient air pollution health impact assessment tools with national scope – that is, tools that are currently configured to run analyses for a single country. Tables B1 and B2 summarize the key technical and operational characteristics of these two tools. Source of population exposure information is included in Table B1.

### Air Quality Benefits Assessment Tool (AQBAT)

The Air Quality Benefits Assessment Tool (AQBAT) is a computer simulation application designed to estimate the human health and welfare benefits or damages associated with changes in Canada's ambient air quality. AQBAT allows for the definition of a wide range of specific scenario models from the flexibility of combining and linking of pollutants, health endpoints, geographic areas and scenario years. The application consists of one Microsoft Excel workbook file containing Excel user forms and toolbars with numerous controls and Visual Basic for Applications (VBA) programming to enable the user to define, run, examine and save the inputs and outputs for a specific scenario model. AQBAT also contains sheets of historical and projected population data, and accesses data files of distributions of historical and hypothetical pollutant concentrations along with data files of annual baseline health endpoint occurrence rates. AQBAT utilizes and controls the @Risk add-in software to perform Monte Carlo simulation, which entails sampling the input distributions, tracking the outputs and providing descriptive statistics on the distributions of these outputs.

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### AP2 (formerly APEEP)

AP2, like APEEP, is a standard integrated assessment model (IAM) in that it connects emissions to monetary damages through six modules: emissions, air quality modeling, concentrations, exposures, physical effects, and valuation. The distinguishing feature of AP2 is its spatial detail and that it is calibrated to compute marginal damages. AP2 is equipped to use various approaches to modeling dose-response and health impact valuation.

*Points of contact: Nick Muller (Middlebury College, nicholas.muller74@gmail.com)*
*How to obtain: Free download from American Economic Review Website or contact N. Muller*

### Co-benefits Risk Assessment (COBRA) screening model

COBRA provides screening-level estimates of the impact of air pollution emission changes on ambient fine particulate matter ($PM_{2.5}$), translates this into health effect impacts, and then monetizes these impacts. Built into COBRA are emissions inventories, a simplified air quality model, exposure-response relationships, and unit values. They are based on assumptions that EPA currently uses as reasonable best estimates. Analyses can be performed at the state or county level and across the 14 major emissions categories included in the EPA's National Emissions Inventory.

*Points of contact: Denise Mulholland (U.S. Environmental Protection Agency, mullholland.denise@epa.gov)*
*How to obtain: Free download from http://epa.gov/statelocalclimate/resources/cobra.html*

**Illness Costs of Air Pollution (ICAP)**

See OMA website and technical reports available online.

*Points of contact: John Wellner (Ontario Medical Association) or Ed Hanna (DSS Management Consultants Inc.)*
*How to obtain: Free download from Canadian Medical Association and Ontario Medical Association websites*

**Integrated Transport and Health Impact Modelling Tool (ITHIM)**

ITHIM provides integrated health impact assessment of transport through changes in physical activity, road traffic injury risk, and urban air pollution. These health changes are linked to changes in greenhouse gas emissions. ITHIM can either be used as a stand-alone model, or linked to other transport and health models. It can be used for development of scenarios, for estimation of changes in exposures, and for modelling health outcomes.

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*How to obtain: Contact the developers*

Table B1. Key technical characteristics of tools with national scope.

| Characteristic | AQBAT | AP2 | COBRA | ICAP | ITHIM |
|---|---|---|---|---|---|
| **Country** | Canada | U.S. | U.S. | Canada | UK |
| | | | | | |
| **Spatial resolution:** | | | | | |
| **County or province** | x | x | x | | |
| **City** | | | | | x |
| **Census division** | x | | | x | |
| **Grid** | | | | | |
| **Pollutants:** | | | | | |
| **$PM_{2.5}$** | x | x | x | x | x |
| **$PM_{10}$** | x | x | | x | |
| **Ozone** | x | x | | | |
| **$NO_2$** | x | x | | x | |
| **$SO_2$** | x | x | | x | |
| **CO** | x | | | | |
| **Other** | | VOC, $NH_3$ | | | |
| | | | | | |
| **Health outcome:** | | | | | |
| **Mortality (cases)** | x | x | x | x | x |
| **Disability-adjusted life years (DALY) or years of life lost (YLL)** | x | x | | | x |
| **Morbidity (cases)** | x | x | x | x | x |
| | | | | | |
| **Source of population exposure information:** | | | | | |
| ***In situ* monitor** | x | | | x | |
| **Reduced-form atmospheric chemistry model – source-receptor matrix** | | | x | | |
| **Dispersion model with reduced-form atmospheric chemistry model** | | x | | | |
| **Simple linear sub-model** | | | | | x |

Table B2. Key operational characteristics of tools with national scope.

| Characteristic | AQBAT | AP2 | COBRA | ICAP | ITHIM |
|---|---|---|---|---|---|
| **Format:** | | | | | |
| **Software download** | | x | x | x | |
| **Microsoft office program** | x | | | | x |
| **Analytica program** | | | | | x |
| **Web-based** | | | | | |
| **Open-source** | x | x | | | |
| **Proprietary** | | | x | x | x |
| | | | | | |
| **Peer reviewed/policy applications:** | | | | | |
| **Peer-reviewed** | x | x | x | | x |
| **Used for policy applications** | x | x | | x | |

# Background paper 3: Population exposure

*Guiding question 3.a: "What are the different methods available for estimating population exposure to air pollution for HRA at different scales and temporal trends (for both calculation of current burden and future scenario analysis)?"*

*Michael Brauer and Gerard Hoek, with contributions from the attendees of the WHO Consultation "Developing a Global Platform on Air Quality and Health" held in Geneva, 30-31 January 2014.*

This paper presents a summary of discussions held at a recent WHO consultation on improving global estimates of exposure to outdoor air pollution for better assessments of related health impacts. In addition, we provide an overview of various approaches to refine exposure estimates to incorporate factors that are known to modify exposures based upon ambient concentrations such as fine-scale spatial variability within urban areas, population mobility and infiltration of outdoor air pollution into the indoor environment.

A core component of health risk assessment for air pollution is the assessment of exposure. While measurements of ambient air pollutants are the foundation for air pollution epidemiology, the applicability of measurements to health risk assessment is often limited by their temporal and spatial coverage. Very few measurements are available in some highly-polluted regions of the world. Further, measurements are typically only available in urban areas, despite the fact that approximately 50% of the global population resides in rural areas. In addition, measurements conducted in different locations often follow different procedures and use different technologies, making it difficult to harmonize data. Recent progress in methods based on remote sensing and (global) chemical transport and local land use regression models and other estimation approaches, combined with existing surface monitoring, has lead to an increase in availability of information on key air pollutants, including the most highly-polluted and data-poor regions (Brauer M et al. 2012; Paciorek C and Liu Y. 2012 HEI Review Committee Commentary; Dentener FJ et al. 2010; van Donkelaar A et al. 2010; Hoek et al. 2008). These approaches allow for improvement of air pollution health risk assessment and are described in more detail below.

## *WHO AQ databases*

Air quality monitoring data may be used for public information, to guide policy decisions in areas such as transportation or energy, and to estimate the related disease burden in the population (Brauer et al 2012). In developed countries, the network of monitoring stations is generally sufficiently dense with adequate temporal coverage to be used directly in health risk assessment. In developing countries, the situation varies widely. While in some countries the monitoring network for fine particulate matter has recently been extended into numerous cities, it is still at the planning stage in others. Many developing countries, however, are currently expanding their monitoring systems. Information on other common pollutants is even more limited and inconsistent throughout the world.

Unfortunately, even where they exist in sufficient quantity, measured PM data have limited comparability across countries. Measurements and techniques are not standardized globally, with different quality control programs, protocols and sampling frequencies, and may not use the same calibrations, or differ in the types of sampling locations (e.g. roadside, background, industrial) (Brauer et al 2012). Nevertheless, surface measurements are likely to be a key component to any assessment approach and these may be combined with other sources of information such as those estimated from satellite observations or simulated via chemical transport models, as described in more detail below.

While the global coverage of surface monitoring for PM10 and to a lesser degree PM2.5 is growing, most of the world still lags far behind the monitor density that is available in North America and Western Europe. Although such monitoring networks have been the basis of numerous epidemiologic studies and analysis of temporal and spatial trends in ambient concentrations additional approaches are needed to estimate exposures for disease burden or for epidemiologic studies in areas where surface monitoring networks are currently, and may well remain, non-existent or inadequate. Even in high income countries with dense monitoring networks, recent studies have indicated that satellite-based estimates and high-resolution air quality models can complement surface monitoring data and be used to fill in temporal and spatial gaps (Atkinson et al 2013, Lee et al, 2012, ).

The WHO data base on air pollution currently includes ground-level measurements of annual average particulate matter from approximately 1,600 cities worldwide. PM2.5 measurements are available from slightly more than 50% of cities, mostly in North American and Europe, with measurements of PM10 in the remainder. Data from Africa, South America and the eastern Mediterranean region are scarce. The primary data sources are official national/ subnational reports and national/ subnational web sites. In addition, measurements collated by Clean Air Asia, and AirBase – the European Air quality database are also included. In the absence of data from the above listed sources, data from (a) UN Agencies, (b) Development agencies and (c) articles from peer reviewed journals were used. In the most recent update to the Global Burden of Disease (2013) a similar approach was taken but additional measurements were gathered following direct appeals to air quality experts and national government representatives as well as NGOs. For example, recent measurements of PM2.5 in ~150 cities in China which were initiated in 2013 are also included as were measurements from rural monitoring networks such as EMEP (EU) and IMPROVE (U.S).

In the WHO database as well as that used for the Global Burden of Disease, in locations where only PM10 measurements are available, PM2.5 concentrations are estimated from local, regional or national PM2.5/PM10 ratios. While this provides a larger set of PM2.5 estimates this is also a source of error as these ratios may be influenced by local or even site-specific factors. Wherever the primary information allows it, the city averages are based on data from monitors located in urban residential, urban background, commercial or mixed locations, while roadside (traffic) and industrial location monitors are excluded, except when local conditions suggest that these are also representative of population exposure (e.g. industrial monitors in India). In some cases monitor type information is not available and it is therefore possible that roadside or industrial site measurements are included in calculation of city means. Information on monitoring methods (equipment and its calibration, data completeness and processing, quality assurance and control procedures) as well as monitoring network objectives and design are often missing, therefore limiting the comparability of data. Different equipment is used in different locations and when samples are collected on filters they are subject to different humidity equilibration and weighing procedures. Also the formats, levels of aggregation and timeliness differ among countries. In addition, quality assurance and quality control programs are not standardized internationally and may differ greatly between countries.

### *Dispersion and Chemical transport models*

Dispersion and chemical transport models are also used to estimate exposures for epidemiologic analyses and in impact assessment. At the local, regional and national levels, dispersion models can provide information on the temporal and spatial distribution as well as source-specific impacts for a number of common gaseous (NO2, SO2) and particle-phase pollutants. These models do not typically incorporate atmospheric chemistry and therefore are best suited to non-reactive pollutants and near-source applications.

In contrast, chemical transport models incorporate knowledge of atmospheric chemistry and aerosol dynamics, in addition to pollutant emission, dispersion and deposition, with meteorologic fields to link emissions of pollutants with their surface concentrations at various temporal (hours, days, years) and spatial scales (local, regional, global). Models are typically run at regional or global scales with the ability to estimate concentrations at relatively high spatial resolution. Some global models are currently run at a 0.5ºx0.5º (~55 x 55 km at the equator) resolution, and regional models are currently capable of resolution on the order of ~5-10 km. A particular strength of such models is their ability to estimate source-sectors contributions to concentrations, for example the contribution of road transport (Bhalla et al. 2014) or that from household solid fuel use to ambient PM2.5 concentrations (Smith et al. 2014) as discussed in more detail below. Furthermore, models are unique in their ability to estimate future concentrations, using a variety of emission scenarios that can be used to assess the impact of various policy options.

In the Global Burden of Disease 2010 and subsequently in the recent WHO air pollution burden of disease estimates (Brauer et al., 2012; WHO, 2014), the TM5 chemical transport model output was merged with satellite-based estimates and calibrated with PM data from surface monitoring. In this particular work the two-way nested TM5 model was run at a 1x1 degree resolution over four major world regions, fed with emissions from the GAINS emissions data base, as used in the Global Energy Assessment (2012). The output was consequently refined to a 0.1x0.1 degree resolution using spatial information on the location of the emissions. Increasingly, with improved computing capacity, global models will incorporate abilities to estimate concentrations at finer spatial resolution. Model development and enhanced spatial resolution will also require improvement in emissions inventories and in the meteorological model predictions which can still be subject to substantial errors (Dentener et al, 2010, Granier et al 2011, Zhao et al, 2011). Emission inventories suffer from errors of both activity data and emission factors, as well as spatial and temporal resolution of the emission data. Given these limitations, at present national-level estimates or long term averages are likely to be more accurate model applications than concentrations at a grid point or a specific time.

While Brauer et al. (2012), relied on one particular global chemical transport model, future efforts will likely utilize ensembles of model outputs, where best-practice has shown that, compared to measurements, model performances significantly improves. For example, the LRTAP Convention Task Force on Hemispheric Transport of Air Pollution (HTAP) will, in the next few years, focus on the consistent coupling of ensembles of global models with regional scale models. In addition, HTAP will develop future emissions scenarios for 2010 - 2030 and establish linearized emission-concentration response functions between source and receptor regions based on emission perturbation studies. These functions can be incorporated in reduced-form source-receptor models (eg. the TM5-FASST model) for more rapid analyses of pollutant emission scenarios, and in particular source-attribution studies, bypassing expensive full chemical transport model runs.

### *Satellite-based estimates*

Satellite remote sensing of ground level air quality has developed substantially over the last decade (Martin, 2008; Hoff and Christopher 2009). Satellite remote sensing of aerosol and nitrogen dioxide ($NO_2$) provides valuable information about ground level concentrations and has been applied in epidemiologic studies (Crouse et al. 2012; Anderson et al. 2012; Hystad et al. 2013).

Satellite retrievals of Aerosol Optical Depth (AOD) provide a column-integrated measure of light extinction due to the presence of aerosol. Satellite-based estimates of PM2.5 rely on these retrievals, relating AOD to PM2.5 using either an empirical, semi-empirical or physically-

derived relationship. Empirical relationships rely on statistical regression techniques between in situ measurements and retrieved AOD (e.g. Liu et al. 2009; Kloog et al. 2011). Semi-empirical relationships similarly draw on local measurements in a statistical modeling framework, but also incorporate some physically-based understanding of how these values relate (e.g. Schaap et al. 2009; Di Nicolantonio et al. 2009). Lastly, physically-derived relationships rely on the aerosol vertical distribution and optical properties, often simulated using a chemical transport model, to predict the AOD to PM2.5 relationship (e.g. van Donkelaar et al. 2010; Drury et al. 2010), including its temporal and spatial variation. For example, van Donkelaar et al. (2010) used GEOS-Chem CTM (http://geos-chem.org ) to demonstrate this approach to be globally effective for long-term mean satellite-derived PM2.5 estimates, with a population-weighted mean global uncertainty of 1 μg/m3 ± 25%. This approach was used to contribute to the WHO and Global Burden of Disease 2010 estimates, and directly in epidemiologic analyses. Estimation of long-term (1998-2012) trends and time series of $PM_{2.5}$ for various regions of the world have been developed.

