Methodology for assessment of Environmental burden of disease

Prepared by:

David Kay

Centre for Research into Environment and Health

Aberystwyth, United Kingdom

Annette Prüss

World Health Organization

Protection of the Human Environment

Geneva, Switzerland

Carlos Corvalán

World Health Organization

Protection of the Human Environment

Geneva, Switzerland

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Diarmid Campbell-Lendrum	London School of Hygiene and Tropical Medicine, London, UK
Joe Eisenberg	University of California, Berkeley, USA
Keith Florig	Carnegie Mellon University, Pittsburgh, USA
Scott Grosse	Centers for Disease Control & Prevention (CDC), Atlanta, USA
Tord Kjellström	New Zealand Environmental and Occupational Health Research Centre, Auckland, New Zealand
Eric Lebret	National Institute of Public Health and the Environment, Bilthoven, The Netherlands
Tony McMichael	London School of Hygiene and Tropical Medicine, London, United Kingdom

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1. Introduction

The disease burden caused by an environmental exposure, and the preventable part of it, are major elements which can guide decision-making, priority setting and resource allocation in health and environmental management. Quantitative assessment of the burden, together with information on the effectiveness and cost-effectiveness of interventions within a social and ethical framework, provide a rational basis for research, implementation and policy development.

Since the Global Burden of Disease study was published in 1996[1], the overall burden of disease has mainly been estimated by '*disease outcome*' rather than by '*risk factor*'. A few approaches to estimating the burden of disease from environmental risk factors have been tested and some have produced promising results.

For comparison of disease burden estimates across risk factors, estimates need to employ a harmonized methodology. This requires the development of:

- working definitions,
- the definition of '*zero-exposure*' and/or
- appropriate hypothesised '*alternative'* exposure scenarios, and
- a common approach to evidence or uncertainty underlying an estimate.

To address these issues, a consultation was held in Buffalo, New York, 23-24 August 2000, following the *12th Annual Meeting of the International Society for Environmental Epidemiology (ISEE 2000).*

2. Objectives

The overall aim of the consultation was to advance the agenda of the evaluation of disease burden from environmental risk factors. This consultation was part of an ongoing process aiming primarily at the following:

- To provide methodological guidance on the quantitative assessment of the burden of disease from environmental risk factors at national or regional level; the process should result in a practical guide.
- To create a network of experts interested in developing the conceptual and practical implementation of environmental disease burden assessment and sharing experience to define priorities in future developments.

This meeting constitutes the first consultation of experts in the framework of this project. The participants undertook a structured review of the proposed elements and methodological approaches for environmental burden of disease assessment. A first draft of the methodological elements is provided below. This was tabled in a series of presentations and developed during the meeting.

This project builds upon a previous consultation organized by WHO/ILO[2]. Several papers from that consultation were published in the *September 1999* issue of the journal *Epidemiology.* It also builds upon and adapts concepts put forward in the global

[1] Murray CJL, Lopez AD. *The Global Burden of Disease.* World Health Organization, Harvard School of Public Health, World Bank, WHO, 1996.

[2] Methods for health impact assessment in environmental and occupational health – Report of a WHO/ILO consultation, Geneva, 1998 (WHO/EHG/98.4, ILO/OSH/98.1)

assessment methodology of the GBD study[3,4]. In 1999 the Department of Protection of the Human Environment intensified its efforts and started a project to specifically address the Environmental Burden of Disease (EBD). This is the first meeting dedicated to this project.

Annex 1 contains the background document on this project for the consultation.

A special session on EBD was organized in the 12th Annual Meeting of the International Society for Environmental Epidemiology on 22 August 2000. Its objective was to report on progress in these activities and bring the project to the attention of environmental health professionals.

Programme and summaries of the presentations of the special session are presented in Annexes 3 and 4 of this document.

3. Organization of the meeting

A total of 39 participants, with various specialities in environmental health, participated in the 1½-day consultation (a list of participants is presented in Annex 2). It was chaired by Professor Tony McMichael, London School of Hygiene and Tropical Medicine, UK. Professor David Kay, Centre for Research into Environment and Health, UK, acted as rapporteur.

The meeting was composed of plenary sessions of discussions and brief presentations to introduce each topic (agenda in Annex 3 , summaries of presentations in Annex 4). The main topics discussed included:

- Framework & challenges
- Concepts and examples
- Describing level of uncertainty and evidence
- Further steps and improvements

The group was split into the following working groups during part of the meeting:

- Water & sanitation
- Air quality
- Global environment
- Chemicals

The working groups were asked to address the following issues:

- List useful categories of risk factors to consider
- Propose relevant alternative scenarios
- Address the strength of evidence in each area
- Address the geographical resolution, i.e. the feasibility of size of the area at which the burden of disease assessment can be performed
- Recommendations on the methodology – with reference to the background document
- Other relevant issues – way forward.

[3] Murray CJL, Lopez AD. On the comparable quantification of health risks: lessons from the global burden of disease study. *Epidemiology*, 1999, 10(5):594-605.

[4] Guideline for comparative risk assessment, web site http://www.ctru.auckland.ac.nz/CRA/

The results of the working groups are presented in Annex 5.

4. Meeting recommendations

The main recommendations which emerged during the discussion sessions are summarized below.

General issues

- Decision-making in environmental health should be based on national or regional EBD[5] estimates (with the exception of a number of global risk factors, such as climate change, or greenhouse gas emissions); therefore, the emphasis will lie on national and regional EBD assessment.
- The distribution of EBD within a population should be assessed in addition to the total numbers per age category. The distribution will provide information about the equity in exposures and health outcomes. Such information for policy making in view of the protection of vulnerable groups or high-risk communities.
- Limited transferability of the evidence to populations where empirical data are lacking may restrict the assessment of EBD of "data-poor" populations. Before assessing burden of disease, the applicability of available dose-response relationships to the study population needs to be evaluated.
- Although a general methodology is needed for the sake of comparability, it should be flexible enough to allow for making the most sensible choices regarding categorization of risk factors, summary measures of population health, etc.; The parameters and methods currently used in the global assessment of risk factors would be too restrictive for a number of potential applications in environmental health.

Categorizing risk factors

Various types of categories can be chosen for estimating the related health impacts: the type of human activity (e.g. energy generation, transportation), the type of pollutant (e.g. exposure to lead, arsenic) or by pathway (e.g. air pollution, water). Also, the categories can be more or less aggregated or split into subcategories. For instance water & sanitation could theoretically be split into exposure to recreational water, drinking water intake, access to sanitation etc.

- Categorizing risk factors should be carefully considered, as they may have an impact on the use of resulting estimates of disease burden. In particular, the grouping of risk factors or their splitting into several subcategories may seemingly reduce or increase their importance.
- The choice of risk factor categories should be policy relevant and seek to address parameters policy makers can directly influence (e.g. include sector policies as risk factors, such as transportation policy or energy policy, in addition to risk factors such as 'air quality', 'noise' etc.). In particular, for assessment at regional or national level, risk factor categories should be adapted to policy needs.

[5] EBD: Environmental burden of disease

- The categories of risk factors to be considered for global, national and regional EBD assessment should be relevant to policy making and reflect a logical framework and hierarchy. The DPSEEA framework (Driving Force – Pressure – State – Exposure – Effect – Action) would be very suitable[6]. Adapting to the decision-making process would also facilitate the use of EBD data.

Summary measures of population health

Summary measures of population health are measures that combine information on mortality and non-fatal health outcomes to represent the health of a population in a single figure or unit[7].

- The suitability of health valuation should be further investigated and the utility of this approach for informing EBD assessed.
- It was noted that DALYs (the Disability-Adjusted Life Years, being the most widely used measure) do not currently accommodate *'quality of life'* issues, which are however included in WHO's definition of health.
- The use of other measures (such as QALYs) should be investigated as potential unit for quantifying disease burden and compared with assessments based on DALYs.
- The EBD process needs to be flexible and be able to describe areas such as "life style" or "annoyance", which may, in turn also result in indirect health impacts.
- Issues such as *discounting* of health should also be addressed to satisfy policy relevance. For example, discounted health impacts of risk factors with very delayed effects, as may be predicted for emission of greenhouse gases, will probably be represented as negligible even if a small discount rate is applied.

The considerations in this section may require a number of cross-disciplinary views in environmental health.

Alternative scenarios

Alternative scenarios are baseline scenarios for comparison with the exposure scenario to be studied.

- The term "*counterfactual scenarios*", cited by Murray & Lopez[8] and borrowed from the social science literature, is often misunderstood, and should be replaced by another term, such as "*alternative scenarios*". Such scenarios need to be defined to compare the results with those of an alternative scenario where other

[6] Kjellström T, Corvalán C. Framework for the development of environmental health indicators. *World Health Statistics Quarterly*, 1995, 48:144-154.

[7] Field MJ, Gold GM eds. Summarizing population health: Directions for the development and application of population metrics. Institute of Medicine, Washington, D.C., National Academic Press, 1998.

[8] Murray CJL, Lopez AD. On the comparable quantification of health risks: lessons from the global burden of disease study. *Epidemiology*, 1999, 10(5):594-605.

policies, practices or technologies prevail, or simply of other societies or regions where lower exposures have been achieved.