MODIS instruments (Levy et al. 2007) on board NASA's Terra and Aqua platforms provide a near-daily snapshot of global AOD at approximately 10 km x 10 km resolution; a 3 km product is expected to be released for the MODIS data record in the near future (Remer et al., 2013). The MISR instrument (Kahn et al. 2010), on board of Terra, has reduced retrieval uncertainties compared to MODIS over some regions, but its more limited swath width requires between six and nine days for global coverage. Cloud and snow cover inhibit AOD retrieval from both instruments and can produce seasonal sampling effects that should be accounted for during compilation into long-term mean values. Several on-going projects aim at reduction of the existing uncertainties. One of these is the emerging global network to evaluate and enhance satellite-based estimates of $PM_{2.5}$ (Surface PARTiculate mAtter Network: SPARTAN), deploying $PM_{2.5}$ and $PM_{10}$ sampling stations together with AOD instrumentation in regions with little local surface monitoring of air pollution. Satellite retrievals of NO2 offer additional information on the spatial structure of combustion-related air pollutants (Cooper et al. 2012) at ~ 13 x 24 km resolution, with newly developed methods improving the spatial resolution of the $NO_2$ assessment to 1 km x 1 km grid in selected areas. New data analysis methods increase the accuracy of the estimates and their consistency with ground measurements. New instruments to be launched on board of new satellites will further increase the quality of the data.

### *Integration of data from various approaches*

Estimation of exposure to $PM_{2.5}$ conducted in the framework of the Global Burden of Disease 2010 provides an example of how various sources of information can be combined. Specifically, estimates from remote sensing and chemical transport model simulations at 0.1 x 0.1 degree resolution were averaged and then calibrated with available measurement data in a single global regression model. The intention of data integration from three different approaches was to borrow from the strengths of each individual estimation method. As a result of this data integration, the estimates provided full global coverage with consistent methods, reduced biases due to location or development status, high spatial resolution allowing for a better better link to population data and a spatially-varying estimate of uncertainty in exposure. Given the incorporation of chemical transport model simulations in the integrated estimates, sector-specific contributions to exposure and disease burden are also possible, as indicated in several recent examples (Bhalla et al. 2014; Smith et al 2014). The ongoing GBD collaboration, led by the Institute for Health Metrics and Evaluation, will be published in May 2014 with updated burden of disease estimates for 2013[7]. GBD 2013 will estimate exposure to $PM_{2.5}$ using updated remote

[7] http://www.healthmetricsandevaluation.org/gbd/2013

sensing data, new chemical transport model simulations using an internally consistent emissions inventory from 1990 - 2013 and an expanded data base of surface measurements.

While the above approach allowed data from the three sources to be utilized there was only limited ability to consider spatially-varying relationships between the different approaches and a relatively simple estimate of uncertainty. Advanced statistical techniques would provide a coherent framework for the integration of data from various sources and lead to a greater precision of the estimates preserving the uncertainty of the assessment. Recent advances in methodology for data fusion or melding in this way include Bayesian statistical downscaling models which allow for datasets to be combined which exhibit complex spatial-temporal misalignment. Within these models, differences between different data sources are treated as spatially and temporally dependent random effects, allowing pollution concentrations to be predicted at any time and location. This approach sits naturally within a Bayesian hierarchical framework, which acknowledges uncertainty at each stage of the modelling. This provides a coherent framework for combining the uncertainty that will arise from combining different data sources and will provide accurate estimates of the uncertainty that will be associated with predictions of air pollution at the required resolutions over space and time. There may be computational challenges in implementing some of the more idealized models for this purpose and simplifying assumptions may need to be made. Examination of the effects of such simplifications is essential in order to assess possible trade-offs between accuracy and practicality. Recent advances in computational methods, e.g. Integrated Nested Laplace Approximation (INLA), provide fast and efficient methods for Bayesian hierarchical modelling in space and time. As described below, there are growing examples of land use regression models, which have typically been developed for individual urban areas, being expanded to national or continental coverage by integrating land use predictors with estimated ambient concentrations from satellite-based estimates (Vienneau, 2013; Beckerman, 2013; Hystad, 2012; Hystad, 2011; Novotny 2011). These developments suggest the potential for improved spatial resolution (~100m - 1 km) of exposure estimates at global scales, given the growing availability of land use data for the entire globe.

## *Use of survey data and other approaches to refine assessment of exposure to ambient air pollution*

*Travel survey data*

Exposure assessment for health studies is typically based upon the residential address. However, people spend a sizeable amount of time away from the home, e.g. at work, school or in travel. Actual exposure to outdoor air pollution may therefore differ from residential concentrations. Studies have documented high exposures of a range of traffic-related air pollutants including fine and ultrafine particles, elemental carbon, VOCs while being in transit (Kaur et al., 2007; de Nazelle et al., 2011). Substantial concentration differences related to mode of transport and route have been reported (Kaur, 2007). In several countries travel surveys exist for large population samples that can be used to refine population exposure when combined with spatial maps of air pollution from either land use regression or dispersion models. Examples of this more dynamic exposure assessment have been published for the Netherlands and Belgium (Beckx, 2009; Dons, 2014). Time activity patterns varied significantly over the day as does the air pollution concentration, supporting the use of more dynamic exposure estimates (Beckx, 2009). Time activity patterns may differ across population groups, e.g. related to age, sex, employment status and socio-economic position, contributing to contrasts in exposure between population groups beyond ambient contrasts. These studies used origin destination models and actual travel survey data to generate trips. These data can be applied with more confidence in assessing population exposure than in epidemiological studies in which individual exposures need to be estimated.

*Use of home survey data*

As people spend a large fraction of their time indoors, taking infiltration of outdoor pollution to the indoor environment into account may improve exposure assessment. Infiltration factors differ by pollutant, home characteristics including air exchange rate. In large scale epidemiological studies, indoor measurements of infiltration factors are not feasible. Hystad and co-workers developed a model for the PM2.5 infiltration based on measurements in 84 North-American homes and publicly available predictor variables including meteorology and housing stock characteristics (Hystad, 2009). A model including season, temperature, low building value and heating with forced air predicted 54% of the variability in measured infiltration factors (Hystad, 2009). Low building value increased infiltration factors, increasing exposure contrasts across different socio-economic groups. A study in Toronto explained 38% of the variability in infiltration factors with information on air exchange rate, presence of central air conditioning (AC) and forced air heating (Clark, 2010). Without air exchange rate information (which is typically not available), explained variability was reduced to 26%, illustrating the difficulty in modelling infiltration (Clark, 2010). Infiltration factor models with higher explained variability (R2 60% for two-week average infiltration factors) were developed in the framework of the MESA-AIR study (Allen, 2012). The most important predictors differed by season: AC use and window opening in the warm versus outdoor temperature and forced air heat in the winter (Allen, 2012). The study differs from previous studies by exploiting use of AC (and window opening behaviour) which is less readily available than simple presence of AC.
For population exposure assessment, use of survey data needs further exploration in different settings. Linking the calculated exposures accounting for infiltration to health effects is also not straightforward, as most concentration response functions are expressed for outdoor concentrations. For scenario calculations, refinement may be useful.

*Smartphones and GPS*

Time activity patterns have been assessed with diaries, but these were difficult to complete for subjects. Global Positioning Systems (GPS) and smartphones now offer the possibility to assess time activity patterns continuously. A study in Barcelona illustrated the potential benefit of using smartphone data (de Nazelle, 2013). Subjects wore smartphones for a week. The location signal from the smartphone was overlaid with a detailed spatiotemporal air pollution map. The use of GPS or smartphones may improve travel surveys, offering the potential to improve population exposure assessment further. More work on the validity of location data is still needed.

*Personal monitoring*

Personal exposure monitoring has not been used extensively in epidemiological studies for direct exposure assessment of the often large number of subjects participating in studies. This is especially the case for studies of long-term exposure as it is challenging to characterize long-term average personal exposure. High costs of equipment and personnel and complexity of monitoring for the subjects have contributed to the limited application of personal exposure monitoring. With the promise of development of cheaper and smaller air pollution sensors, some of these limitations may be reduced in the future. However, currently no sensors are available that allow robust assessment of population exposure for health impact assessment.

## *Land use regression models*

Land use regression (LUR) modeling has been applied increasingly to model fine scale spatial variation of outdoor air pollution in the past decade (Jerrett, 2005; Hoek, 2008). Land-use

regression involves development of stochastic models based upon measured concentrations at typically 40-100 locations spread over the study area and predictor variables usually obtained through geographic information systems (GIS). The model is then applied to a large number of unsampled locations in the study area. LUR models have been mostly applied for exposure assessment in epidemiological studies, but can be used for characterizing population exposure for health impact assessment as well.

Application of the land-use regression approach for air pollution mapping was introduced in the SAVIAH (Small Area Variations In Air quality and Health) study (Briggs et al. 1997). After the successful pioneering work in SAVIAH, LUR methods have been increasingly used in epidemiological studies in the past decade. Developments in GIS have contributed to the popularity of LUR methods. Initially the approach was mainly adopted in Europe, but a large number of applications in North America have now been published. Although feasibility has been demonstrated there are limited examples to date of LUR models in developing country settings (eg. Saraswat et al. 2013), with available predictor data being an important limitation. LUR model methodology has been reviewed previously (Jerrett, 2005; Hoek, 2008). LUR studies may differ in their monitoring basis, predictor variable set, geographical and temporal scale, pollutant of interest and method of model identification.

Several studies have made use of air pollution monitoring data from routine networks, but most studies, have undertaken monitoring specifically for the purpose of model development as routine networks in most urban areas are not dense enough to enable meaningful modeling of small-scale variability of outdoor air pollution. A further advantage of purpose-designed monitoring is the control the investigators have over the type of sites (e.g. traffic, background) they wish to include in model development. Disadvantages of purpose-designed monitoring include the additional cost (discussed below) and the limited temporal coverage of the measurements. In the studies to date, most purpose-designed monitoring campaigns consisted of between one to four 7-14 days sampling campaigns, whereas routine monitoring is typically continuous, especially for the gaseous components. Earlier studies were often performed in a large urban area, sometimes including the surrounding smaller communities. Increasingly, LUR models have now been developed for entire countries, such as the Netherlands, the UK, the USA and Canada (Vienneau, 2010; Hart, 2009; Beckerman, 2013; Hystad, 2011; Hystad, 2012) while the APMOSPHERE project modeled concentrations on a 1*1 km scale for the EU-15 (Beelen, 2009). The national models are often based upon routine monitoring data, increasingly supplemented by satellite data (Vienneau, 2013; Beckerman, 2013; Hystad, 2012; Hystad, 2011; Novotny 2011). Especially for ultrafine particles and black carbon, mobile monitoring campaigns have been performed to develop LUR models (Abernethy, 2013; Larson, 2009; Rivera, 2012). Large numbers of sites can be measured with typically a short sample duration (hours) per site. Models based upon these mobile campaigns have shown moderate explained variances.

Significant predictor variables include various traffic representations, population density, land use, physical geography (e.g. altitude) and climate. Traffic predictors include traffic load (traffic intensity times road length) in specified buffers around the sampling point, road length of major roads in buffers (if comprehensive traffic intensity data is not available) and distance to major roads. Emission data have often not added predictive power in LUR models, likely because of the typically coarse spatial resolution (Rosenlund, 2007).

Land-use regression methods have generally been applied successfully to model annual average concentrations of NO2, NOx, PM2.5, Elemental Carbon (EC) or the soot content of PM2.5 and to a lesser extent VOCs in different settings, including especially European and North-American

cities. Of the major pollutants of current health concern, few models have been developed for ultrafine particles and ozone. The performance of the method in urban areas is typically better or equivalent to geo-statistical methods, such as kriging, and dispersion models. However solid comparisons between LUR models and dispersion models are scarce. A recent study suggested that components for which the main source is not motorized traffic (e.g. Ni, V, S or K content of PM) could be less reliably modeled (de Hoogh, 2013). The lower performance for these models was attributed to the difficulty to obtain GIS information for the main sources of these components. LUR models for wood smoke have also been hampered by the difficulty to obtain detailed data on residential wood burning (Larson, 2009).

Most studies use standard linear regression techniques to develop LUR models. Forward, backward or best-subsets automatic selection methods are often applied to develop a parsimonious model from a large set of predictor variables that maximizes the percentage explained variability (R2). Following the approach used in the SAVIAH study, a priori definition of a required sign of regression slopes for specific variables (e.g. positive for traffic intensity) is used by some investigators in order to increase the applicability of the model beyond the monitoring sites (Brauer et al. 2003; Eeftens, 2012). This approach is strongly supported by recent studies that documented that the model R2 is inflated because of overfitting, especially in the case of a small number of monitoring locations and a large number of potential predictors (Wang, 2012; Basagana, 2012). LUR models benefit from using a priori knowledge about the direction of effect and the shape of the relationship, e.g. by offering inverse distances to major roads instead of linear distances. Some studies of large geographical areas have used a structured approach in which different predictors were used for different spatial scales (Stedman, 1997; Beelen et al. 2007). Spatial variation was assumed to comprise a regional, urban and local component for which a different set of monitoring locations and predictor variables was used. A model was first developed for the regional and next for the urban and local scale. The advantage of this approach is that it incorporates more theoretical knowledge about processes governing spatial variation, hence increasing the likelihood that the developed model can be applied elsewhere. Furthermore, this approach reduces the likelihood of developing unrealistic models containing too many correlated predictor variables. Use of this multi-level approach is often limited by the availability of enough monitoring sites.

More automatic methods of model selection are currently used to develop LUR models as well. These include the Deletion Substition Algorithm (DSA) and the ADDRESS algorithm (Su, 2009). Few comparisons of LUR model performance of different algorithms have been made. In a study in Girona, Spain little difference was found in performance of the DSA and the supervised forward regression approach (Basagana, 2012). A study in the US used partial least squares to identify LUR models (Sampson, 2013).

Increasingly, spatiotemporal models have been developed that provide more detailed temporal resolution than the annual average. More temporal resolution is useful for birth cohort studies, that often characterize exposure as pregnancy trimester-average concentrations and thus require more flexible exposure assessment. Spatiotemporal models have also been used to perform daily time series studies relaxing the assumption made in classical time series studies that an entire population is exposed to the same daily concentration pattern. The temporal component is derived from a small number of continuous fixed monitoring sites or from daily satellite observations (e.g. NO2, AOD) (Gryparis, 2007;Hystad, 2012). In the NPACT study, a spatiotemporal model was developed to model concentrations in six US study areas of the MESA study (Vedal, 2013). Hybrid models have been used in which elements of land use regression, dispersion modeling and geo-statistical methods such as kriging have been applied (Mercer, 2011; Wilton, 2010).