- In addition to the alternative scenarios described by Murray & Lopez[8], scenarios which are closer to environmental health policy scenarios should be considered (e.g. the shift from one transportation policy to another, the shift from one energy policy or technology to another).
- The choice of risk factors and alternative scenarios should depend on the planned use of resulting estimates. For example, if disease burden estimates are to be used as elements in decision-making in transportation policies, the risk factor to consider should be transportation.

Causation

- EBD assessment should rely and draw upon all available science and evidence (i.e. "best available evidence") and reviews where available. An "objective" description of the available evidence on exposure-outcome relationships, according to best environmental health practice (e.g. *Environmental Epidemiology*[9], *Evaluation and Use of Epidemiological Evidence for Environmental Health Risk Assessment*[10]), is necessary in order to maintain the credibility of the estimates. An analysis of the uncertainty around estimates should accompany the EBD estimate.
- The evidence underlying any burden of disease estimates should be described in a systematic and comparable way. It is, however, questionable whether the policy maker will make use of information on strength of evidence or information on level of uncertainty.

Potential consequences of factors affecting the quality of life

- Issues affecting the quality of life, such as "*annoyance*" or "*small cognitive disorders*", should be considered in the assessment of burden of disease. In particular in modern societies, "*annoyance*" caused for example by noise, can account for a significant part of the disease burden.
- Apparently small impacts on health or quality of life may potentially result in a large impact on a population. For example, a shift of a whole population by the reduction of just a few IQ points (from exposure to lead) may produce a significant increase in the small proportion of the population who exhibit learning difficulties. As loss of IQ points may impact on education, and level of education is associated with a number of health outcomes, real health impacts may be higher than expected.

Suitable methodologies

- The often limited availability of data needs to be reflected in the type of analysis carried out. For example, it may be possible (or necessary) to use data on distal causes in the estimation of disease burden. E.g. use of cooking fuel has been observed to be associated with ARI (acute respiratory infections). Although

[9] Environmental Epidemiology: A textbook on study methods and public health applications, Preliminary version, WHO/USEPA, 1999, Geneva (WHO/SDE/OEH/99.7), in particular Chapter 9.
[10] WHO/Regional Office for Europe, Denmark, 2000 (EUR/00/5020369).

personal exposures are not generally assessed in most of these studies, such associations could be used in evaluating the burden of disease. It would, in such circumstances, be useful to assess the relationships between distal causes (such as '*use of cooking fuel*') and personal exposures examined in smaller scale investigations to obtain additional information on the links within the causal web. This process would permit the use of data from population surveys, which often assess distal causes at very large scales.

- The different risk factors will determine the suitable approaches which may have to be adapted to the specific case, rather than prescribing a common method. For comparability, however, a common framework is recommended. Specific approaches will depend on data quality and availability of exposure, their relation to dose-response relationships, the complexity of causal relationships and competing causes, the possibility of extrapolating data to data poor regions etc.
- Probability-density functions (PDFs), or parametric value exceedences, have been shown to be useful tools in modelling chronic exposure to, for example, lead. Using PDFs to represent exposure distributions in a population rather than using mean values or only few exposure categories will provide better estimates of disease burden, in particular when dose-response relationships are not linear or when they have thresholds.
- Wherever possible, the assessment of burden of disease should be based on comprehensive models integrating the various interacting or competing risk factors. Occupational exposures and environmental exposures to chemicals, for example, should be part of integrated risk factor assessments where they both play a role. As risks are not merely additive, a combined assessment would usually provide better results.
- Also for modelling health impacts from water & sanitation, a common framework is essential to take into account the interactions between the various exposures and health. Such a model, integrating various distal and proximal determinants of water and sanitation related disease, is yet to be developed. Many of the determinants of faecal-oral disease transmission are interrelated, and should be assessed jointly.

Prioritisation and choice of risk factors to be addressed

- Risk perception should play a role in the selection of risk factors to evaluate. Also the quantification of a relatively low disease burden caused by a risk factor raising concern in the population may constitute important information for policy setting and risk communication.
- Because of the difficulty in assessment, risk factors such as '*housing*', '*indoor temperature*', '*domestic accidents*', '*noise*', '*natural disasters due to climate change*', '*transportation system*' may not necessarily receive the attention they deserve. They may cause quite significant disease burdens, which can however not be evaluated, mainly due to the lack of evidence on dose-response or other difficulties in assessment.

- More distal risk factors (for example '*environmental refugees*' due to land degradation or climate change) could also have significant impacts, but such disease burden is, however, currently very difficult to estimate. In fact, risk factors which are not directly linked to health outcomes are more difficult to quantify, as a number of additional parameters may intervene.
- Disease burden assessment should focus on risk factors with potentially high impacts. Risk factors causing high disease burden may require priority public health action, provided that the burden is preventable and interventions are cost-effective.
- If data are available, '*the environment'* should be considered in a much broader manner than would be the case by simple consideration of the '*exposure*' or easily quantifiable '*risk factor*' commonly dealt with. For example, environments promoting certain behaviours or risks, such as '*accident promoting environments*' (or '*traumagenic environments'*) could also be considered.

Diverse issues

- Positive health impacts should also be considered when evaluating disease burden from health determinants, such as the positive effects of development or increasing living standards.
- A network of environmental health professionals interested in the environmental burden of disease work should be promoted, to exchange experiences and learn from them. WHO plans to set up a an information exchange mechanisms for experts involved in environmental burden of disease activities.

Additional recommendations are contained in the reports of the working groups in Annex 5.

Annex 1: Background document

Annette Prüss
Protection of the Human Environment, World Health Organization

1. Introduction

A large number of countries engage in burden of disease studies, to describe their national situation in terms of disease burden due to various disease groups. Countries are increasingly interested in looking for causative life-style, social or physical factors that contribute to this disease burden, such as smoking, dietary patterns, or air pollution. Such information, together with estimates of preventable burden, can become major elements for consideration in the decision-making process for priority setting and resource allocation in health and environment.

A number of studies have been undertaken to assess the disease burden from selected environmental risk factors at global and national level, using a variety of approaches. There is an increasing demand to aid these efforts by providing methodological support to countries.

WHO is currently developing guidelines for comparative risk assessment at global level. These guidelines cover the underlying principles of risk factor assessment in general, without addressing issues which are specific to environmental health.

This initiative builds on the workshop '*Methods for health impact assessment in environmental and occupational health*', July 1997, which addressed basic features of burden of disease assessment.

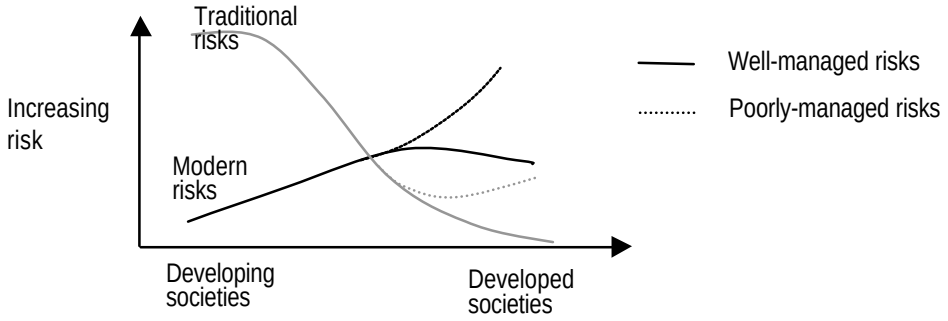
This project aims to provide practical recommendations for the evaluation of specific environmental risk factors for disease burden estimates at national and global levels, and analyse methodological elements on the basis of current approaches. The expected outcome of the project is a practical guide for countries to estimate the disease burden from environmental risk factors. It will address issues such as indicators and parameters to collect, on which frequency data should be collected, how to make estimates for data-poor areas or populations.

This work will be based on the Comparative Risk Assessment and Burden of Disease initiatives of WHO, which may be adapted and completed to satisfy the requirements of environmental health.

2. Relative importance of environmental risk factors per region

Before engaging in national or regional studies on environmental disease burden and assessing or compiling the necessary parameters, the orders of magnitude of risk factors can be estimated according to development status. Environmental conditions and their impact on health are strongly linked to demographic and socio-economic development and the pressures these have on the environment. The health transition accompanying development and socio-economic change has been described as a transition from traditional to modern risks (*Smith, 1996; WHO, 1997; Frenk, 1991*). Environmental health risk in developed societies will depend upon the risk management efforts (Figure 1).

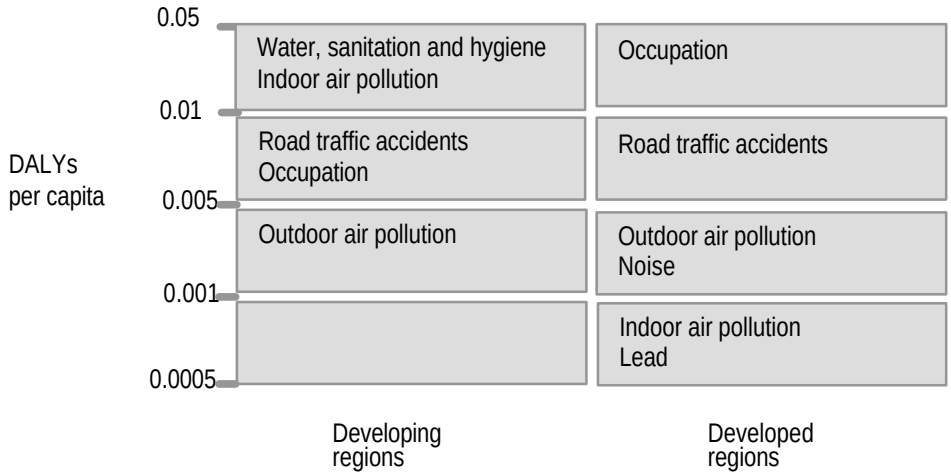
Figure 1: Environmental health risk transition



Adapted from: Smith, 1996; WHO, 1997

From previous studies assessing disease burden from environmental risk factors Murray & Lopez, 1996, Smith, 1999, De Hollander, 1999), orders of magnitude can be outlined for developed and developing regions (Table 1).