### *Methods to estimate the contribution to ambient pollution from household air pollution contribution*

As described above, chemical transport models provide the ability to estimate source and source-sector contributions to ambient concentrations. The sector contributions can then be used to estimate the disease burden attributable to the sector as in examples for road transport (Bhalla et al. 2014) or household solid fuel use (Smith et al. 2014). In the latter example, given that both household air pollution and ambient air pollution were considered as risk factors for the global disease burden, the GBD2010 estimates included an assessment of the degree of overlap in exposures from these two risk factors. Specifically, household combustion of solid fuels leads to exposure of cooks and their families indoors, but when pollutants also disperse into the outdoor environment they also contribute to outdoor air pollution. In fact, in rural areas where household solid fuel use is common, household combustion can be a significant source of outdoor air pollution, given the strength of this source and the absence of other sources. For the GBD2010 estimation, two existing global models were used to calculate the proportion of ambient PM2.5 and subsequently disease burden attributable to household combustion of solid fuels. Specifically, the Fast Scenario Screening Tool for Global Air Quality and Instantaneous Radiative Forcing (TM5-FASST) was used to assess the contribution of household sources. This analysis involves running this reduced-form model while sequentially removing emissions from specific source sectors and then computing the difference estimated concentrations between these simulations and those in which all sources are included. Thus, all emissions are processed through the chemical transport model. In the context of household solid fuel use, as the TM5-FASST source sector includes all household combustion it was also important to separate household cooking emissions from those related to household space heating. For this, the emission inventory developed for the Greenhouse Gas and Air Pollution Interactions and Synergies (GAINS) model was used as it included the relative contributions of household cooking and heating to household combustion. Emission estimates of household (cooking) combustion of solid fuels as a percent of total ambient PM2.5 were then calculated for 170 countries.

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# Background paper 4: Updated exposure-response functions available for estimating mortality impacts

*Guiding question 3.b: "What dose-response, exposure-response, and concentration-response functions are available for estimating mortality impacts of concentration or emission changes?"*

*F. Forestiere, H. Kan, A. Cohen*

## Summary

Epidemiologic evidence currently provides the most reliable basis for air pollution risk assessment. This evidence is summarized in the form of exposure-response functions (ERF) that quantify the increase in the rates or risks of mortality related to exposure to different levels of ambient air pollution.

Two recent WHO documents from the REVIHAAP and HRAPIE projects have provided rationale and indications in order to perform health impact assessment of air pollution at European level. The present paper briefly reviews the exposure-response functions available on the relationship between both PM2.5 and NO2 and long term mortality and updates them on the basis of the recently published studies, including the results of the European ESCAPE project. New meta-analytical ERFs are provided for PM2.5 and long-term all-cause, cardiovascular, respiratory mortality and for lung cancer. The long-term impact of NO2 has been extensively discussed in REVIHAAP and HRAPIE and an update is provided based on recent publications. When estimating the impacts of both PM2.5 and NO2 some double counting may occur but the likely overlap seems to be only moderate. Emerging literature on the long-term effects of PM components is reviewed although it is premature to provide a convincing risk function.

In the absence of direct epidemiologic evidence on mortality risk from long-term exposure to PM2.5 in the world's most polluted regions, the GBD 2010 project developed integrated exposure -response functions (IER) that combined evidence from studies of ambient air pollution, second-hand smoke, household air pollution and active smoking to estimate risk for ambient air pollution over the entire global range of exposure. The IER provides the best approach currently available to estimate mortality attributable to PM2.5 over the entire global range of exposure to PM2.5, and was recently used by WHO to estimate the burden of disease in 2012 attributable to ambient air pollution in 2012. However, the IER depends on assumptions that require further testing.

Many public health and policy decisions require that the mortality attributable to ambient air pollution be considered in the context of mortality due to other major health risk factors. Comparative Risk Assessment (CRA) provides a way to provide comparable estimates for the various risk factors, but requires that consistent methods be used to estimate risks for each. Current estimates assume that air pollution-attributable mortality is independent of other risk factors and more research is needed to address this issue.

## *Introduction*

Causal inference regarding adverse effects of exposure to ambient air pollution draws on information from laboratory experiments in humans and non-human species and observational epidemiologic research, and there is broad expert consensus that long-term exposure to ambient

air pollution increases the risk of mortality from cardiovascular and respiratory disease and lung cancer. Risk assessment of ambient air pollution, though sometimes based on experimental evidence, depends on a large and growing epidemiologic literature, which, despite its limitations and uncertainties, currently provides the most extensive evidence and reliable basis for air pollution risk assessment. This evidence is summarized in the form of exposure-response functions (ERF) that quantify the increase in the rates or risks of mortality related to exposure to different levels of ambient air pollution.

The WHO Regional Office for Europe have recently coordinated two projects ("Review of evidence on health aspects of air pollution – REVIHAAP" and "Health risks of air pollution in Europe – HRAPIE") to provide the European Commission (EC) and its stakeholders with evidence-based advice on the adverse effects of air pollution. The resulting documents contain a review of evidence on adverse health effects of air pollutants, in particular, the health outcomes and exposure–response functions (ERFs) that could be used for risk assessment of long-term exposure on mortality (WHO, 2013a and b). After that reviews, the results of additional studies on air pollution and mortality have been published, including the findings of the large European ESCAPE project (Beelen et al, 2014). In addition, a IARC working group has reviewed the available evidence on exposure to PM and lung cancer (IARC in press) and an extensive review of the ERFs employed in the Global Burden of Disease (GBD) assessment (Lim et al, 2012) has been published (Burnett et al, 2014). The aim of this paper is to summarize the available evidence for PM2.5 and NO2 long-term exposure and mortality, provide updated ERFs, and discuss the strengths and limitations in their applications.

## *Pollutants, components, and sources*

Several studies have shown associations between long-term exposure to particulate matter air pollution and mortality (Hoek et al, 2013). The exposure has been characterized as the mass concentration of particles smaller than 10 μm (PM10) or 2.5 μm (PM2.5). Ambient PM represents a heterogeneous mixture of constituents from diverse sources, e.g. fossil fuel combustion and biomass burning, and there is still uncertainty as to which specific particle components are the most dangerous for health. Components for which associations with a range of health endpoints have been reported in epidemiological or toxicological studies include (transition) metals, elemental carbon, inorganic secondary aerosols (sulfate, nitrate), and organic components, but the evidence is not consistent (Kelly and Fussell, 2012). Wang et al (2014), within the recent European ESCAPE project, selected 8 elements for their study on cardiovascular mortality: Copper (Cu), iron (Fe), potassium (K), nickel (Ni), sulfur (S), silicon (Si), vanadium (V) and zinc (Zn)), reflecting major anthropogenic sources such as road traffic non tailpipe emissions including brake linings (Cu, Fe, Zn) and tyre wear (Zn), industrial (smelter) emissions (Fe, Zn), crustal materials (Si, K), fossil fuel combustion (Ni, V, S) and biomass burning (K). These elements were included because they reflected the major local particle sources.

Nitrogen dioxide (NO2) is a surrogate for vehicle emissions. Nitrogen oxides (NOx) emissions from vehicles are dominated by NO, which is converted to NO2. Ambient NO2 concentrations, in combination with indicators of traffic (e.g. distances to busy roads and traffic volume), are important surrogate for traffic emissions in urban areas. Several epidemiological studies, on both short and long term effects, have indicated associations between NO2 and mortality (WHO, 2013a). The important scientific question is whether NO2 is directly responsible for the health effects or is only an indicator of other pollutants, including particulates and specific constituents such as metals, polycyclic aromatic hydrocarbons and other organic matter. The REVIHAAP document concluded that although it is difficult "to judge the independent effects of NO2 in the long-term studies because, in those investigations, the correlations between concentrations of

NO2 and other pollutants are often high, so that NO2 might represent a mixture".. "the mechanistic evidence, particularly on respiratory effects, and the weight of evidence on short-term associations suggest a causal relationship".

## *Exposure–response functions (ERFs) for all-cause and cause-specific mortality*

*Effects of long-term PM2.5 exposure on all-cause and cause-specific mortality*

The USA Environmental Protection Agency (EPA), in the Integrated Science Assessment for Particulate Matters (US EPA 2009, 20012), integrated the scientific evidence from toxicological, controlled human exposure, and epidemiologic studies in combination with evidence from atmospheric chemistry and exposure assessment studies and developed causal determinations for different outcomes (e.g., respiratory effects, cardiovascular effects, mortality, etc.) in relation to short- or long-term exposure to various PM size fractions. The conclusion was that the studies are consistent with a causal association between long-term exposure to PM2.5 and mortality (i.e., all-cause and cardiovascular) within a specific range of long-term mean PM2.5 concentrations (13.2 – 32.0 μg/m3). Some studies provide additional evidence for respiratory mortality, including lung cancer.

The HRAPIE project provides recommendations of ERFs for input into the cost–benefit analysis of the selected policy options. According to the REVIHAAP project report (WHO, 2013a), there is sufficient evidence for the causality of effects for each of the ERFs recommended. They classified the pollutant–outcome pairs recommended for cost–benefit analysis into the Group A category (pollutant–outcome pairs for which enough data are available to enable reliable quantification of effects) or Group B category (pollutant–outcome pairs for which there is more uncertainty about the precision of the data used for quantification of effects).

The HRAPIE experts recommended estimation of the impact of long-term (annual average) exposure to PM2.5 on all-cause (natural) mortality in adult populations (age 30+ years) for cost–effectiveness analysis (Group A). A linear ERF, with an RR of 1.062 (95% CI = 1.040, 1.083) per 10 μg/m3, has been recommended. The recommended risk coefficient was based on a meta-analysis of all cohort studies published before January 2013 by Hoek et al (2013). Eleven different studies conducted in adult populations of North America and Europe contributed to estimation of this coefficient in this review. The review conducted by Hoek et al (2013) provided also meta-analyses for cardiovascular mortality with a stronger and statistically significant effect (RR 1.11, 95% CI = 1.05, 1.16 per 10 μg/m3, based on 11 studies). The effect of PM2.5 on respiratory mortality was weaker and with a large uncertainty (RR 1.029, 95% CI = 0.94, 1.126 per 10 μg/m3, based on six studies).

After the review by Hoek et al (2013), three additional cohort studies on PM and mortality, either all-cause or cause-specific, have been published. Jerrett et al (2013) have reported the results of the American Cancer Society study on 73,711 subjects living in California and followed from 1982 to 2000 with exposure assessment to PM2.5 performed using Land Use Regression model. Carey et al (2013) studied a national cohort from England of 835,607 patients recruited from general practice, followed in the period 2003-2007, with exposure assessment to PM2.5 obtained with a dispersion model. Finally, the results of the ESCAPE project have been published (Beelen et al, 2014) on 367,251 participants from 22 European cohorts during 1982-2008; Land Use Regression model has been applied for exposure assessment. The main question is whether the new evidence has an effect on the ERFs already available.

In order to address the question, we included these additional studies in the original list of studies from Hoek et al (2013) and performed a meta-analysis using the same methodology, namely using random effects methods of DerSimonian and Laird (1986). The $I^2$ statistic was calculated as a measure of the degree of heterogeneity across studies [Higgins et al, 2003]. We performed the meta-analysis for all causes, cardiovascular and respiratory mortality. In addition, we evaluated whether the effect was different according to the different areas of the world (USA, Canada, Europe) or according to the exposure assessment methodology employed (at the city level, at the area of residence, at the residential address). We used STATA version 11 (Stata Corp, College Station, Texas) for meta-analysis.

The results for all-cause mortality are presented in Table 1 and the in the forest plot (Figure 1). The inclusion of the three additional studies in the meta-analysis yield an overall RR of 1.066 (95% CI = 1.040, 1.093) per 10 μg/m3, based on 14 studies. As Table 1 illustrates, there is heterogeneity in the effect estimates (I-squared 61%) but this heterogeneity is not explained by the geographical area of the study or by the study design used for exposure assessment.

Similarly, the meta-analysis has been updated also for cardiovascular and respiratory mortality and the results are presented in Table 2-3 and Figures 2-3, respectively. The effect estimate for cardiovascular mortality is very similar (1.10, 95% CI = 1.05, 1.15, per 10 μg/m3, based on 14 studies) to the original one obtained by Hoek et al (2013). On the other hand, the inclusion of three additional studies for respiratory mortality increased the effect estimate from 1.03 (95% CI = 0.94, 1.126), based on 6 studies, to 1.10 (95% CI = 0.98, 1.24) per 10 μg/m3, based on nine studies. For both cardiovascular and respiratory mortality there is evidence of heterogeneity of the effects.

Although no specific investigation have assessed the long-term effects of PM2.5 on mortality in Asia, two recent studies from China have evaluated the effect of PM10 exposure and one study has estimated the effect of TSP exposure and provided estimates of effects of PM2.5 exposure based on conversion of TSP levels to PM2.5. These investigations are important because they are the only cohort studies that have estimated the effects on mortality from chronic disease of long-term exposure to high levels of particulate air pollutants. Cao et al. (2011) examined the association between TSP and mortality in 70,947 middle-aged men and women of the China National Hypertension Survey and its follow-up study, and reported that an increase of 10 $\mu g/m^3$ of TSP corresponded to 0.3% (95%CI, −0.1–0.6), 0.9% (95%CI, 0.3–1.5), and 0.3% (95%CI, −0.6–1.3) increase of total, cardiovascular and respiratory mortality, respectively. Zhang et al (2014) conducted a retrospective cohort of 39,054 subjects from four cities in northern China, with a follow-up for mortality from1998 to 2009. Information on concentrations of PM10 was collected from fixed monitors and the estimated exposure for the study participants was done at area level. For each 10 μg/m3 increase in PM10, the relative risk ratios (RRs) of all-cause mortality and cardiovascular mortality were 1.24 (95% CI, 1.22–1.27) and 1.23 (95% CI, 1.19–1.26), respectively. Zhou et al (2014) examined the association of particulate air pollution with mortality in a prospective cohort study of 71,431 Chinese men. Baseline data were obtained during 1990 and 1991 and the follow-up evaluation was completed in January, 2006. Annual average PM10 exposure between 1990 and 2005 were estimated using fixed-site monitoring data at community level. Each 10 mg/m3 PM10 was associated with a 1.6% (95%CI: 0.7%, 2.6%), 1.8% (95%CI: 0.8%, 2.9%) and 1.7% (95%CI: 0.3%, 3.2%) increased risk of total, cardiovascular and respiratory mortality, respectively.

In summary, the additional long-term studies on mortality published in the last year only slightly modify the already available ERFs, and the largest change is for respiratory mortality.

*Effects of long-term PM2.5 exposure on lung cancer mortality*

The International Agency for Research on Cancer (IARC) recently classified ambient air pollution in general, and PM specifically, as a Group 1 carcinogen (IARC, in press). The IARC Working Group reviewed all the epidemiologic studies, including several large, high-quality cohort studies. Most of these studies included estimates of quantitative levels of outdoor air pollutants and most could account for the potential confounding effects of important cancer risk factors.

Associations between increased risk of lung cancer and exposure to air pollution measured by several indicators, including concentrations of PM2.5, PM10, NO2 and indices of exposure to traffic, were consistently observed in cohort and case-control studies after adjustment for important potential confounders including tobacco smoking. Among the most important studies evaluated for the IARC Monograph were a pooled analysis of lung cancer and air pollution in Europe (Raaschou-Nielsen et al, 2013) and a nationwide cohort study of lung cancer in the United States (Krewski et al, 2009). The European ESCAPE study included 17 cohorts from 10 countries.

The Working Group concluded that the observed associations of lung cancer with indicators of air pollution were not explained by confounding. Increased risk of lung cancer with exposure to outdoor air pollution was seen in analyses restricted to non-smokers and the magnitude of association was not appreciably affected by statistical adjustment for tobacco smoking or other risk factors, including socioeconomic status.

Quantitative exposure data were most consistently available for PM2.5. A meta-analysis of the 18 most informative studies included in the evaluation estimated a meta-RR of 1.09 (95% CI 1.04-1.14) per 10 µg/m3 of PM2.5 (Hamra et al, 2014).

*Effects of long-term NO2 exposure on all-cause mortality*

The recommendation from the REVIHAAP project was to include in the cost–benefit analysis the impact of long-term (annual average) exposure to $NO_2$ on all-cause (natural) mortality as well as on cardiovascular mortality.

The HRAPIE experts recommended applying a linear ERF for all-cause (natural) mortality, corresponding to an RR of 1.055 (95% CI = 1.031, 1.08) per 10 µg/$m^3$ annual average $NO_2$. An ERF for cardiovascular mortality was not provided as this effect was already included in all-cause mortality. The recommended coefficient was based on the meta-analysis of all cohort studies published before January 2013 by Hoek et al. (2013). This considered 11 studies as they were conducted in adult populations of Europe and North America with exposure assessment at the level of the address of residence of the cohort members. The additional inclusion in the meta-analysis of the large American Cancer Society Study, based on exposure assessment at the city level and not at the residential address, was associated with only a small decreased overall effect (1.047, 95% CI = 1.024, 1.071).

A comparative meta-analysis on the role of long-term exposure to NO2 and to PM2.5 on mortality has been published (Faustini et al, 2014). The authors systematically examined the studies up to January 2013 that investigated the long-term effects on mortality of both outdoor NO2 and PM in the same population. A total of 12 studies were considered and the pooled estimate of NO2 effects on natural/total mortality was 1.04 (95%CI = 1.02-1.06) per 10 µg NO2/m3 and the corresponding effect of PM2.5 in the same populations was 1.05 (95%CI = 1.01-1.09) per 10 µg/m3. The authors noted that variability of NO2 levels was greater than for

PM2.5 (e.g. the median interquartile range, IQR, was 14.1 μg/m3 for NO2 and 5.4 μg/m3 for PM2.5 across the natural/total mortality studies) and when the results were expressed using interquartile ranges as the exposure metric (only 10 studies were considered where the IQRs were available or could be derived), greater effects of NO2 (6%) than of PM2.5 (3%) was found on total mortality. The authors concluded that the magnitude of the long-term effects of nitrogen dioxide on mortality is at least as important as that of PM2.5 and the results hold when using either 10 μg/m3 or IQR as the metric of choice.

The three most recent cohort studies, not considered in the original reviews from Hoek et al (2013) and Faustini (2014), reported relative risks (per 10 ug/m3 NO2) lower than those previously reported in the meta-analytical estimates, namely 1.031 (1.008, 1.056) for the California study (Jerrett et al, 2013), 1.02 (1.00–1.05) for the English cohort (Carey et al, 2013), and 1.01 (0.99-1.04) for the ESCAPE study.

*PM2.5 and NO2, double counting of the impacts*

It is clear that health impact assessments relying only on PM2.5, and not considering NO2, would be neglecting an important source of the adverse effects of pollution mixture. However, double counting of the impacts is an issue. Therefore, HRAPIE recommended that the impact calculation for NO2 should be conducted as Group B* in order to avoid potential overlap and double counting of mortality effects from PM2.5, which is included in Group A* analysis.

In most of the studies investigating the effects of NO2 and of PM2.5, a moderate to high correlation of the exposure levels of the two pollutants has been found. In the Faustini et al (2014) paper, the correlation between NO2 and PM2.5 was found in 9 studies with values ranging from 0.3 (Japan and California) to 0.88 (Norway). Similarly, in the ESCAPE cohorts (Beelen et al, 2014) the correlation coefficients between NO2 and PM2.5 ranged from 0.40 to 0.85. Therefore, the recommendation from the REVIHAAP report has been to use a ERF based on effect estimates for NO2 mutually adjusted for PM metrics. However, when the results of the available long-term studies were reviewed in the HRAPIE report, six investigations performed a multi-pollutant analysis and the results were generally similar between single and multi-pollutant models, with only small changes in the effect estimates in the multi-pollutant models (the decrease was in the range 0–33%). Given the results of the multi-pollutant models, therefore, the recommendation has been that the ERF is better based on the unadjusted meta-analysis, with the acknowledgement that the resulting estimates of the effects of NO2 may represent an overestimate in the likely range 0–33%. This recommendation hold considering the most recent ESCAPE results since the effect estimate for NO2 in this study did not change from unadjusted analysis (1.01, 95% 0.99-1.04) to that adjusted for PM2.5 (1.01, 95% 0.97-1.05) although the uncertainty of the estimate was larger.

## *Emerging literature on the effects of PM precursors and components*

Epidemiological studies on short-term effects have assessed the mortality effects related to exposure to elemental PM components with results that varied considerably between the investigations (Kelly and Fussell 2012). Only few studies have evaluated the mortality risks related to long-term exposure to particle components.

Sulfate has received the most attention in epidemiological studies and some cohort studies suggested an association between long-term exposure to sulfate and mortality. An association between sulfate and mortality was originally reported in the Six Cities study (Dockery et al. 1993) and the adjusted HR comparing the most and least polluted city was 1.26, resulting in a HR of 1.03 per 1 μg/m3. Within the American Cancer Society study, the adjusted HR for natural

mortality was 1.01 per 1 µg/m3 (Pope et al. 2002). In the recent National Particle Component Toxicity (NPACT) project, Lippmann et al (2013) reported an association between sulfur exposure and all-cause mortality using ACS data. Within the same NPACT initiative, the data-set of the Women's Health Initiative–Observational Study (WHI-OS) cohort was evaluated to study the association with cardiovascular mortality and cardiovascular events (Vedal et al, 2013). No statistically significant association was found between sulphur and all cardiovascular deaths (HR 1.01 (95%: 0.92, 1.12) per 0.25 µg/m3), but the association with cardiovascular events was statistically significant (HR 1.09 (95% 1.05, 1.14) per 0.25 µg/m3).

A cohort study among California Teachers found no statistically significant association between long-term exposures to PM2.5 and several of its constituents, including elemental carbon, organic carbon (OC), sulfates, nitrates, iron, potassium, silicon, and zinc and all-cause mortality, although statistically significant associations were found with cardiovascular deaths (Ostro et al, 2011).

A recent study within ESCAPE (Wang et al (2014) did not find statistically significant associations between any of the eight selected elemental constituents of PM10 and PM2.5 and overall cardiovascular mortality in the 19 European cohort studies. Elevated risks, but not statistically significant, were found for silicon and sulphur in PM2.5 and cardiovascular mortality.

In its comprehensive review, EPA (US EPA, 2012) has concluded that "Overall, new studies support the conclusions that many PM components can be linked with differing health effects and the evidence is not yet sufficient to allow differentiation of those components or sources that are more closely related to specific health outcomes". Therefore, based on the overall findings, it is premature to derive a specific ERF for any PM component.

### *Integrated Exposure-Response (IER) Function for Particulate Matter*

Among various pollutants in the ambient mixture, fine particulate matter (or $PM_{2.5}$) shows the most consistent association with adverse health outcomes. Quantitative knowledge about the relationship between exposure to $PM_{2.5}$ and health outcomes is crucial to assessing the health impact of air pollution and its implications in relevant policy-making. However, most ambient $PM_{2.5}$ cohort studies were conducted in the United States (US) and Western Europe (Beelen et al, 2014; Dockery et al, 1993; Pope et al, 2002; Miller et al, 2007; Krewski et al, 2009), where the annual $PM_{2.5}$ concentrations were much lower than in developing countries (Brauer et al,. 2006). Further, there is indication that the relationship between air pollutants' concentration and health risk is likely to be non-linear and tend to become flat at the higher end (Pope et al, 2009; Pope et al, 2011). Therefore, it is often questioned whether the cohort findings from low air pollution exposure settings in developed countries are applicable to other parts of the world, where both characteristics of ambient $PM_{2.5}$ (e.g. levels, components, sources) and socio-demographic status of local residents may be different from those in developed countries.

To inform the risk estimates across the full range of $PM_{2.5}$ concentrations worldwide, Burnett and coworkers followed the approach used by Pope and colleagues (Pope et al, 2009; Pope et al, 2011) and integrated available epidemiologic evidence on the hazardous effects of $PM_{2.5}$ from diverse sources, including ambient air pollution (AAP), household air pollution (HAP), second-hand smoke (SHS), and active smoking (AS) (Burnett et al 2014). The approach was termed an integrated exposure-response (IER) model because its development requires the integration of exposures to $PM_{2.5}$ from different sources (i.e., AAP, HAP, SHS, and AS). IER model was adopted in the Global Burden of Disease (GBD) 2010 project (Lim et al, 2012) for AAP, because the ambient $PM_{2.5}$ levels considered in the GBD 2010 project expanded far beyond the

concentrations observed in available $PM_{2.5}$ cohort studies. In addition to AAP, IER model was also used to estimate the disease burden due to HAP exposure (Lim et al. 2012; Smith et al 2014).

Detailed methods for estimating the IER curves have been published (Burnett et al 2014). Briefly, Burnett et al. compiled study-level estimates of the relative risk (RR) associated with any or all of AAP, HAP, SHS and AS for the following causes: ischemic heart disease (IHD), stroke, lung cancer, chronic obstructive pulmonary disease (COPD) and acute lower respiratory infection (ALRI) in children. Equivalent ambient $PM_{2.5}$ concentrations were assigned to SHS and AS studies by the methods used by Pope et al (Pope et al, 2009; Pope et al, 2011). Equivalent $PM_{2.5}$ exposure from HAP was estimated for study subjects using coal or biomass for cooking and/or heating.

The IER model was based on the following assumptions:

- $PM_{2.5}$ exposure from diverse sources is associated with increased RR of mortality from IHD, stroke, COPD, and LC and with increased incidence of ALRI;
- The health effects of $PM_{2.5}$ are only related with inhaled mass (exposure), but not with $PM_{2.5}$ composition and sources;
- The relationship between $PM_{2.5}$ exposure and excess mortality is not necessarily restricted to be linear;
- The RR of mortality from exposure to AAP, SHS, HAP, and AS does not depend on the temporal nature of the $PM_{2.5}$ exposure;
- No interaction exists among the various $PM_{2.5}$ exposure types for any cause of mortality.

Burnett et al. evaluated a range of non-linear functions with up to three parameters for fitting the IER relationship, and postulated a flexible RR function of the following form:

$$\textit{for } z < z_{cf},\ RR_{IER}(z) = 1$$
$$\textit{for } z \geq z_{cf},\ RR_{IER}(z) = 1 + \alpha \{1 - exp[-\gamma (z - z_{cf})^{\delta}]\} \quad \text{(Burnett et al, 2014)}$$

This IER function is characterized with the $PM_{2.5}$ counterfactual concentration ($z_{cf}$) below which no association is assumed. In formulating the RR model, Burnett et al. relied on information on the RR of mortality at specified $PM_{2.5}$ exposure concentrations from the available literature. The unknown parameters ($\alpha$, $\gamma$, $\delta$) are estimated by nonlinear regression methods. The RR estimates were weighted by the inverse of the variance estimate of the logarithm of the RR in order to reflect the uncertainties in each estimate.

Summary results of IER model are presented in Figures 4 and 5.

Overall, the IER model provided the best fit among all the health outcomes examined, compared to the seven alternative models (Burnett et al, 2014). The IER curves reflect a steeper increase in risk at low exposure levels than that for higher exposures observed in some epidemiological studies. Also, the estimates of risk based on this approach compare well with the results of two recent air pollution cohort studies conducted in China (Cao et al, 2011; Zhou et al. 2014; Burnett et al, 2014), with estimated $PM_{2.5}$ (converted from total suspended particles or PM10) concentrations ranging from 38–166 $\mu g/m^3$. [8]

[8] The cohort study of Zhang et al. (2014) reported larger relative risks than either Cao et al. or Zhou et al. This may be due to an error in the analysis of the Zhang et al. study in which exposure in surviving cohort members was systematically under-estimated leading to spuriously elevated estimates of the relative risk.

The IER approach has advantages and limitations. This approach avoids estimation of unrealistically high risks in populations exposed to very high ambient $PM_{2.5}$ levels (e.g. in east Asia). Therefore, the use of an IER curve has allowed an estimate of a continuous risk function across the full range of PM2.5 levels all over the world. The resultant large attributable disease burden reported in the GBD 2010 project represents a major shift in the understanding of the disease burden arising from $PM_{2.5}$ and has broad policy implications. A major limitation of the IER approach is that it depends on several underlying assumptions mentioned above, about which expert opinion is not in complete agreement.

### *Mortality impacts from air pollution in a Comparative Risk Assessment context*

Efforts to reduce the burden of non-communicable disease, which is growing worldwide, must address a range of risk factors in addition to ambient air pollution, including tobacco smoking, diet, high blood pressure, and household air pollution from burning of solid fuels (Lim et al. 2012). And despite reductions in mortality from acute lower respiratory infections (ALRI) in young children over the past 20 years, efforts to reduce the substantial burden of disease due to ALRI in low- and middle-income countries will require reductions in household as well as ambient air pollution (Lozano et al. 2012; Lim et al. 2012; Smith et al. 2014). However, risk assessments of ambient air pollution are, for the most part, performed without explicit regard for other major potentially modifiable risk factors, even though ultimately their results are interpreted in this context by policy makers and the public.

Recognizing the need for objective, evidence-based ranking of major potentially modifiable risk factors with respect to their attributable burdens of disease, the Global Burden of Disease (GBD) project, initiated in the early 1990s by WHO and the World Bank, pioneered the development of a comparative risk assessment (CRA) approach which applied a consistent methods to estimate the attributable burden of disease for a variety of risk factors (WHO 2004). The most current update of the GBD project provides estimates of the burden of disease attributable to 67 risk factors, including ambient and household air pollution, in 1990 and 2010 on global, regional, and national levels and their respective uncertainties (Figure 6; Lim et al 2012).

Estimating the burden of disease attributable to ambient air pollution in a CRA context requires that for certain key aspects of the analysis methods are employed that are conceptually and methodologically consistent with those applied to other risk factors so that the estimates of attributable burden can be ultimately be compared. For example, in the recent GBD 2010 project a consistent approach was applied to determine the counterfactual, or Theoretical Minimum Risk Exposure Distribution (TMRED) level for major risk factors. For risk factors such as air pollution and high blood pressure where zero exposure is not possible, the TMRED was based on two considerations: the availability of convincing (i.e., statistically robust) evidence from epidemiological studies that support a continuous reduction in risk of disease to the chosen distribution; and a distribution that is theoretically possible at the population level (Lim et al. 2012, p. 2236-2237). A common approach was also applied to estimate age-specific exposure-response functions for cardiovascular diseases, IHD and stroke, for major cardiovascular risk factors including ambient air pollution (Lim et al. 2012; Burnett et al 2014).

In GBD 2010 the IER, discussed above, used a common $PM_{2.5}$ exposure metric for ambient air pollution, second-hand smoke, household air pollution and active smoking, to estimate the burden of disease attributable to ambient air pollution. This allowed estimates to be made for ambient air pollution over the entire global range of exposure, but it also provided a level of internal consistency with regard to the estimates for each of the four combustion-related risk factors, and provided the basis for estimates of the burden of cardiovascular mortality

attributable to household air pollution for which there were no actual epidemiologic studies (Lim et al 2012; Smith et al. 2014)

Epidemiologists understand that the mortality and disease burden attributable to individual risk factors add to more than the total number of events actually observed because the risk factors interact, but this remains a source of considerable confusion for non-experts. The comparative risk assessment provided by GBD 2010 assumes that the burden of disease attributable to ambient air pollution is independent of other major risk factors, such as tobacco smoking and household air pollution, and other assessments that provide estimates of combined burdens do so under the assumption that the risk factors act independently (Ezzati et al. 2004; WHO 2014). Air pollution epidemiology has yet to explore interactions of air pollution exposure with other risk factors on the additive scale that is most relevant to burden estimation and other public health applications (Rothman, Greenland and Lash 2008). Such research is needed to allow the assumptions of risk factor independence to be confirmed or modified (Turner et al. 2014. AJE In Press).