Table 1: Comparison of order of magnitude of main disease burden from environmental risk factors in developed and developing regions



The differences in orders of magnitude between least developed and most developed regions will be even greater as exemplified by the disease burden in the Sub-saharan region which is known to be much higher than the mean values in the developing world. Also, the rural/urban differences or the differences for high-risk communities even within one nation, are likely to be important.

This initial classification has, however, a number of limitations, mainly because of the difficulty in the assessment of environmental disease burden:

- Developing societies have been relatively poorly studied in terms of environmental disease burden
- Several risk factors, in particular those which are locally specific (exposure to solid waste, natural disasters, disease vectors, chemical hazards, land degradation etc.) are difficult to assess.

3. Basic approaches for estimating disease burden due to environmental risk factors

As described in the previous workshop, there are two basic approaches to assess disease burden from environmental risk factors: the exposure-based and the outcome-based approach (*WHO/ILO, 1998*). While the exposure-based approach estimates the disease burden on the basis of population exposure, the outcome-based approach is based on the attributable fraction of a disease burden to a certain risk factor. These two approaches require different sets of data, although they share the same underlying assumptions on a health-environment link and its quantification.

Ideally, disease burden due to a specific risk factor should be estimated by both approaches, and the results should match. In practice, this may rarely be possible. The principles of assessment according to these two approaches areas follows:

(i) Exposure-based approach

- Identification of outcomes associated with the relevant risk factor
- Assessment of exposure in the study population

  The exposure distribution of the study population needs to be estimated on the basis of measured data.
- Dose-response relationships

  A dose-response relationship as a function of the exposure parameter assessed for the study population needs to be defined. It needs to be based on a 'sufficient level of evidence'.

Exposure distribution and dose-response relationships are then combined to yield health impact distributions in the study population. Health impact distributions, usually expressed in terms of incidence, can then be converted into health summary measures, for examples DALYs (by existing models).

As an example, the disease burden of outdoor air pollution for Santiago, Chile, was calculated by measuring the concentration of particulate matter (PM10) in the air, estimating the susceptible population, and combining these data with relevant dose-response relationships. A reduction of PM10 levels to recommended standards would result in a reduction of about 5'200 deaths, 4'700 respiratory hospital admissions, and 13'500'000 restricted activity days per year, for a total population of 4.7 million (*WHO, 1996*).

(ii) Outcome-based approach

- Identification of outcomes associated with the relevant risk factor
- Collection and compilation of disease outcome data
- Definition of fraction attributable to relevant risk factor

The disease burden due to a given risk factor is estimated by combining the attributable fraction of a certain disease burden with the amount of disease burden.

As an example, Smith et al. (*1999*) recently estimated the total disease burden attributed to the environment by an outcome-based approach. They estimated that 25

to 33% of the global disease burden expressed in DALYs can be attributed to environmental risk factors. After establishing a number of working definitions and assumptions, the authors analysed disease outcomes regarding the likely contribution of the environment for each of these diseases. These estimates rely on scientific knowledge and expert opinion. For example, tuberculosis "has important household environmental risk factors, including crowding, chilling, and, probably, air pollution", leading to an attribution of 20-25% of the burden caused by this disease to the environment. Acute respiratory infections are known to be eliminated by environmental and nutritional improvements in developed countries, therefore indoor and outdoor air pollution, and housing conditions are estimated to contribute 40-60% of the burden.

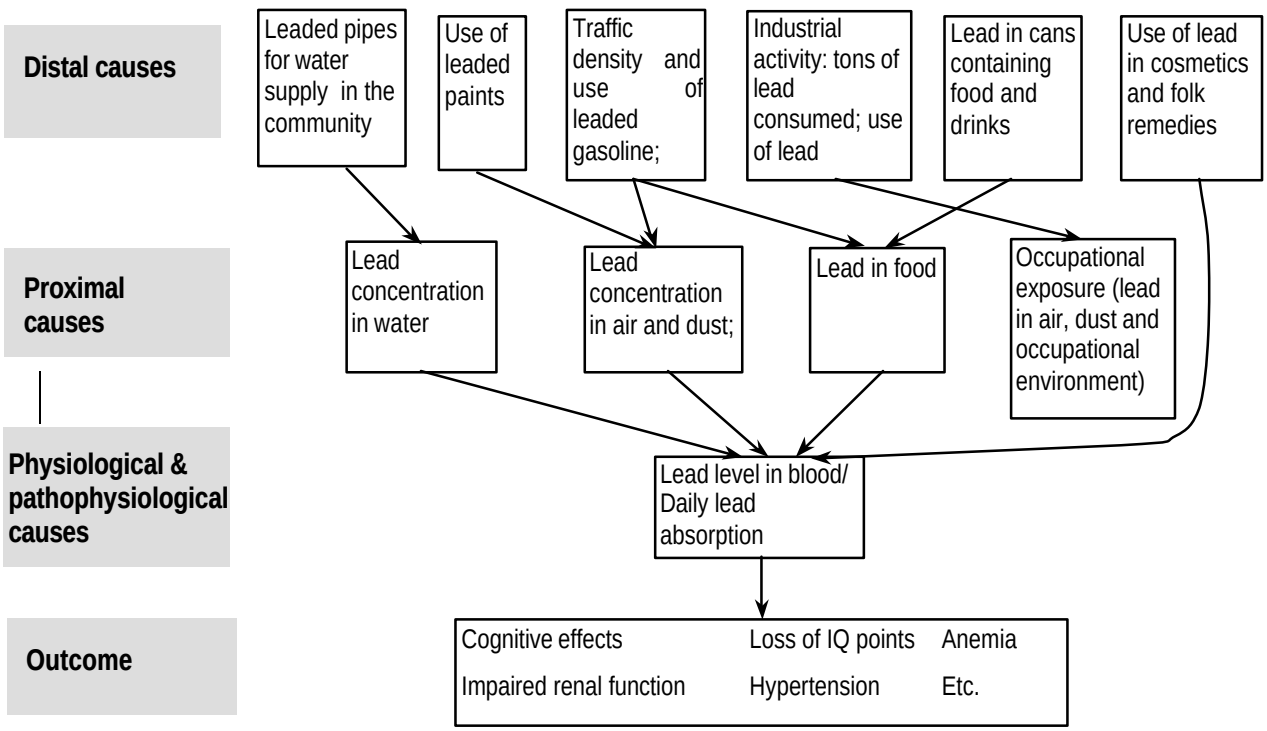
The estimation of disease burden attributable to water, sanitation and hygiene in the Global Burden of Disease Study (*Murray & Lopez, 1996*) was based on outcome. Relevant diseases, such as diarrhoea and parasitic diseases, were attributed by a certain percentage to likely modes of transmission, in this case water, sanitation and hygiene. In the same study, the disease burden attributable to outdoor air pollution was estimated by an exposure-based approach. Exposures were roughly estimated for the world's population, and then combined with the relevant dose-response relationships.

Diseases which are specifically related to one single risk factor will typically be used in an outcome-based approach. Examples include legionellosis, fluoridosis, methaemoglobinemia, trachoma, helminth infestations, hepatitis A, which are related to water, sanitation, food or hygiene. Risk factors which could reasonably be assessed through simple indicators at a large scale and which result in a number of unspecific disease outcomes may be assessed through an exposure-based approach. Examples include outdoor air quality, chronic exposure to lead, indoor air pollution, community noise, recreational water quality etc., which are related to various disease outcomes.

Example of approach using a causal inference model for assessing environmental disease burden

In environmental health, as in many other health areas, cause-to-effect models often involve a multitude of distal and proximal causes relating to each other, and a number of outcomes. To illustrate this type of application to the environment, a preliminary version of a causal web (intended to be only illustrative) is shown in Figure 2. A causal web is a cause-to-effect model, in which relationships among risk factors and between risk factors and disease outcomes are modelled. The more proximal a cause is to a disease outcomes, the more direct analytical relationship is expected with the health outcome. Distal causes operate through proximal causes on the disease outcome.

Figure 2: Causal web for chronic exposure to lead



Each link among causes, or between causes and disease outcome, could be characterized by a function. It may result in a mathematical model yielding results on disease burden if exposure data were introduced.

The causal web approach provides an interesting framework for disease burden assessment in environmental health. While distal parameters are often available at national level (from economic parameters assessed at national level, such as use of leaded gasoline, or from household surveys performed at large scale), proximal parameters characterizing individual exposure are more difficult to assess at a sufficient frequency to be representative for a study population (e.g. indoor air quality). Box 1 outlines the application of a causal web to the example of chronic exposure to lead.