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**Table 1.** Long-term effects of PM2.5 on natural mortality. Meta-analysis

| Studies | n. studies | HR | 95% CI | | $I^2$ | p-het |
|---|---|---|---|---|---|---|
| **All** | 14 | 1.07 | 1.04 | 1.09 | 61 | 0.002 |
| US | 9 | 1.07 | 1.02 | 1.12 | 65 | 0.003 |
| Canada | 1 | 1.10 | 1.05 | 1.15 | - | - |
| Europe | 4 | 1.06 | 1.02 | 1.11 | 33 | 0.216 |
| Between city | 2 | 1.09 | 1.02 | 1.17 | 70 | 0.068 |
| Area-level | 3 | 1.08 | 1.02 | 1.15 | 79 | 0.009 |
| Address | 9 | 1.06 | 1.02 | 1.10 | 50 | 0.042 |

**Figure 1.** Long-term effects of PM2.5 on natural mortality. Forest plot, 14 studies

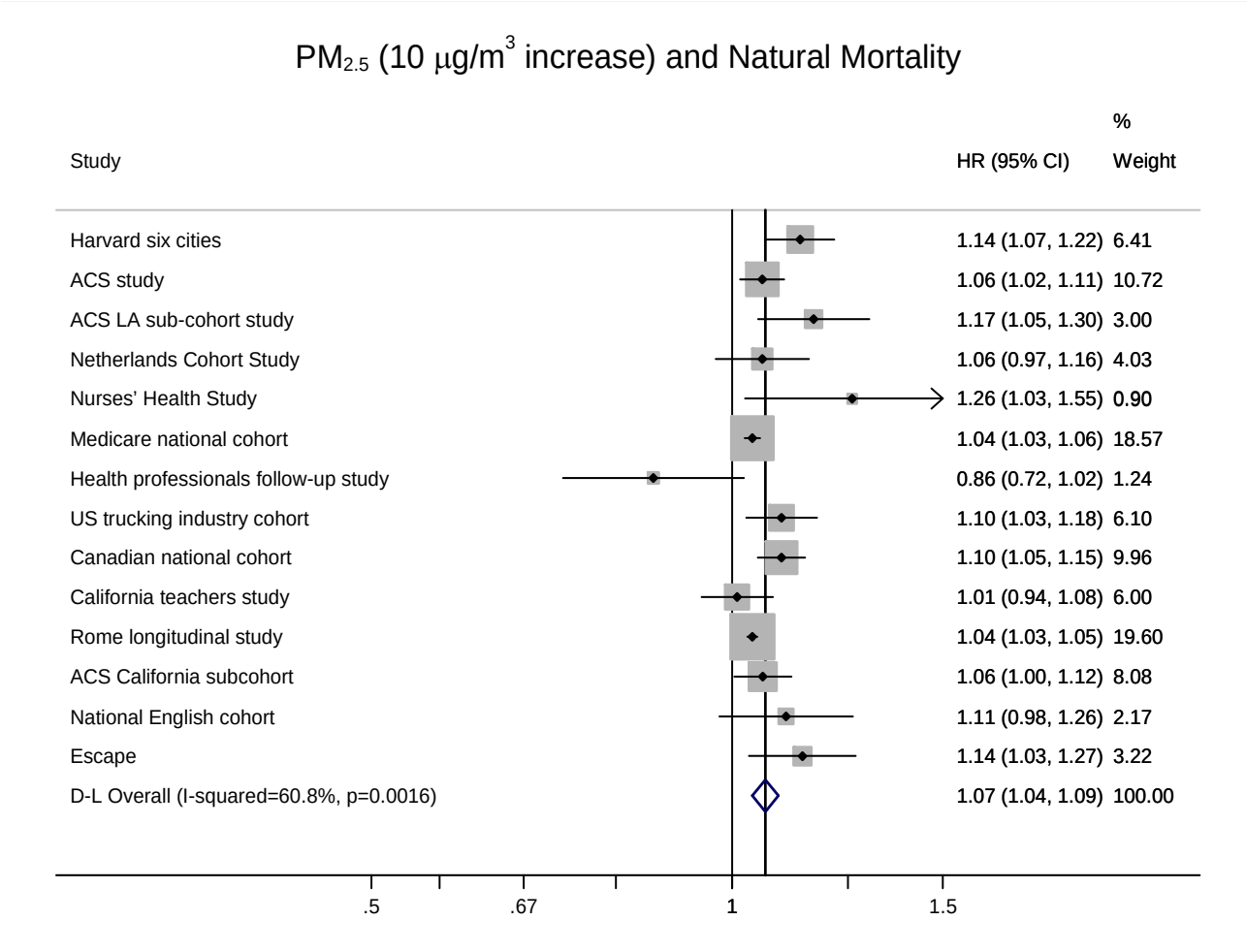


**Table 2.** Long-term effects of PM2.5 on cardiovascular mortality. Meta-analysis

| Studies | N | HR | 95% CI | | I2 | p-het |
|---|---|---|---|---|---|---|
| **All** | 14 | 1.10 | 1.05 | 1.15 | 54 | 0.009 |
| US | 8 | 1.14 | 1.05 | 1.23 | 56 | 0.026 |
| Canada | 2 | 1.14 | 1.06 | 1.22 | 0 | 0.533 |
| Europe | 4 | 1.06 | 1.04 | 1.08 | 0 | 0.718 |
| Between city | 2 | 1.16 | 1.01 | 1.34 | 83 | 0.017 |
| Area-level | 3 | 1.29 | 1.03 | 1.63 | 67 | 0.048 |
| Address | 9 | 1.06 | 1.04 | 1.08 | 0 | 0.916 |

**Figure 2.** Long-term effects of PM2.5 on cardiovascular mortality. Forest plot, 14 studies

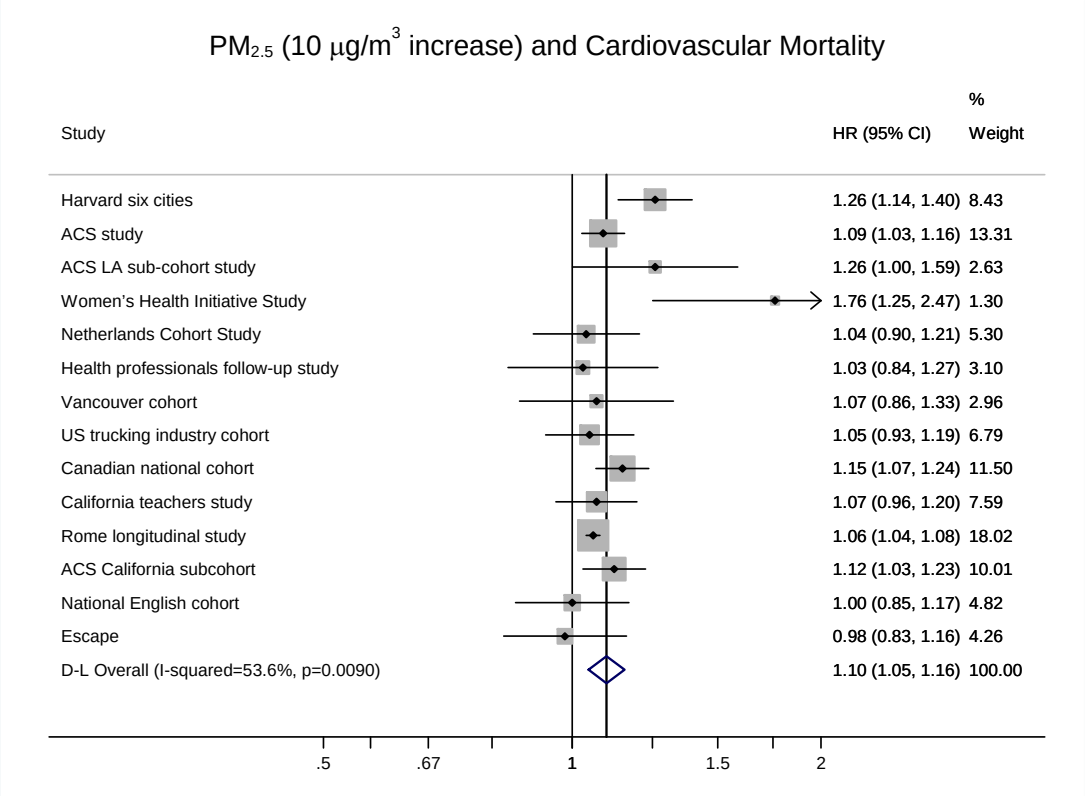
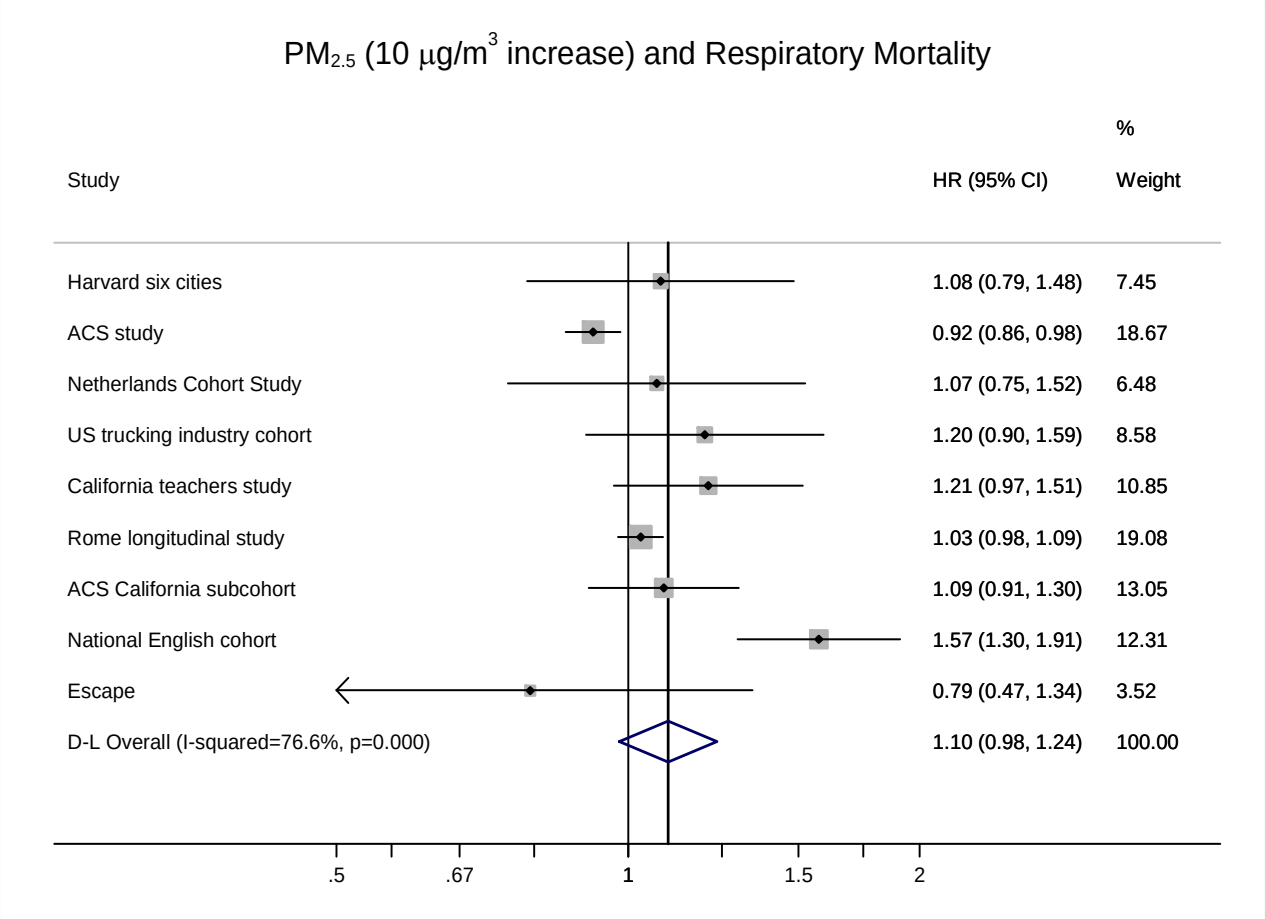


**Table 3.** Long-term effects of PM2.5 on respiratory mortality. Meta-analysis

| Studies | n. studies | HR | 95% CI | | $I^2$ | p-het |
|---|---|---|---|---|---|---|
| **All** | 9 | 1.10 | 0.98 | 1.24 | 77 | 0.000 |
| US | 5 | 1.06 | 0.93 | 1.22 | 62 | 0.033 |
| Canada | 0 | - | - | - | - | - |
| Europe | 4 | 1.13 | 0.86 | 1.49 | 84 | 0.000 |
| Between city | 2 | 0.93 | 0.87 | 0.99 | 0 | 0.332 |
| Area-level | 0 | - | - | - | - | - |
| Address | 7 | 1.15 | 1.00 | 1.33 | 70 | 0.002 |