Box 1: Example: Application of a causal web to exposure to lead

Current scientific evidence does not permit quantification of many of the relationships of the causal web. This is due to the lack of studies assessing multiple environmental exposures and blood lead levels (or disease outcomes) simultaneously. Dose-response relationships between blood lead levels and several disease outcomes are however well established. Although it is not possible to quantify the entire model, the overall structure of causal web can be used to develop a simpler method.

The most direct and best studied cause of 'health risk' associated with lead is certainly the blood lead level. Whenever such assessments are available for representative samples of a population with similar exposures, these can be used for directly estimating disease burden through the dose-response relationships.

Should blood lead levels not be available for a population, they could be estimated by more distal causes. Blood lead levels linked to environmental exposures such as concentrations in ambient air, concentration in drinking water, and lead in food. These are then linked to more distal causes such as the use of leaded gasoline, leaded pipes for drinking-water supply, and use of lead-glazed cooking utensils. If the link between such exposures and blood lead levels can be quantified, disease burden for populations without known blood lead levels could nevertheless be estimated, although the uncertainty increases considerably. A causal web containing certain quantitative relationships could permit a simplified disease burden assessment, feasible at national or regional level. Validity to other populations would need to be verified.

Some exposures are likely to be relatively uniform for a large proportion of the population (e.g. dense urban area in a country using leaded gasoline), and others will vary at the level of small communities (e.g. leaded drinking-water pipes) while they can still be described statistically.

Scenario-based approach

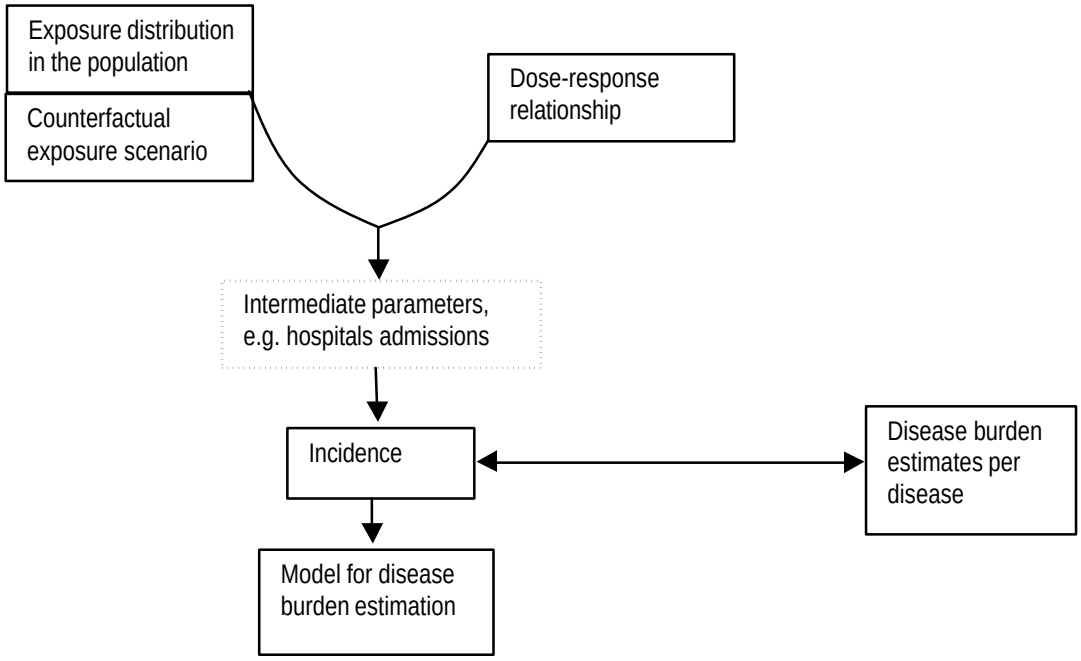
Where it is not feasible to describe key relationships between distal and proximal causes and/or disease outcomes, for example because of complex and competing relationships between exposures, a simplified approach can consist in the selection of a number of characteristic and representative exposure scenarios. The study population can be categorized into a number of defined exposure scenarios, corresponding to a specific health risk. For exposure to lead, such scenarios could include:

- Urban environment and degraded housing
- Urban environment without degraded housing
- Rural environment, no use of leaded pipes for drinking water
- Urban environment with use of leaded gasoline

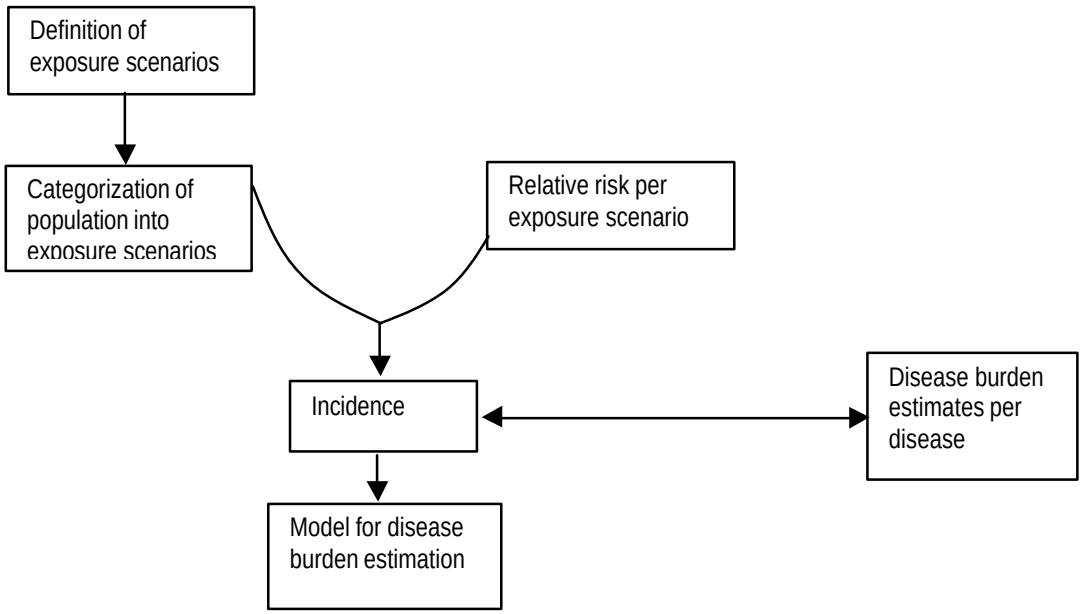
The basic steps required for disease burden estimation for the exposure-based and the scenario-based approach are shown in Figure 3.

Figure 3: Steps in disease burden estimation for exposure based and outcome based approaches

Exposure-based approach



Scenario-based approach



4. Choosing counterfactual scenarios

The estimation of disease burden from a specific risk factor requires that the exposure distribution of interest be compared to an alternative scenario, or *counterfactual scenario*. Counterfactual scenarios are 'what if' scenarios, as a thought experiment to describe a situation in which the exposure by the risk factor has been reduced or not occurred. Many counterfactual scenarios are potentially of interest, in particular when they are relevant for policies. Murray & Lopez outlined four scenarios of interest (*Murray & Lopez, 1999*), including the theoretical, plausible, feasible and cost-effective minima. Counterfactual scenarios can thus be chosen according to theoretical considerations (*theoretical minimum risk*), distributions observed in other environments, populations or regions (*feasible minimum risk*), the optimization of a specific parameter (e.g. *cost-effective minimum risk*) or according to situations resulting from a particular process (e.g. implementation of a policy). *Theoretical distributions* could consist of a theoretical minimum risk, being the distribution of exposure which would yield the lowest population risk. For environmental exposures, this would usually correspond to the absence of the risk factor altogether (e.g. absence of pollution), or a scenario where air pollution levels would not cause any health impacts. In general, the use of theoretical minimal scenarios seems relatively sound in the area of environmental health, as there is a high potential for pollution reduction by innovative technologies. The *feasible minimum risk* could for example correspond to an urban centre with a successful policy for clean air.

For policy relevance, it would be useful to define comprehensive scenarios which could lead to modified exposure distributions and disease burden, in particular when estimating the preventable burden.

The formulation of alternative scenarios may, however, become relatively complex, as they often imply a shift in environmental exposures rather than simple removal. For example, a reduction in exposure caused by a change in the energy policy should be compared to exposure distributions corresponding to alternative energy scenarios.

For the preventable fraction, estimating disease burden against clean air in the near future would not make much sense, as this cannot be achieved in many urban centres of the world. It would be more relevant for policy makers to be presented with estimates for alternative scenarios which can realistically be achieved in the given time frame. This does not preclude from taking into account creative scenarios, in which innovative technologies could see the day, in particular in the more distant future (e.g. 20 years).

Elaborate scenarios of the future environment have been developed, which could also be used as comparative scenario for the evaluation of disease burden. The Global Environmental Outlook (*UNEP, 1999*) describes future scenarios for every continent, based on demographic, economic and policy developments. Scenarios include the 'business-as-usual' scenario, a 'policy' scenario and an 'accelerated policy' scenarios, aiming at more sustainable developments.

McMichael *et al.* (*1998, 1999*) propose scenario-based forecasting of health impacts addressing global environmental changes such as climate change, the depletion of freshwater supplies or food-producing systems, or the accumulation of pesticides. More generally, they recommend extension beyond proximal, individual-level risk factors and application with a large scale social-ecologic systems perspective.

The International Institute for Applied Systems Analysis has also analysed and forecasted various environment scenarios (*Nakicenovic et al, 1998a; Stigliano, 1989*) and energy scenarios beyond 2050 (*Nakicenovic, 1998b*). The International Panel on Climate Change forecasts future emission scenarios. These scenarios address the issue of alternative scenarios in a comprehensive way, which may be relevant for assessing the impact of environmental changes on health.

Future scenarios to be used for the estimation of preventable burden should be characterised by the projection of the current scenario with unchanged policies or trends.

5. Parameters for environmental disease burden assessment at national level

A selection of parameters can be provided for the assessment of environmental disease burden at national level. For every risk factor, the following data sets can be proposed (example in Box 2):

- Selection of suitable indicators
- Frequency of indicator assessment
- Dose-response relationships or relative risk for exposure scenarios
- Applicability of the dose-response relationships

Box 2: Example of chronic exposure to lead

Parameters to assess at national level:

- Blood lead levels (ug/dl)
- Use of leaded gasoline (%)
- Use of lead-glazed ceramics (%)
- Households with leaded drinking-water pipes (%)
- Use of other leaded, region-specific products

6. Evaluation of uncertainty

Before estimating a disease burden, it should be established that there is sufficient evidence that the risk factor – disease relationship is causal. This concerns the dose-response relationship in the exposure-based approach, or the attributable fraction in the outcome-based approach. Every disease burden estimate should furthermore contain an estimate on the uncertainty interval around the estimate.

In certain cases, however, it would be relevant to undertake a disease burden estimate even without the sufficient evidence that a relationship is causal. This would be the case for risk factors potentially generating a very important and preventable disease burden, which could apply to climate change.

Acknowledging that the other sources of error can dwarf the statistical uncertainty in GBD estimates, it is still of use to consider methods that can be used to quantify statistical uncertainty. GBD estimates can be complicated functions of other estimates (e.g., estimates of incidence, prevalence and relative risks). Several techniques have been described for deriving inference for an estimates which is itself

a function of existing estimates, for instance meta-analysis of epidemiological data. The statistical techniques one could apply, *given the information exists*, are straightforward (Boxes 3 and 4; source: Alan Hubbard).

Box 3: Statistical uncertainty in GBD estimates

Let $\hat{q} = g(\vec{\mathrm{g}})$, where q is the GBD estimate, g is the vector of parameters and g is the function used to calculate q and the hat (^) notation indicates that estimates of the parameters are being used. The first step in deriving inference of the GBD estimate, such as confidence intervals for $\hat{q}$, is an estimate of the variance of $\hat{q}$. A delta-method approximation for the variance of $\hat{q}$ is:

$$\hat{\mathrm{var}}(\hat{q}) = [g'(\vec{\mathrm{g}})^T]\hat{VC}(\vec{\mathrm{g}})[g'(\vec{\mathrm{g}})]$$

where g' represents the vector of first partial derivatives of g w.r.t. g and $\hat{VC}(\vec{\mathrm{g}})$ is the estimated variance-covariance matrix of the vector $\vec{\mathrm{g}}$. If the estimates used to construct the GBD estimate are from independently drawn data, then one expects $\hat{VC}(\vec{\mathrm{g}})$ will be diagonal. Finally, if there is good reason to believe that $\hat{q}$ is normally distributed, for instance if *g(.)* is a linear function, then confidence intervals for q are easily derived. However, if one can not assume that $\hat{q}$ is normally distributed, then the joint distribution of $\vec{\mathrm{g}}$ needs to be specified and a Monte Carlo method can be used to estimate the distribution of $\hat{q}$.

Box 4: Monte Carlo Estimation of Uncertainty

An attractive method that works more generally than the traditional method discussed above uses the computer to construct a set of new GDB estimates, say q^*_i, *i=1,...,M*, and investigate uncertainty in $\hat{q}$ by simple graphs or summary measures (*see De Hollander, et al., 1999; Nurminen, et al., 1999*). The technique can be thought of as a generalization of calculating a GBD based on several scenarios, for instance, estimating a GBD for the minimum and maximum possible values of a risk factor prevalence. The technique works as follows: using the joint distribution of $\vec{\mathrm{g}}$ one random generates a vector of g^*_i, then calculate and record $q^*_i = g(g^*_i)$, and repeats this procedure M times. Then, the confidence interval for q can be derived straightforwardly from this computer generated sample.

The above discussion assumes that the distribution of $\vec{\mathrm{g}}$ is known. This probably is only true if one has derived the necessary information for the parameters used in the GBD estimates from independent studies, and thus one can assume that the estimates contained in $\vec{\mathrm{g}}$ are at least roughly statistically independent. Often, it will be the case that the information on the distribution of $\vec{\mathrm{g}}$ will be limited and consist of a mix of reported standard errors and simple regions of plausibility (e.g., the prevalence of a risk factor lies somewhere between 5 and 20%). The Monte Carlo technique can still be used, but one can not interpret the distribution of the q^* as an approximation of the distribution of $\hat{q}$, and thus, one can not construct confidence intervals for q. However, the Monte Carlo method can still provide a rough estimate of the level of uncertainty of $\hat{q}$ and ranges of plausible values for q.

7. Risk factors which are difficult to assess at large scale

At national, regional or global scale, it will be difficult, if not impossible, to describe the whole picture of environmentally-caused disease. This is due to the following reasons, some of which may change as knowledge around certain issues develops:

- Exposure is difficult to assess for local 'events', which are not representative for a larger scale (e.g.industrial emissions or hazardous waste)
- Evidence is still relatively low for establishing certain dose-response relationships (e.g. noise)
- Relationships and competing risks between risk factors are often complex, and influence the dose-response relationship according to the scenario (e.g. in the example of water, sanitation & hygiene, a dose-response relationship may become 'saturated' when the level of faecal-oral pathogens in the environmental is very high)

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Annex 2: List of Participants

Dr Ruth H. Allen
Health Effects Division
Office of Pesticide Programs
USEPA 7509-C Ariel Rios Bldg
1200 Pennsylvania Ave.
Washington, D.C. 20460
USA
Tel. : +1 703 305 7191
Fax : + 1 703 305 5147
E-Mail : allen.ruth@epa.gov
and ra78n@nih.gov

Professor Vladimir Bencko
Head, Institute of Hygiene & Epidemiology
First Faculty of Medicine
Charles University of Prague
Studnickova 7
CZ 128 00 Prague 2
Czech Republic
Tel/Fax +420224919967
E-mail: vbencko@lf1.cuni.cz

Dr. C. Pedro Mas Bermejo
Director General
Instituto Nacional de Higiene, Epidemiologia y Microbiologia
Infanta no. 1158
e/. Llinas y Clavel
La Habana
CP 10300
Cuba
Tel. : (537) 781479 786755 705531-34
Fax : (537) 662404
E-Mail : director@inhem.sld.cu

Dr Rebecca Calderon
MD-58C
U.S. Environmental Protection Agency
Research Triangle Park, NC 27711
USA
Tel. : +1 919 966 0617
Fax : +1 919 966 0655
E-Mail : calderon.rebecca@epa.gov

Dr Diarmid Campbell-Lendrum
Disease Control and Vector Biology Unit
Infectious Diseases Department
London School of Hygiene and Tropical Medicine
Keppel Street
London WC1E 7HT
United Kingdom
Tel. : +44 207 927 2497
Fax : +44 207 580 9075
E-Mail : Diarmid.Campbell-Lendrum@lshtm.ac.uk

Dr Augustinus de Hollander
Laboratory for Exposure Assessment & Environmental Epidemiology
National Institute of Public Health and the Environment (RIVM)
P.O. Box 1
3720 BA Bilthoven
The Netherlands
Tel. : +31 30 274 4535
Fax : +31 30 274 4407
E-Mail : AEM.de.Hollander@rivm.nl

Dr Kristie L. Ebi
Manager, Epidemiology
Electric Power Research Institute (EPRI)
3412 Hillview Ave. Tel.: +1 650 855 2735
Palo Alto, CA 94304 Fax: +1 650 855 2950
USA E-mail: krisebi@epri.com

Dr Joseph Eisenberg
Environmental Health Sciences & Epidemiology
University of California, Berkeley
School of Public Health
140 Warren Hall # 7360 Tel. : (510) 643-9257
Berkeley, CA 94720-7360 Fax : (510) 642-5815
USA E-Mail : eisenber@socrates.berkeley.edu

Dr Lorna Fewtrell
Centre for Research into Environment and Health
5 Quakers Coppice
Crewe Gates Farm
Crewe Tel:+44 1270 250583
Cheshire CW1 6FA Fax:+44 1270 589761
UK E-mail: lorna@creh.demon.co.uk

Dr Jay M. Fleisher
United States Navy Environmental Health Center
2510 Walmer Avenue Tel. : +1 757 462 5417
Norfolk, VA 23513 Fax : +1 757 444 9691
USA E-Mail : fleisherj@nehc.med.navy.mil

Dr Keith Florig
Risk Analysis Group
Department of Engineering and Public Policy
Carnegie Mellon University Tel: +1 412 268 3754
Pittsburgh, PA 15213-3890 Fax: +1 413 581 6294
USA E-mail: florig@cmu.edu

Dr Scott Grosse
Centers for Disease Control & Prevention (CDC)
National Center for Environmental Health
4770 Buford Highway, Mail Stop F29 Tel. : +1 770 488 4575
Atlanta, GA 30341
USA E-Mail : sgg4@cdc.gov