**Figure 3.** Long-term effects of PM2.5 on respiratory mortality. Forest plot, 9 studies



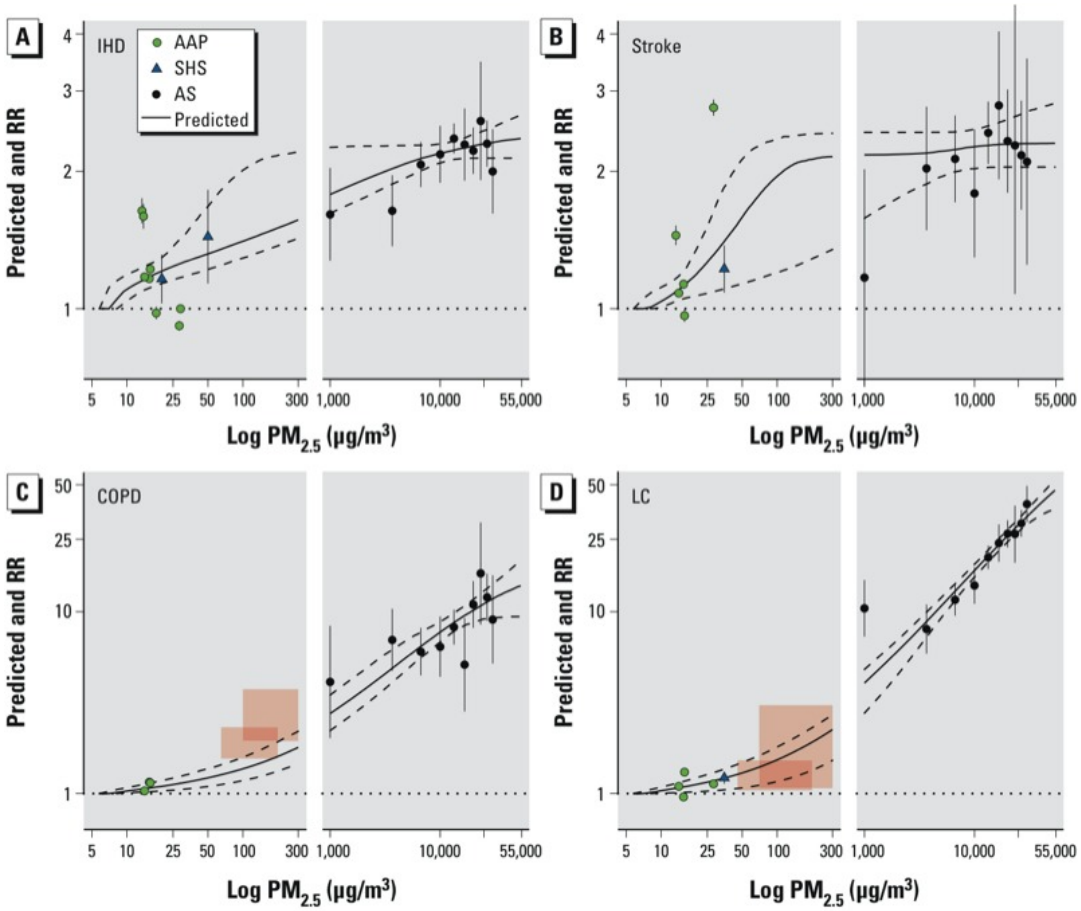



**Figure 4**: Predicted values of IER model (solid line) and 95% CIs (dashed line) and type-specific RRs (points) and 95% CIs (error bars) for IHD (A), stroke (B), COPD (C), and LC (D) mortality. Shaded boxes for COPD and LC mortality represent uncertainty (height) and exposure contrast (width) of RR HAP estimates for males (smaller boxes) and females (larger boxes) separately. (Burnett et al. 2014; reproduced from *Environmental Health Perspectives*, http://ehp.niehs.nih.gov/1307049/)

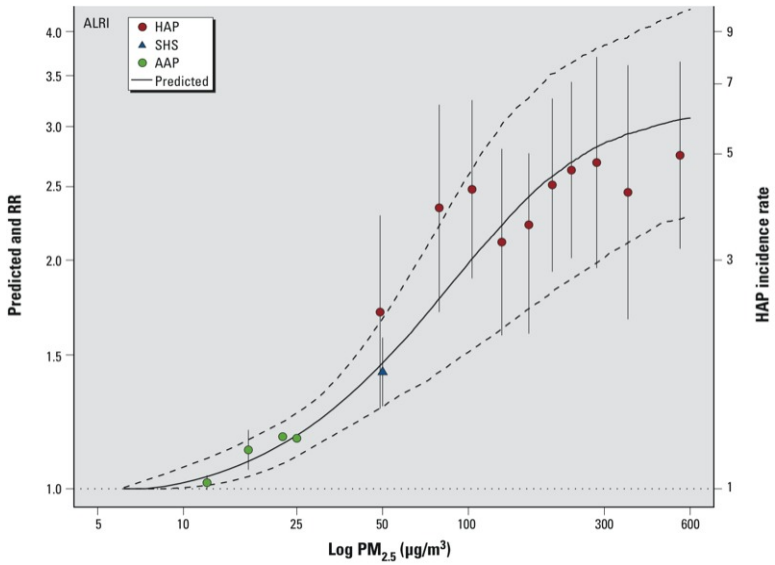



**Figure 5**. Predicted values of IER model (solid line) and 95% CIs (dashed line) and type-specific RRs (points) and 95% CIs (error bars) for ALRI in infants (Burnett et al. 2014; reproduced from *Environmental Health Perspectives*, http://ehp.niehs.nih.gov/1307049/)

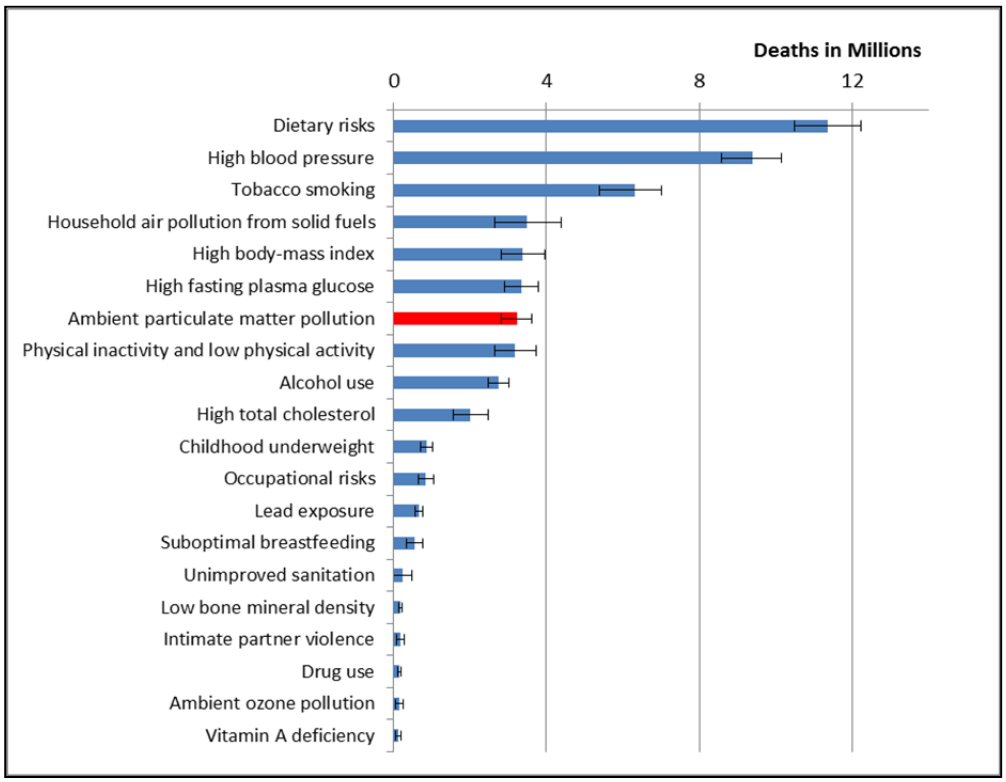



**Figure 6** Global deaths in 2010 (95% uncertainty intervals) attributable to the top 20 risk factors (http://ghdx.healthmetricsandevaluation.org/global-burden-disease-study-2010-gbd-2010-data-downloads)

# Background paper 5: Datasets for baseline and population mortality rate

*Guiding question 3.c: "What population and baseline mortality rate datasets are available for assessing the health risks of present-day concentrations and future changes in emissions?"*

*Gretchen Stevens and Heather Adhair-Rohani (WHO)*

Underlying population and disease burden data whether historical or projections is an integral component of any health risk assessment. The sources, methods and applications of different health and population datasets are important to consider when selecting such input data. Background information on some key population and disease burden datasets is found below.

## *Population data*

Population data for 231 countries and areas, both historical (i.e. 1950 and after) and projections, are available from the UN population division. The latest update was published in the World Population Prospects report in the summer of 2013 ("World Population Prospects 2012 revision"). These data are available by age, sex, and country, for 5-year periods 1950-2100. Aggregated data is available for 4 development groups, 6 major areas and 21 geographical areas. Revisions are made on the biennial basis and the next update is anticipated in 2015.

Further information is available here: http://esa.un.org/unpd/wpp/

## *Comparable mortality estimates*

Multi-country studies should use methods and datasets that are comparable across countries. Comprehensive and comparable mortality estimates use similar methods for all countries and time periods, and include estimates for all disease and injury causes of death. Two sets of comprehensive and comparable mortality estimates of are currently available, the WHO Global Health Estimates (2013 revision) and the Global Burden of Disease 2010 published by the Institute for Health Metrics and Evaluation (IHME) (NB 2013 update expected in May, 2014). Whenever possible, WHO estimates of environmental burden of disease should be consistent with the WHO Global Health Estimates.

### *Global Burden of Disease (GBD) 2010 / GBD 2013*

The Institute for Health Metrics and Evaluation (IHME)'s GBD 2010 estimates of mortality by cause of death (for 155 causes) for 187 countries, disaggregated by country age, and sex, and year (1990, 2005 and 2010) are available on IHME's webpage (http://ghdx.healthmetricsandevaluation.org/). Data for more specific causes of death are available online at the regional level and upon request from IHME at the country-level. GBD 2010 estimates include systematic analysis of uncertainty. Release of GBD 2013 is anticipated in May, 2014.

### *Global Health Estimates (GHE) 2013 revision*

WHO's Global Health Estimates (GHE) synthesize WHO and UN estimates of mortality and causes of death to generate comprehensive estimates by region of mortality by cause, age, sex, and year. Currently, WHO's Global Health Estimates are available at the region level for the years 2000- 2011. These estimates are based on analysis of the most recently available national

information on levels of mortality and cause distribution. These estimates are derived using standardized categories, definitions and methods to ensure comparability between countries.

Global Health Estimates (including estimates for 194 countries) for the period 2000-2012 will be released on WHO's website in May, 2014:
http://www.who.int/healthinfo/global_burden_disease/en/

The next update of the GHE is anticipated in late 2015- early 2016.

### *Future Projections*

WHO has projected mortality and causes of death to 2030, available online here:
http://www.who.int/healthinfo/global_burden_disease/projections/en/

Projections are based on methods developed for GBD 2002, published in PLoS Medicine in 2006: http://www.plosmedicine.org/article/info%3Adoi%2F10.1371%2Fjournal.pmed.0030442

Resources permitting, WHO aims to update and improve methods for projections in the next 1-2 years.

*Shared Socio-economic Pathways (SSP) Database*

The IPCC's Fifth Assessment Report (AR5) presents scenarios of greenhouse gas and aerosol emissions (i.e. Representative Concentrations Pathways (RCP)) to support climate change operational research. The Shared Socio-Economic Pathways (SSP) describe plausible alternative trends in social and economic development to support quantitative research on climate change impacts, adaptation, and mitigation. The SSP database includes projections for population and economic growth by region (i.e. World Five, 32 macro-level regions)and/or country. Specific parameters included in the database are population (by age, sex and education), urbanization and gross domestic product (GDP).

Further information on the scenario process for AR5, see:
http://sedac.ipcc-data.org/ddc/ar5_scenario_process/index.html

To access the SSP database, see:
https://secure.iiasa.ac.at/web-apps/ene/SspDb/dsd?Action=htmlpage&page=about#

# Background paper 6: Morbidity impacts

*Guiding question 3.d: "What is the state of the science for including morbidity impacts in air pollution health risk assessment at various scales?"*

*Laura Perez*

## *Introduction*

A main objective of Air Pollution Health Risk Assessment (APHRA) is to help optimize policies with respect to their health benefits and costs. All monetary valuations of air pollution impact assessment show that the impact of morbidity outcomes is small relative to mortality. However the quantification of morbidity estimates at local, national and international level remains very important information for policy-making and for public health. Within the European context, methodological approaches have recently been reviewed and a set of pollutants, morbidity outcomes, and related concentration-response functions to be used in morbidity APHRA, been proposed. A number of principles, however, need to be further refined to overcome limitations of current methodology and to respond policy needs at different scales.

This chapter summarizes the state of the science for including morbidity impacts in air pollution health risk assessment (APHRA). It summarizes what pollutants, sources and exposure times are currently considered or recommended in morbidity APHRA, limitations with current approaches, and what opportunities for new methodological developments exist. This chapter is not an exhaustive review of the literature but builds on information and recommendations proposed in the recent Wold Health Organization review projects "Review of evidence on health aspects of air pollution" (REVIHAAP) and "Recommendations for concentration–response functions for cost–benefit analysis of particulate matter, ozone and nitrogen dioxide" (HRAPIE) (now on referred as "WHO review" in the text) as well as other recent reviews (CFHA 2014; WHO 2013a, b).

## *Morbidity impacts and policy*

A main objective of APHRA is to help optimize policies with respect to health costs and benefits. Evaluating morbidity impacts of air pollution is necessary to obtain more precise estimates of the true costs of air pollution, help to better evaluate effectiveness of policy measures, help at identifying and reducing sources of inequality due to air pollution exposure, and improve communication with stakeholders.

### *Improving the monetary evaluation of morbidity impacts*

Recent literature has shown that the morbidity impacts of air pollution may have been underestimated altogether in the first place. Current evaluation do not account for air pollution contributing to the development of chronic disease for example. Premature mortality due to long-term exposure to air pollution is related to chronic pre-clinical as well as clinically relevant conditions relevant in the disease processes that are unaccounted in current assessments. Thus there is currently an unfair comparison between the cost of morbidity and mortality impacts of air pollution at local, national or international level.

Monetary valuation based on valuing years of life lost hides the tangible morbidity costs bore by families or health systems (Brandt et al. 2012). This is particularly relevant to evaluate the benefits of preventive actions (see below).

*Improving the evaluation of effectiveness of policy measures*

The keystone of public health is aimed at reducing morbidity and its consequences (i.e premature death). Understanding what measures are more effective at reducing the morbidity burden of air pollution is of relevance for policy-makers. Changes in mortality patterns from policy measures are more difficult to attain and document than morbidity outcomes.

*Reducing social inequalities of air pollution exposure*

Reducing disparity across populations should be a priority of policy-making at different scales. Health inequalities are not only reflected in final health end points. Understanding inequity of air pollution impacts can be further refined by using morbidity endpoints (Perez et al. 2009).

*Communication with stakeholders*

The concept of prevented mortality or related results expressed in related life years metric may be hard to grasp for laypeople and of little applicability for policy-making. If public relates more closely to morbidity outcomes this could empower the populations to seek further improvement of air quality from policy-makers.

## Current methodological approaches

Morbidity outcomes have been included in numerous APHRA conducted at very different scales. For Europe, the latest recommendation by WHO review is to conduct APHRA for two main pollutants, Particulate Matter and Ozone, for which health effects are assumed to be mostly independent of each other. While a wide range of evidence exist for mortality, the number of studies on morbidity are far less numerous and sometimes less consistent than for mortality. Therefore the current recommendation to include morbidity outcomes in APHRA is limited to a specific set of outcomes for which the evidence is deemed sufficiently certain.

WHO review emphasizes the need for transparently identify and describe uncertainties in APRHA. Thus to integrate aspects of uncertainty in the analysis, some outcomes are proposed to be included in a core analysis and others in an extended or sensitive analysis only. For Particulate Matter (PM), the quantification is to be conducted for either $PM_{2.5}$ or $PM_{10}$ but not both, as this would result in double counting of burden due to overlapping of sources of PM. Local ratios between PM sizes can be used to transform risk functions from one PM indicator to another. For absolute quantification of burden, baseline health data is to be collected for the population under study matching as close as possible the outcome definition used in the proposed CRFs.

In recent years, there has been an increasing literature suggesting that near-road traffic pollution has partly independent effects from $PM_{2.5}$ and ozone (Chen et al. 2013; Gan et al. 2010; Gan et al. 2011). The effects are unlikely to be explained by $PM_{2.5}$ alone as this pollutant is not elevated near roads in contrast to compounds that may be better markers of near road traffic pollution such as ultrafine particles, carbon monoxide, $NO_2$, black carbon, polycyclic aromatic hydrocarbons and some metals. WHO review was particularly focused at reviewing the health evidence for $NO_2$. WHO review concludes that there is enough evidence for some morbidity outcomes related to $NO_2$ exposure to be added to the impact of PMs and Ozone.