Dr Heraline E. Hicks
Great Lakes Program Director
Agency for Toxic Substances and Disease Registry
1600 Clifton Road, N.E., Mail Stop E 29 Tel. : +1 404 639 5097
Atlanta, Georgia 30333 Fax : +404 639 6315
USA E-Mail : heh2@cdc.gov

Dr Alan Hubbard
School of Public Health
University of California at Berkeley
Division of Environmental Health Sciences
140 Warren Hall No. 7360
Berkeley, CA 94720-7360
USA
Tel. : +1 510 642 8365
Fax : +1 510 642 5815
E-Mail : hubbard@stat.berkeley.edu

Dr Wieslaw Jedrychowski
Head, Chair of Epidemiology and Preventive Medicine
Jagrèllomiom University
7, Kepernika str.
Krakow
Poland
Tel.: +48 12 423 1003
Fax : +48 12 422 8795
E-mail: mydedryc@cyf-kr.edu.pl

Professor David Kay
CREH
University of Wales
Llandinam Building
Aberystwyth
Ceredigion, Wales
SA23 2DB
UK
Tel. : +44 1970 622634
Fax : +44 1570 423565
E-Mail dvk@aber.ac.uk
and dave@crehkay.demon.co.uk

Professor Tord Kjellström
Director, New Zealand Environmental and Occupational Health Research Centre (NEOH)
Division of Community Health
The University of Auckland
Private Bag 92019
52-54 Grafton Road
Auckland
New Zealand
Tel. : +64 9 373 7599 ext. 2328
Fax : +64 9 373 7624
E-Mail : t.kjellstrom@auckland.ac.nz

Dr Aparna M. Koppikar
Medical Officer/Epidemiologist
NCEA-Washington (8623D)
US Environmental Protection Agency
1200 Pennsylvania Avenue
Washington, D.C. 20460, USA
Tel. : 202-564-3242
Fax : 202-564-0079
E-Mail : koppikar.aparna@epa.gov

Sari Kovats
Research Fellow
Dept of Epidemiology and Population Health
London School of Hygiene and Tropical Medicine
Keppel Street
London WC1E 7HT
United Kingdom
Tel. : +44 20 7612 7844
Fax : +44 20 7580 6897
E-Mail : s.kovats@lshtm.ac.uk

Dr Erik Lebret
National Institute of Public Health and the Environment
Laboratory of Exposure Assessment
P.O. Box 1
3720 BA Bilthoven
The Netherlands
Tel. : +31-30-274 4194
Fax : +31-30-274 4451
E-Mail : erik.lebret@rivm.nl

Professor A.J. McMichael
Department of Epidemiology and Population Health
London School of Hygiene and Tropical Medicine
Keppel Street
London WC1E 7HT
U.K.
Tel. : (020) 7927.2254
Fax : (020) 7580.6897
E-Mail : tony.mcmichael@lshtm.ac.uk

Sumi Mehta
School of Public Health
Division of Environmental Health Sciences
140 Warren Hall # 7360
Berkeley, CA 94720-7360
USA
Tel. : (510) 643-5580
Fax : (510) 642-5815
E-Mail : sumim@uclink4.berkeley.edu

Dr Patricia A. Murphy
U.S. Environmental Protection Agency
National Center for Environmental Assessment
MS-272
2890 Woodbridge Ave.
Edison, New Jersey 08837-3679
USA
Tel. : (732) 906-6830
Fax : (732) 906-6845
E-Mail : murphy.patricia@epa.gov

Dr Harris Pastides
School of Public Health
University of South Carolina
Columbia, SC 29208
USA
Tel. : (1) 803 777 5032
Fax : (1) 803 777 4783
E-Mail : hpastides@sph.sc.edu

Dr Paulina Pino
Division of Environmental and Occupational Health
School of Public Health
Faculty of Medicine
University of Chile
Independencia 939
Santiago de Chile
Chile
Tel. : (56-2) 678-6152
Fax : (56-2) 735-5582
E-mail: ppino@machi.med.uchile.cl

Dr Isabelle Romieu de Hernandez
Regional Advisor in Environmental Health, PAHO/WHO
Instituto nacional de salud Publica
Av. Universidad no. 655
Col. Sta. Ma. Ahuacatitlan
C.P. 62508
Cuernavaca, Morelos
Mexico
Tel. : (52) (73) 11 01 11 Ext. 2200
Fax : (52) (73) 11 11 48
E-mail: iromieu@insp3.insp.mx

Professor Kirk Smith (unable to attend)
School of Public Health, University of California
140 Warren Hall # 7360
Berkeley, CA 94720-7360
USA
Tel: +1 510 643 0793
Fax: +1 510 642 5815
E-mail: krksmith@uclink4.berkeley.edu

Professor Stanislaw Tankowski
Head, Department of Environmental Health Hazards
Nofer Institute of Occupational Medicine
8, Sw. Teresy st. Tel.: +48 42 631 4842
90-950 Lodz Fax: +48 42 631 4572
Poland E-mail: tarko@imp.lodz.pl

Dr Shilu Tong
Centre for Public Health Research
Queensland University of Technology Tel.: +61 7 3864 5437
Kelvin Grove, Qld. 4059 Fax: +61 7 3864 5941
Australia E-mail: s.tong@qut.edu.au

Professor John E. Vena
University at Buffalo
State University of New York
Department of Social and Preventive Medicine
School of Medicine and Biomedical Sciences
Farber Hall Rm. 270
3435 Main St., Bldg. 26 Tel. : (716) 829.2975 Ext. 602
Buffalo, NY 14214-3000 Fax : (716) 829-2979
USA E-Mail : jvena@buffalo.edu

Dr Susan T. West
Environmental Health Education and Outreach
Physicians for Social Responsibility
1101 Fourteenth Street, NW
Suite 700 Tel. : (202) 898-0150 Ext. 224
Washington, DC 20005 Fax : (202) 898-0172
USA E-Mail : swest@psr.org

WHO

Dr Roberto Bertollini
Global Change and Health
WHO European Centre for Environment and Health
Via Francesco Crispi, 10 Tel. : +39 06 487 2042
I-00187 Rome Fax : +39 06 487 7599
Italy E-Mail : rbe@who.it

Xavier Bonnefoy
Division of Technical Support and Strategic Development
World Health Organization
Regional Office for Europe
8 Scherfigsvej Tel: +45 39 17 1427
2100 Copenhagen Fax : +45 39.17 1818
Denmark E-mail: xbo@who.dk

Dr Carlos Corvalán
World Health Organization
Department of Protection of the Human Environment (PHE)
20, avenue Appia — Tel: +41 22 791 4208
CH-1211 Geneva 27 — Fax: +41 22 791 41 27
Switzerland — E-mail: corvalanc@who.ch

Dr Dafina Dalbokova
EH Information Systems
WHO European Centre for Environment and Health
Bilthoven Division — Tel.: +31 30 2295 324
P.O. Box 10, 3730 AA De Bilt — Fax: +31 30 2294 120
Netherlands — E-mail: dda@ecb.who.nl

Majid Ezzati
Global Programme on Evidence for Health Policy (GPE)
World Health Organization — Tel. : +41 22 791 23 69
CH-1211 Geneva 27 — Fax : +41 22 791 43 28
Switzerland — E-Mail: ezzatim@who.ch

Dr Luiz Augusto Galvão
Regional Advisor, Environmental Quality Program-HEQ
Health and Environment Division-HEP
Pan American Health Organization-PAHO
Regional Office for the Americas of the World Health Organization-WHO
525, 23rd Street, NW, Room 535 — Tel: +1(202) 974 3156
Washington, DC-20037-2895 — Fax: +1(202) 974 3645
USA — E-mail: galvaolu@paho.org

Dr Bettina Menne
Global Change and Health (HIA-GCH)
WHO European Centre for Environment and Health
Via Francesco Crispi, 10 — Tel.: +39 06 487 7546
I-00187 Rome — Fax: +39 06 487 7599
Italy — E-mail: bme@who.it

Annette Pruess
World Health Organization
Department of Protection of the Human Environment (PHE)
20, avenue Appia — Tel: +41 22 791 35 84
CH-1211 Geneva 27 — Fax: +41 22 791 41 59
Switzerland — E-mail: pruessa@who.ch

Francesca Racioppi
Transport
WHO European Centre for Environmental Health
Via Francesco Crispi, 10 — Tel.: +39 06 487 7545
I-00187 Rome — Fax: +39 06 487 7599
Italy — E-mail: frr@who.it

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Annex 3: Agenda

23 August

9:00-9:30 Aims, objectives & introduction

Welcome and background: Carlos Corvalán (10 min)
Aims, objectives & concept: Annette Pruess (15 min)

9:30-10:30 Framework & challenges

CRA framework: Majid Ezzati (15 min)
Challenges in a national study: Guus de Hollander (10 min)

10:30-11:00 Break

11:00-12:30 Concepts and examples

Selected conceptual issues: Lorna Fewtrell (20 min)
- Use of probability-density functions
- Scenario-based approach

Practical guide – IAP example: Sumi Mehta (10 min)
Break-up into working groups

12:30-13:30 Lunch

13:30-15:00 Group work – concepts and examples

15:00-15:30 Break

15:30-17:30 Describing the level of uncertainty and evidence

Uncertainty: Alan Hubbard, Majid Ezzati (10 min)
Level of evidence – considerations: Jay Fleisher (10 min)
Level of evidence in practice: Sari Kovats (10 min)

24 August

9:00-10:30 Report of the group work – concepts and examples

10:30-11:00 Break

11:00-13:00 Discussion and further steps and improvements

Proposed working groups:

- Water & sanitation
- Air quality
- Global environment
- Chemical exposures

Tasks for the working groups

- Counterfactual scenarios
- Strength of evidence
- Geographical resolution
- Comments on proposed approaches
- Way forward
- Other issues?