Below we summarize the evidence and the general methods proposed in the WHO review.

*Overview of morbidity effects of Particulate Matter and Ozone*

There is a large body of evidence that support the effects of long-term exposure to Particulate Matter (PM2.5 or PM10) and morbidity. Most of the cohorts that have produced evidence come from Europe, Canada or the United States. Acute effects of PMs on several morbidity outcomes are also supported by large evidence. In the short-term domain, several morbidity studies have been conducted in low and middle income countries as well as in Europe and the United States.
Strong evidence exist now for long-term exposure to PMs and cardiovascular diseases. Of special relevance are studies on an association with $PM_{2.5}$ and various markers of atherosclerosis such as thickness of the intima-media, coronary artery calcification, or pulse pressure. This pathophysiological pathway is supported by short-term epidemiological and panel studies showing variations in cardiovascular biomarkers of inflammation such as C-reactive protein or fibrinogen that are linked to subsequent cardiovascular disease.

There is also evidence to support the role of PM in the development of respiratory diseases, such has infections, bronchiolitis and low lung function in children. In adults, lung function development impairment is also associated with $PM_{2.5}$.

Other outcomes have more recently been related to PMs including diabetes, neurological development in children and disorders in adults, and diabetes. Association with birth outcomes including low birth weight, preterm birth and small for gestational age at birth have also been reported.

For ozone, the epidemiological evidence on its effect on morbidity outcomes came initially principally from short-term effects of hospitalization for respiratory and cardiovascular disease. In the last decade, several studies evaluated the chronic effect of ozone and chronic respiratory health and found evidence with lung function, asthma admission, and increase IgE in adult asthmatics. Some studies reported effects of long-term ozone exposure and onset of asthma in children. In recent years, the evidence for association with birth outcome has increased, and there are preliminary findings of ozone being related to cognitive decline in adults.

Many studies have found evidence of excess health risks using proximity to roads as pollutant indicator for long-term exposure to near-road traffic pollution. The effects have remained robust event after adjusting for socio-economic status or noise. Morbidity effects related to proximity to road include several markers of cardiovascular diseases, asthma hospitalization, lung function reduction, and lung cancer.

Proximity to roads is a limited pollutant marker for both adjusting properly epidemiological studies and policy-making. In many epidemiological studies $NO_2$ has been used as a marker of traffic emissions and off-road traffic pollution instead. Long-term studies have evaluated association with lung function decrement, incidence or prevalence of cardiovascular diseases, diabetes mellitus, asthma and bronchitis independently of PMs. Of those, effects of long-term exposure to $NO_2$ and respiratory conditions in children appear the most robust. Indeed, while results for mortality report that traffic and other sources of fossil fuel combustion are associated with cardiovascular of respiratory mortality, the association with morbidity endpoints has not been consistently replicated. Short-term effects of $NO_2$ have been principally associated with respiratory hospital admissions, evidence on cardiovascular admission is also more uncertain.

*Retained outcomes*

Table 1 summarizes the outcomes recommended to be included in core and extended morbidity cost-benefit analysis analyses in Europe by WHO review. Details of concentration-response

functions (CRFs), exposure windows, baseline health data are presented in Table Appendix 1 and Table Appendix 2.

For PMs, the primary morbidity candidate that has been recommended in core analysis includes only short-term effects on cardiovascular, cerebrovascular and respiratory hospital admissions for all ages. In an extended analysis, bronchitis symptoms in children under the age of 18 years, chronic bronchitis in adults older than 30 years, asthma attack for all ages, and restricted activity day in adults are proposed. The underlying assumption is a linear relationship over the full range of exposures. Relevant exposure times for PM are annual levels to represent long-term exposures, and 24-hour average for short-term exposures.

For ozone, the outcomes retained by WHO review relate to short-term effects on respiratory and cardiovascular hospital admissions among 65 year and older. Minor restricted activity days can be included in an extended analysis. Selected exposures relate to converted all-year daily maximum 8-hour ozone. Linear relationship of outcomes with cut-off points of no effect set at 35 ppb for daily maximum 8-hour ozone have been established.

To capture some morbidity impacts of near-road traffic pollution, represented by $NO_2$, WHO review suggest that a core analysis include impact of short-term $NO_2$ exposure on respiratory hospital admissions using 24hour or 1hour averaging times. Given current uncertainties and potential for double-counting of burden, the impact of long-term exposure to $NO_2$ on bronchitis symptoms in asthmatic children is suggested to be restricted to the extended analysis.

Table 1. Summary of outcomes suggested to be included in cost-benefit analysis in Europe and level of analysis. Summarized from (WHO 2013b)

| Level of analysis | **PM** | **Ozone** | **$NO_2$** |
|---|---|---|---|
| **Core** | $PM_{2.5}$ daily mean. Hospital admissions, CVD diseases (includes stroke), adults all ages | $O_3$, daily maximum 8-hour mean .Hospital admissions, CVD (includes stroke) and respiratory diseases, age 65+ | $NO_2$ 24-hour mean. Hospital admissions due to respiratory diseases |
| | $PM_{2.5}$ daily mean Hospital admissions, respiratory diseases, all ages | -- | -- |
| **Extended** | $PM_{10}$, annual mean. Prevalence of bronchitis in children, age 6-12 years (or 6-18) | $O_3$, daily maximum 8-hour mean . Minor restricted activity days, all ages | $NO_2$ annual mean. Prevalence of bronchitic symptoms in asthmatic children |
| | $PM_{10}$, annual mean. Incidence of chronic bronchitis in adults (age >=18) | -- | -- |
| | $PM_{2.5}$ two-week average. Restricted activity days, all ages** | -- | -- |
| | $PM_{2.5}$ two-week average. Work loss days, among working population | -- | -- |

| | | | |
|---|---|---|---|
| | $PM_{10}$ daily mean. Incidence of asthma symptoms in asthmatic children 5-19 years | -- | -- |

## *Limitation and uncertainty around current approaches*

*Effect of sources*

APRHA based on PMs assumes that the toxicity is the same for all sources. While different pollution sources have been associated with different type of health effects, caution has been recommended when attributing health impacts to different sources of air pollution, given the mixture of source and correlation existing between those. WHO has concluded that there is no sufficient evidence to differentiate source and constituents that may be more closely related to health outcomes, and thus source-specific APHRA is not currently proposed by WHO except partially for near-road traffic related pollutants as presented above. Others have developed methods to integrate traffic markers to calculate the underlying chronic burden of near-road traffic pollution (Perez et al. 2013). To estimate the total burden of air pollution but to limit possible double counting, near-road traffic related impacts were then added to the acute burden of regional pollutants.

*Range of exposure*

There is lack of evidence on the shape of most morbidity risk functions at very high or low level of exposure. Integrating risk functions from different sources to estimate this shape for PM2.5 has been attempted in the mortality domain, but not for morbidity outcomes. As such currently, CRFS are assumed to be valid at any levels of exposure.

*Double counting of impacts*

In the morbidity domain, there is greater potential for overlapping of health endpoints used in different CRFs than in the mortality domain. Respiratory outcomes may be especially sensitive to this but also markers used for cardiovascular diseases. Some CRFs developed on general population may also include population specific cases, such as asthmatics, for which a separate quantification is also suggested. The morbidity outcomes currently proposed in APHRA were selected to minimize double counting due to health definitions, although some remaining double counting is possible. Care should thus be taken when including CRFs from new morbidity studies to ensure that they may not already be covered by other CRFs.

*Underestimation of impacts*

APHRA that use PMs as sole pollutant indicator of long-term exposure will underestimate the whole burden of air pollution, as suggested by the independent effects detected for near-road traffic pollution. Using other pollutant markers, such as NO2, to represent near-road traffic pollution to be added to the rest of the total PM and ozone burden may however result in potential double counting of effects. CRFs based on two-pollutant models could be used instead. However, often, studies that provide evaluation for two pollutant models are unavailable because of high correlation between pollutants. The spatial scale of past cohort studies may also influence the interpretation of the risk functions obtained from two pollutant models.

Another approach would be to use other indicators more closely related to traffic proximity and emissions from combustion and less correlated with PM2.5, such as elemental or black carbon.

WHO suggests that including both PM2.5 and elemental or black carbon in APHRA may still lead to double counting of some of the impacts and is currently not recommended as core analysis but rather as sensitivity analysis of local effects.

*Baseline rates of diseases*

As is shown in Table Appendix 1 and 2 for the example of Europe, when data is not available at the scale needed, extrapolations from other areas are suggested to be used. The source of information to derive baseline health data is more varied than for mortality. There is a general lack of relevant baseline health data in most settings, thus conducting morbidity APHRA relies on extrapolation from other areas, which contributes to larger uncertainty. Great variability of rates may be present at national and local level. The spatial distribution of morbidity health outcomes is also generally unavailable, but of importance especially for assessments at regional and local scale that attempt to capture vulnerability impacts. Tapping on new statistical methods (i.e. Bayesian modelling) to estimate spatial incidence and prevalence of outcomes may be a promising approach.

*Indoor-outdoor air pollution burden*

Morbidity air pollution burden is based on outdoor air pollution levels modelled or measured. Exposure attributed to ozone is based on outdoor concentrations measured at background locations. The correlation between outdoor and indoor concentrations and between outdoor and personal exposure is less strong than for PMs as exposure depend on indoor sources and activity patterns relating to housing activity (.e. opening of windows). Extrapolation of CRFs for ozone may be less appropriate in some setting where these factors greatly influence exposure and potentially health effects. This may be true for other sources of air pollution (i.e. biomass fuel, or second hand smoke).

## *Opportunities for advancing APHRA methods at a local, national and international level*

*Quantification of morbidity outcomes*

The range of morbidity outcomes retained for morbidity quantification is currently principally limited to short-term effects. The evidence of PM2.5 and cardiovascular morbidity is however growing. For example a recent analysis of 11 European cohorts and stroke incidence found suggestive evidence of an association with long-term exposure to fine particles (Stafoggia et al. 2014). Given that cardiovascular outcomes are the leading cause of death in many countries and will even more contribute greatly to disability and costs in the future, there is a need to develop recommendations for integrating these outcomes in APHRA.

While evidence has grown for birth and cognitive development in children that may be suitable for including in APHRA, the methods for translating these findings into policy-relevant information is still lacking.

There is a need for evaluating if/how findings using continuous pre-clinical markers of disease, such as lung function or atherosclerosis , can be translated into APHRA and be useful for policy-making.

Disability-Adjusted Life Years (DALY) have been used in international burden evaluations as the metric to express morbidity burden. Concerns by policy-makers and health professionals have been expressed regarding the lack of available information regarding the assumptions used

to translate morbidity impacts into this metric. Beyond cost, there is a need to evaluate the best metrics to express results of morbidity burden to be useful for policy-makers.

*Source-specific morbidity analysis and interaction of sources*

Conducting separate analysis for black carbon or elemental carbon, closely related to traffic emissions and near-road pollution, could be very relevant to evaluate if local action reduce effectively population's exposure to traffic pollutants for example, since this indicator has larger spatial variability than with PMs. Black carbon is mostly generated by diesel exhaust and has been categorized as carcinogen (IARC 2012). Evaluating excess cancer risk due to local elemental carbon exposure is currently not included in APHRA.

Household air pollution is a major contributor to respiratory illnesses in many regions. Given that the pollutant generated in combustion processes may share similar pathways than with other air pollution combustion processes, effects on the cardiovascular system seem possible. While evidence is growing, the methodological approach for source-specific burden quantification needs to be evaluated.

In some settings, the interrelation and accumulation of exposure to indoor and outdoor pollution, including second-hand smoke suggest that the dichotomization of APHRA as developed in Europe has limited value for policy-making. APHRA could identify the physical and social factors that drive interactions and susceptibilities to develop composite risk factors (Rajagopalan and Brook 2012).

*Relationship with co-morbidities and mortality*

Daily average exposure concentrations contribute to short-term and cumulative exposure. 24 hour exposure to PM is associated with morbidity immediately and in subsequent days. While it has been shown that repeated exposures may result in larger health effects than the effects of single day, in the mortality domain, the sum of all the short-term effects do not amount to the long-term effects observed, that are much larger. To explain this difference, it has been suggested that effects are not only due to exacerbation but to progression of underlying chronic diseases. There is a need to further develop burden models that can integrate these domains.

APHRA currently do not consider interaction between co-morbidities. Short-term studies that have shown harvesting effects especially regarding respiratory diseases suggest that frailty modifies the effect of air pollution in specific subpopulations. Most studies adjust by co-morbidity rather than look at interaction effects due to sample size, thus effects are generally ignored in APHRA.

Many studies have now addressed the interaction between genes and air pollution effects. Studies show that the factors and pathways at play are very complex. There is a need to review the literature, and evaluate if methods can be developed to integrate some of these findings in APHRA.

It is to note that the lack of integration of susceptibility and interaction issues in current APHRA approaches does not preclude that current APHRA are wrong or over and underestimated. Indeed the unknown group-specific estimates are contributing to the weighted estimate used for the total group. APHRA results would not necessarily be different but be more specific for policies.

*Advancing information systems for morbidity APRHA*

Baseline health risk data is inexistent in many places of the world. Extrapolating baseline rates from Western populations may result in large errors in burden. Risk profile in middle and high income countries that may interact with air pollution effects is rapidly changing but the prevalence of many common non-communicable diseases is still unknown in many settings. Development of protocols for developing health and environmental monitoring system to conduct morbidity APRHA would be useful especially to better identify local and national morbidity impacts in relation to dual burden of diseases.

Closer collaboration between epidemiology and risk health assessment disciplines will help design studies that can fill methodological uncertainties in the morbidity domain.

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An early version of this report was commented by Prof. Nino Kunzli, Swiss Tropical and Puplic Health Institute, Basel, Switzerland.

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**Table Appendix 1. Summary of recommended short-term and long-term concentration-response function for particulate matter and ozone to be used on cost-benefit analysis in Europe, with source of background health data. Adapted from (WHO 2013b)**

| Pollutant metrics | Heath outcome | Group[1] | RR (95%CI) per 10 µg/m$^3$ | Range of concentr. | Source of background health data for Europe | Source of CRF | Comments |
|---|---|---|---|---|---|---|---|
| **Long-term** | | | | | | | |
| $PM_{10}$, annual mean | Prevalence of bronchitis in children, age 6-12 years (or 6-18) | B* | 1.08 (0.98 – 1.19) | All | Mean prevalence from PATY study: 18.6% (range 6% -41%) | PATY (Pollution and the Young) project (Hoek et al. 2012) analyzing data from ca. 40,000 children living in 9 countries. HRAPIE recommends applying to population 6-12 or 6-18, but to simplify we apply to children 5-17 | Between-studies heterogeneity of the association ($p<0.10$) |
| $PM_{10}$, annual mean | Incidence of chronic bronchitis in adults (age >=18) | B* | 1.117 (1.040-1.189) | All | Annual incidence 3.9 per 1000 adults based on Swiss study SAPALDIA | Combination of results from longitudinal studies AHSMOG and SAPALDIA | Two studies only with different RRs; CB based on symptoms reporting is weak indication of clinically recognized COPD. |
| **Short-term** | | | | | | | |
| $PM_{2.5}$ daily mean | Hospital admissions, CVD diseases (includes stroke), adults all ages | A* | 1.0091 (1.0017-1.0166) | All | European hospital morbidity database. http://www.euro.who.int/en/what-we-do/data-and-evidence/databases/european-hospital-morbidity-database-hmdb2 ICD10: I00-I99 | APED meta-analysis of 4 single city studies and 1 multi-city study | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| $PM_{2.5}$ daily mean | Hospital admissions, respiratory diseases, all ages | A* | 1.019 (0.9982-1.0402) | All | European hospital morbidity database.http://www.euro.who.int/en/what-we-do/data-and-evidence/databases/european-hospital-morbidity-database-hmdb2 ICD10: J00-J99 | APED meta-analysis of 3 single city studies | |
| $PM_{2.5}$ two-week average | Restricted activity days, all ages | B** | 1.047 (1.042-1.053) | All | 19 RADs per person per year: baseline rate from Ostro and Rothschild (1989) study | Study of 12,000 adults followed for 6 years in 49 metropolitan areas of US (Ostro 1987) | One US study from 1987; no data of background rate in Europe |
| $PM_{2.5}$ two-week average | Work loss days, among working population | B* | 1.046 (1.039-1.053) | All | Health for All database (HFA-DB). (http://data.euro.who.int/hfadb/) | Study of 12,000 adults followed for 6 years in 49 metropolitan areas of US (Ostro 1987) | High variability of background rates based on reported sick absenteeism in Europe, reflecting inter-country differences in definition. |
| $PM_{10}$ daily mean | Incidence of asthma symptoms in asthmatic children 5-19 years | B* | 1.028 (1.006-1.051) | All | The prevalence of asthma in children based on "severe asthma" in ISAAC (Lai et al 2009): Western Europe: 4.9%, Northern and Eastern Europe: 3.5%. Daily incidence of symptoms in this group: 17% (interpolation from several panel studies) | Meta-analysis of 36 panel studies of asthmatic children conducted in 51 populations, including 36 from Europe, (Weinmayr et al. 2010). HRAPIE recommends apply age 5-19, again for simplification we apply to stricter definition of children between -5-17 years. | Varying definition of the target population and of the daily occurrence of symptoms. |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| $O_3$, daily maximum 8-hour mean | Hospital admissions, CVD (includes stroke) and respiratory diseases, age 65+ | A* | CVD: 1.0089 (1.0050-1.0127)<br><br>Respir.: 1.0044 (1.0007-1.0083) | >35 ppb (>70 µg/m³) | WHO European Hospital Morbidity Data http://data.euro.who.int/hmdb/index.php ; ICD9 codes: CVD 390-429, respir: 460-519 (ICD10: I00-I52; J00-J99) | APHENA study based on data from 8 European cities. Coefficients adjusted for PM10 in two-pollutant model | APHENA study based on all range of observed ozone concentrations, including levels below 35 ppb. Therefore the effects at the ozone <35 ppb are ignored. |
| $O_3$, daily maximum 8-hour mean | Hospital admissions, CVD (includes stroke) and respiratory diseases, age 65+ | A | CVD: 1.0089 (1.0050-1.0127)<br><br>Respir.: 1.0044 (1.0007-1.0083) | >10 ppb (>20 µg/m³) | WHO European Hospital Morbidity Data http://data.euro.who.int/hmdb/index.php, ICD9 codes: CVD 390-429, respir: 460-519 (ICD10: I00-I52 and J00-J99) | APHENA study based on data from 8 European cities. Coefficients adjusted for PM10 in two-pollutant model | Alternative to the assessment for O3>35 ppb only. |
| $O_3$, daily maximum 8-hour mean | Minor restricted activity days, all ages | B* | 1.0154 (1.0060-1.0249) | All | 7.8 days/year based on Ostro and Rothschild, 1989 | Ostro and Rothschild (1989) 6 separate analyses of annual data 1976-81 of the US National Health Interview Survey, Ostro and Rothschild (1989) | One study from US, 1989, used as a source of both RR and background rates. |

*Component of Total

** Only residual RADs to be added to Total effect, after the days in hospital and days with work days lost and symptoms accounted for

[1] For outcome pairs in Group A and B, the expert group has judged that there is sufficient evidence for causality of effects, as reviewed in REVIHAAP. For Group A there is enough available data enabling reliable quantification of effects. For Group B, there is more uncertainty in the precision of estimates being used for quantification of the effects. The effect estimates in pairs marked by * contribute to the total effect. Rule for CBA: Core set of impacts based on ΣA*, extended set of impacts based on ΣA*+ ΣB*

**Table Appendix 2. Summary of recommended long-term and short-term concentration-response function for NO2 to be used in addition to effects of particulate matter and ozone, with source of background health data. Adapted from (WHO 2013b)**

| Pollutant metrics | Heath outcome | Group [1] | RR (95%CI) per 10 µg/m$^3$ | Range of concentr. | Source of background health data for Europe | Source of CRF | Comments |
|---|---|---|---|---|---|---|---|
| Long-term | | | | | | | |
| $NO_2$ annual mean | Prevalence of bronchitic symptoms in asthmatic children | B* | 1.021 (0.990-1.060) per 1 µg/m³ change in annual mean $NO_2$ | All | The background rate of asthmatic children: "asthma ever" in Lai et al (2009): Western Europe: 15.8%, SD 7.8%, Northern and Eastern Europe: 5.1% SD 2.7%. Prevalence of bronchitic symptoms among asthmatic children 21.1% to 38.7% (Migliore et al,2009, McConnell et al, 2003) | Southern California Children's Health Study (McConnell et al, 2003). Coefficient from 2-pollutant model with BC (coefficients from models with PM10 or $PM_{2.5}$ are higher) | Based on only one available longitudinal study providing NO2 coefficient adjusted for other pollutants. Supported by studies of long-term exposure to nitrogen dioxide and lung function and by the wider evidence on nitrogen dioxide and respiratory outcomes from other types of studies. |
| Short-term | | | | | | | |
| $NO_2$ daily maximum 1-hour mean | Hospital admissions due to respiratory diseases | A | 1.0015 (0.9992-1.0038) | All | European hospital morbidity database. http://www.euro.who.int/en/what-we-do/data-and-evidence/databases/european-hospital-morbidity-database-hmdb2 (ICD10: J00-J99) | APED meta-analysis of 4 studies published until 2006; coefficient from one-pollutant model. Estimate robust to adjustment to co-pollutants. | Alternative to the estimates based on 24h NO2 average (preferred due to more studies available) |
| $NO_2$ 24-hour mean | Hospital admissions due to respiratory diseases | A* | 1.0180 (1.0115-1.0245) | All | European hospital morbidity database. http://www.euro.who.int/en/what-we-do/data-and-evidence/databases/european-hospital-morbidity-database-hmdb2 (ICD10: J00-J99) | APED meta-analysis of 15 studies published until 2006; coefficient from one-pollutant model. Estimate robust to adjustment to co-pollutants. | |

[1] For outcome pairs in Group A and B, the expert group has judged that there is sufficient evidence for causality of effects, as reviewed in REVIHAAP. For Group A there is enough available data enabling reliable quantification of effects. For Group B, there is more uncertainty in the precision of estimates being used for quantification of the effects. The effect estimates in pairs marked by * contribute to the total effect. Rule for CBA: Core set of impacts based on ΣA*, extended set of impacts based on ΣA*+ ΣB*

# Background paper 7: Presenting uncertainty in health risk assessments of outdoor air pollution

*Guiding question 3.e: "How should health risk assessments quantify and express the uncertainty of their estimates, balancing the complexity of information and tools used in concert and the desire to produce simple results for non-technical decision-makers?"*

*Greg Freedman*

## *Prompt*

How should health risk assessments quantify and express the uncertainty of their estimates, balancing the complexity of information and tools used in concert and the desire to produce simple results for non-technical decision-makers?

Despite great improvements in the science behind health risk assessments for outdoor air pollution, we still cannot know with complete certainty what the effects of air pollution on health is. However, policy makers look to us in order to give recommendations on weighing the negative effects of outdoor air pollution against the economic benefits. Because of this, it is important that we describe with as much honesty as possible the uncertainty in our estimates. This document attempts to describe the sources of uncertainty, as well as one way in which to carry all sources of uncertainty through an analysis to get estimates of the burden due to outdoor air pollution.

## *Sources of uncertainty in a Health Risk Assessment*

There are four main sources of uncertainty in health risk assessment of air pollution: Uncertainty in disease burden, the pollution exposure level, response to the pollution and the counterfactual level of air pollution. When attempting to calculate the burden due to outdoor air pollution, each of these four components needs to be calculated, and these analyses will most likely have uncertainty in them.

Uncertainty in disease burden can come because when looking at mortality or morbidity. Modelers may have to combine multiple sources of data to calculate the number of deaths and correct for known sources of biases between these sources. Even if there is a complete vital registration, uncertainty can arise when assigning a particular cause of death to so-called "garbage codes" where the vital records have failed to identify a plausible underlying cause of death. Furthermore, if a health risk assessment is studying the effects of a policy change on the effects of pollution in the future, uncertainty will arise in projecting population and deaths into the future. Background level of morbidity estimate are similarly uncertain.

There also is uncertainty in the dose-response function of mortality and morbidity, or the relationship between excess health risk and amount of exposure to air pollution. As is true with any epidemiologic study, there is a fair amount of uncertainty when trying to determine the harm done by exposure to pollution. Additionally, because most existing literature on this relationship are based on studies that were conducted in the developing world, the range of exposures studied does not cover the entire range of pollution observed. Though there are various methods for extending the existing literature to higher ends of seen exposure, including the integrated exposure response curve, this does lead to uncertainty in the dose-response curve that is impossible to now the entire magnitude of without further studies.

Estimates of the exposure to air pollution also come with uncertainty. Because there is not full coverage of ground monitors, almost any health risk assessment will rely on modelling to determine exposure estimates. There is also some inherent uncertainty in exposure estimates as well, unless the study has wearable monitors for all those who are studied to determine their exact exposure level.

Finally, there can be uncertainty in the counterfactual level of pollution. This could be the counterfactual level of pollution given some policy change with some uncertainty around the exact effect size, or it could be the theoretical minimum level of pollution, whose value may not be known.

## *Simulation methods*

Given multiple sources of uncertainty in a single analysis, one solution is to use simulation methods. The general idea behind simulation methods is to create a large number (N) of draws with each of the parameters uncertainty intervals and line them up with each other to calculate the end result for each of these draws. The uncertainty interval then can be given as the 95% quantile of these N results[9]. These N draws should maintain any correlation structure from the original analysis, so for example two independent components just need to be lined up randomly, but coefficients from the same regression should be drawn from the variance-covariance distribution.

Though this method requires increased more computational power than other methods for incorporating uncertainty analysis, it does provide considerable advantages. First, it gives a great deal of flexibility in the distributions around the input parameters. There is no need to assume that the distribution is of a particular form in order to match it to the other components. This also helps coordinate between multiple groups each calculating a different component. Because all that each team needs to provide is 1,000 draws, each team can be completely independent of the particular methods used by the others.

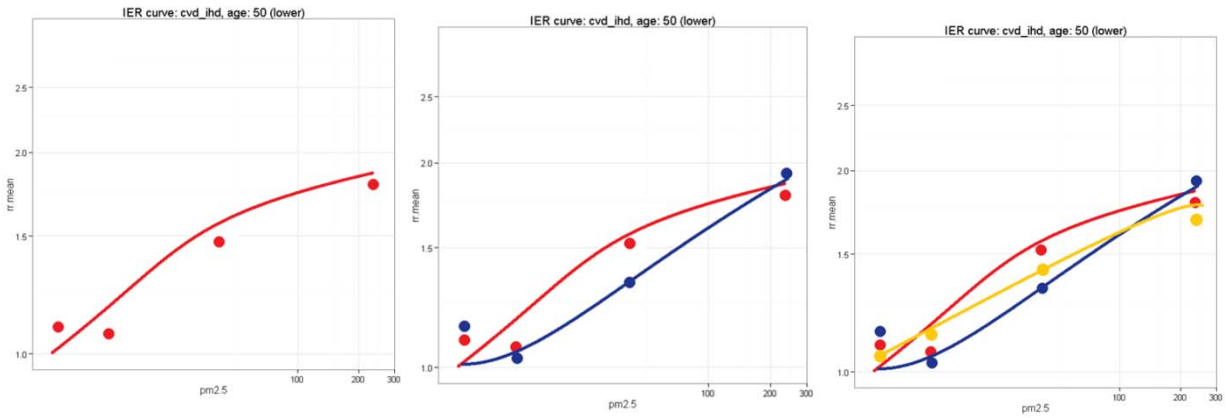
It is important to note that it is not possible to extend the analysis without the original draws. Every calculation based on the data, including aggregating age groups, calculating ranks, or other analyses, must be done at the draw level in order to properly account for uncertainty. If for example one wishes to calculate the burden attributable to all-ages and she only has the burden for the age-specific estimates, by simply adding the lower and upper confidence intervals, she will exaggerate the uncertainty, because this effectively assumes that the uncertainty is perfectly correlated.

## *The Global Burden of Disease 2010 – an example of simulation methods*

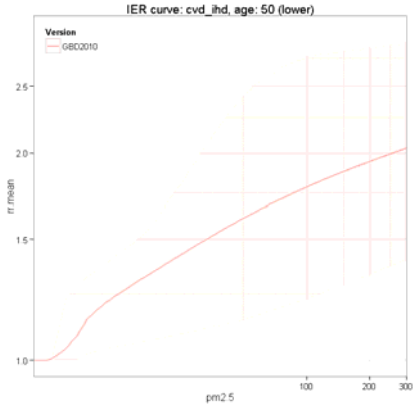
The global burden of disease uses simulation methods to incorporate the uncertainty from these four sources. Estimating the underlying deaths and disability is beyond the scope of this paper, but further information can be found in the GBD capstone papers.

Uncertainty in the exposure response curve was handled by simulating 1,000 draws of each study's relative risk and then running a separate regression on each of these 1,000 pairs. Figures 1a, 1b and 1c show what this looks like for the first 3 draws using example data.

[9] King, Gary, Michael Tomz, and Jason Wittenberg. *Making the Most of Statistical Analyses: Improving Interpretation and Presentation*. American Journal of Political Science, Vol. 44, No. 2, April 2000, Pp. 341–355.




Each dot represents a single study for the draw, and the line through it is an example regression line fitting the data. Once we have done this 1,000 times, we can take the 95% quantile of the distribution of all draws and create a graph like figure 2. The line in the middle is the mean of all 1,000 draws, and the shaded area represents the area covered by the middle 95% of all lines for a given $PM_{2.5}$ level.




For measuring exposure, the uncertainty comes from the calibration of the satellite and chemical transport model to the ground monitors. We have been unable to collect uncertainty in the ground monitor, and so we only need to perform a single regression. The uncertainty then comes from random draws from the variance covariance of the coefficients from the regression.

## *Presenting to decision makers*

Decision makers will likely always be most interested in the simplest story possible, which may make presenting uncertainty difficult. It likely will always be the case that all presentation will focus on the mean results. However, given advances in graphing technology, such as D3, a toolset for building online visualizations[10], it will become more and more possible to present the uncertainty along with the general conclusions. By using graphical elements that are not possible in traditional presentation mediums like animation and hover overs (where descriptive text is shown when the user hovers their mouse over an item), we can more effectively convey the uncertainty as part of the whole story of our visualization.

[10] www.d3js.org