Annex 4.1: Comparative Risk Assessment in the Global Burden of Disease Study and the Environmental Health Risks

Majid Ezzati

Global Programme on Evidence for Health Policy
World Health Organization

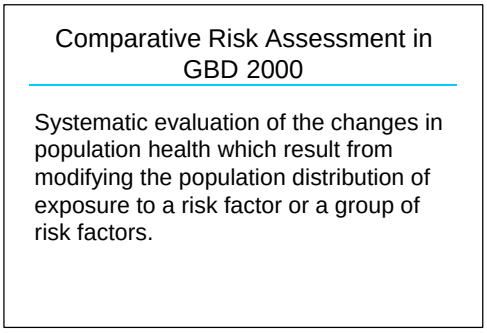
Comparative Risk Assessment is defined as the systematic evaluation of the changes in population health which result from modifying the population distribution of exposure to a risk factor or a group of risk factors.

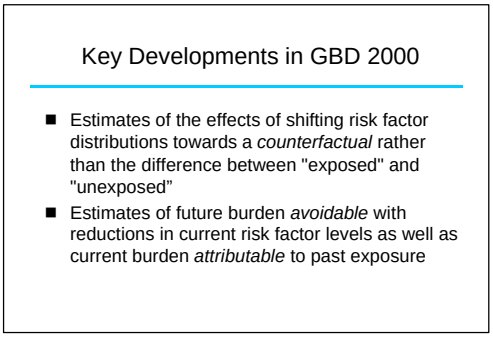
Burden of Disease (or any measure of population health or disease) can be classified based on:
1) Outcome or disease type
2) Risk factors that cause disease

GBD project provided global estimates for both classifications with a central goal of increased comparability in input (exposure) and output (disease burden) formats as well as in methodology.

Key developments for GBD 2000 are considerations about:

1) Characterization of population exposure by using counterfactual (alternative) exposure distribution as the basis of comparison instead of zero. Murray and Lopez (1999) introduce 4 categories of counterfactual distributions: theoretical minimum (exposure distribution that results in minimum population risk), plausible minimum (exposure distribution that is imaginable), feasible minimum (exposure distribution that has been observed in a population), and cost-effective minimum.





2) Timing of exposure and health impacts by considering the burden attributable to previous exposure and burden avoidable with reductions in current exposure.

Analysis strategy:

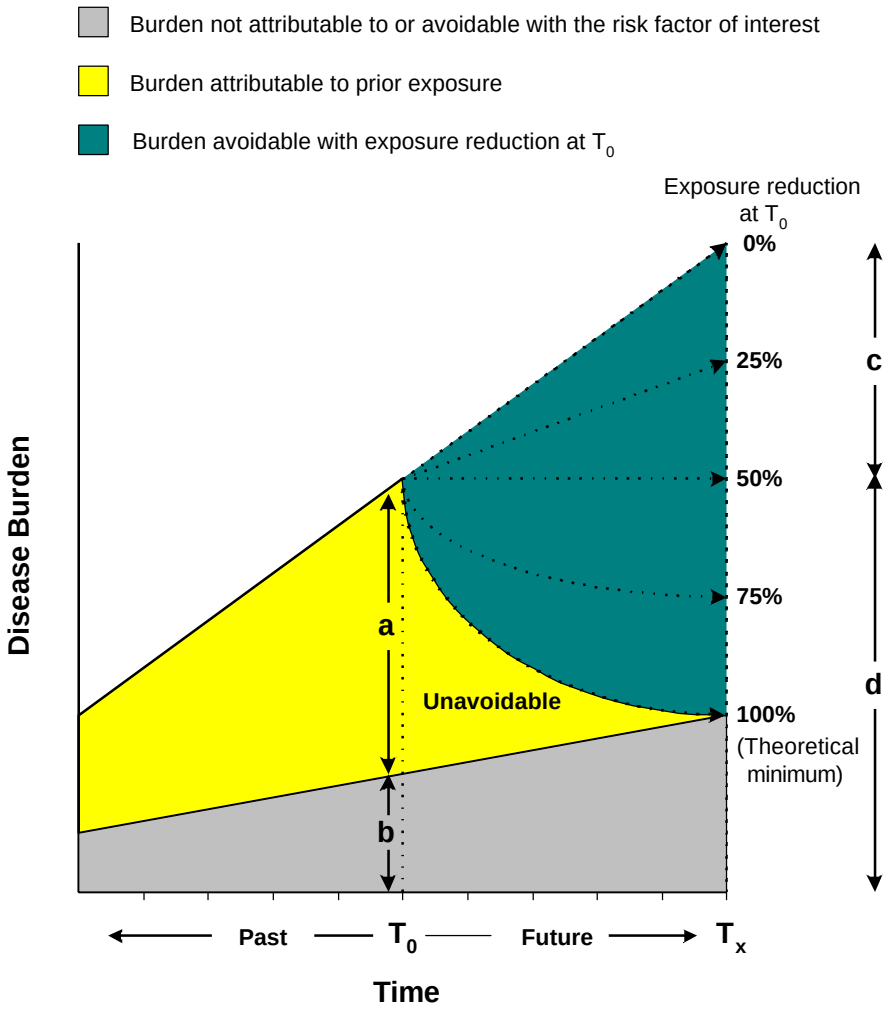
1) Provide estimates of population distribution of exposure (current and theoretical minimum) for all regions and demographic sub-groups.

2) Consider standard incremental transitions from current towards the theoretical minimum: the distributional transition.

3) Among these choose plausible, feasible, and cost effective distributions.

Exposure combined with exposure-response relationship results in attributable/avoidable fraction, which combined with burden of disease estimates results in attributable/ avoidable burden.

Attributable and avoidable burden



a = disease at T_0 attributable to prior exposure
b = disease at T_0 not attributable to the risk factor (caused by other factors)
c = avoidable disease at T_x with a 50% exposure reduction at T_0
d = disease at T_x after a 50% reduction in risk factor
Attributable fraction at T_0 due to prior exposure = a / (a + b)
Avoidable fraction at T_x due to 50% exposure reduction at T_0 = c / (c + d). In general avoidable burden at T_y due to exposure reduction at T_0 is given by the ratio of the green area to total burden at T_y. Dashed arrows represent the path of burden after a reduction at T_0. Policy choices for feasible, plausible, and cost-effective exposure reductions can be chosen from the range of distributional transitions.
Note that the burden attributable to other risk factors (grey area) may be decreasing, constant, or increasing over time. The last case is shown in the figure.

Some of the methodological issues that arise

Methodological issues:

1) Characterization of distributional transition.
2) Choosing the theoretical minimum.
3) Temporal dimension of exposure, exposure accumulation, and risk reversibility.
4) Analysis of uncertainty especially estimates of uncertainty in input parameters.
5) The impacts of changes in multiple risk factors.

Criteria for choice of 18 risk factors (behavioural, environmental, and physiological):

1) Potential contribution to the global burden of disease.
2) Not too specific or too broad.
3) High likelihood of causality.
4) Availability of reasonably complete data.
5) Potentially modifiable through policy

Some of the characteristics of environmental risk factors:

1) Limited data on exposure especially in developing countries . By definition, exposure assessment for environmental risk factors requires dealing with an interface outside the individual.
2) Many environmental risk factors have effects that are concentrated geographically and/or socioeconomically.
3) Many interventions can be combined with other policies such as energy policy, conservation policy, etc.

Collaborators:

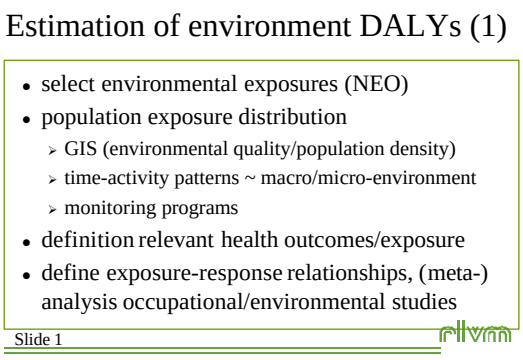
1) WHO headquarters and regions.
2) National and international health organizations.
3) Universities and research centres.
4) Secretariat: EBD/ GPE at WHO and CTRU at the University of Auckland
web-site: http://www.ctru.auckland.ac.nz/cra

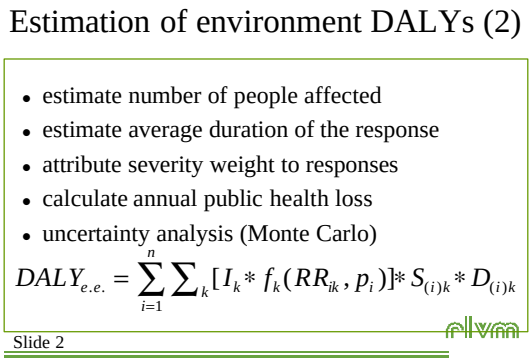
Annex 4.2: An aggregate public health indicator of the impact of multiple environmental exposures

AEM de Hollander, JM Melse, E Lebret, PGN Kramers
National Institute of Public Health and the Environment (RIVM), NL

Some five years ago, we were requested to estimate public health loss attributable to environmental degradation by our executive director. People were beginning to loose interest in environmental issues, probably because there was no clear picture of the environmental health domain: data such as probabilistic risk estimates, borderline significant risk elevations of very rare cancers are not sufficient to adequately represent the health risks of the population. Assessment along the line of the Global Burden of Disease study were requested, based on the disability adjusted life years approach. Although this approach appeared difficult, we started off with traditional health impact assessment methodology to see hoe it could be integrated with the DALY-approach.

We selected around 20 environmental exposures for which reasonable data were available regarding outcomes that could in some way be related to public health endpoints. Main steps of the undertaking are described in slides 1 and 2 below.





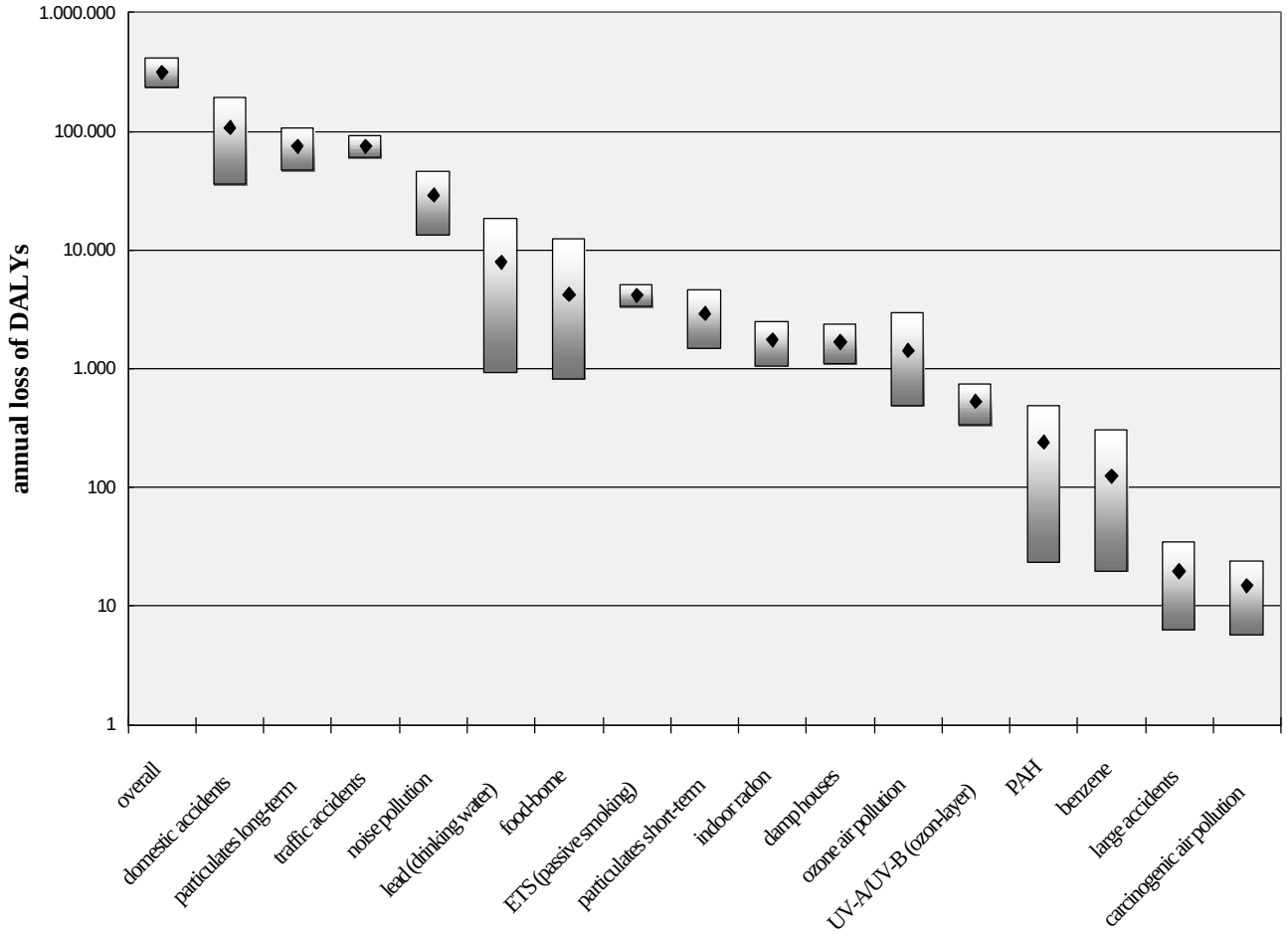
Calculated attributable fractions were combined with data on outcome incidence in the Dutch population to calculate the number of annual cases. The duration of responses were estimated from epidemiological studies, prevalence/incidence figures (PHSF), life table analysis and sometimes expert judgement. Composite severity weights were derived from our national and in some case the global burden of disease study in which protocoled formal weighing exercises were performed involving panels of experienced physicians.

Finally environmental DALYs were calculated by simply multiplying the number of cases with duration and severity estimates. We performed a simple MonteCarlo Analysis to estimate the uncertainty involved. We're currently exploring more sophisticated ways of doing so. Input-parameters are treated as random variables, for which a probability distribution was estimated; distributions for output variables are estimated through random sampling from the distribution of risks.

A rather provisional overall picture of environmental disease burden in the Netherlands resulted from this exercise (see slide 3). Annual health loss in terms of DALYs is on a logarithmic scale. The bars represent the uncertainty interval between the 5- and the 95-

percentile of the uncertainty distribution. When considering these numbers, it is important to keep in mind the uncertainties involved.

Slide 3: Environmental Disease burden in the Netherlands



Some of the main results are summarized in Slide 4. It is not the aim of this presentation to address uncertainties, assumptions and default values, causality and mechanisms of action, poor resolution of epidemiological studies and exposure assessment problems in detail. Some of these challenges are briefly listed in Slide 5. Selected challenges or issues of concern are discussed hereafter:

- The relatively very high disease burden we attributed long term exposure to particulates was based on the results of only two American cohort studies, which were not without controversies. Fortunately, a Dutch study recently confirmed these results. One challenge consists certainly in where to place the threshold of considering the evidence as too weak as a basis for burden of disease estimates.

Results

- large burden attributable to accidents
- significant burden attributable to particulates (long term) and noise
- significant burden indoor air pollution
- share environmental exposures total health loss (2,6 million/year: 175/1000 inhabitants)
  - around 9% (accidents included)
  - around 4% (accidents excluded)

Slide 4

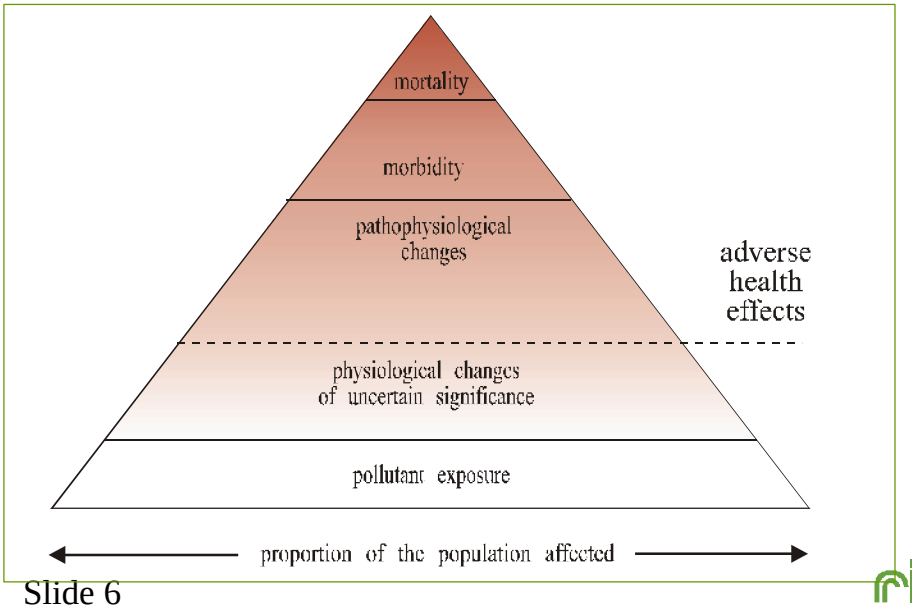
Challenges 1

- Health Response Assessment (exposure-response)
  - causality/mechanism
  - attributable proportion (aggravation vs. initiation)
  - poor resolution of (epidemiological) research
  - response definition (clinical significance)
  - lack of knowledge, data (toxicology)
  - promising cases: (indoor/outdoor) air pollution, noise, infectious disease (food-, water-borne)

Slide 5

- How will the proportion of disease burden attributable to environmental health in the original DALY-paradigm be estimated? One way would consist in estimating disease specific burden and then, on the basis of epidemiological studies, estimate the burden that can be attributed to certain risk factors. The problem however is that in most of the well documented cases environmental exposures are only causing aggravations of symptoms of preexisting disease (air pollution, noise, indoor air pollution). A nice representation of this phenomenon has been proposed by the ATS back in 1986 (Slide 6).

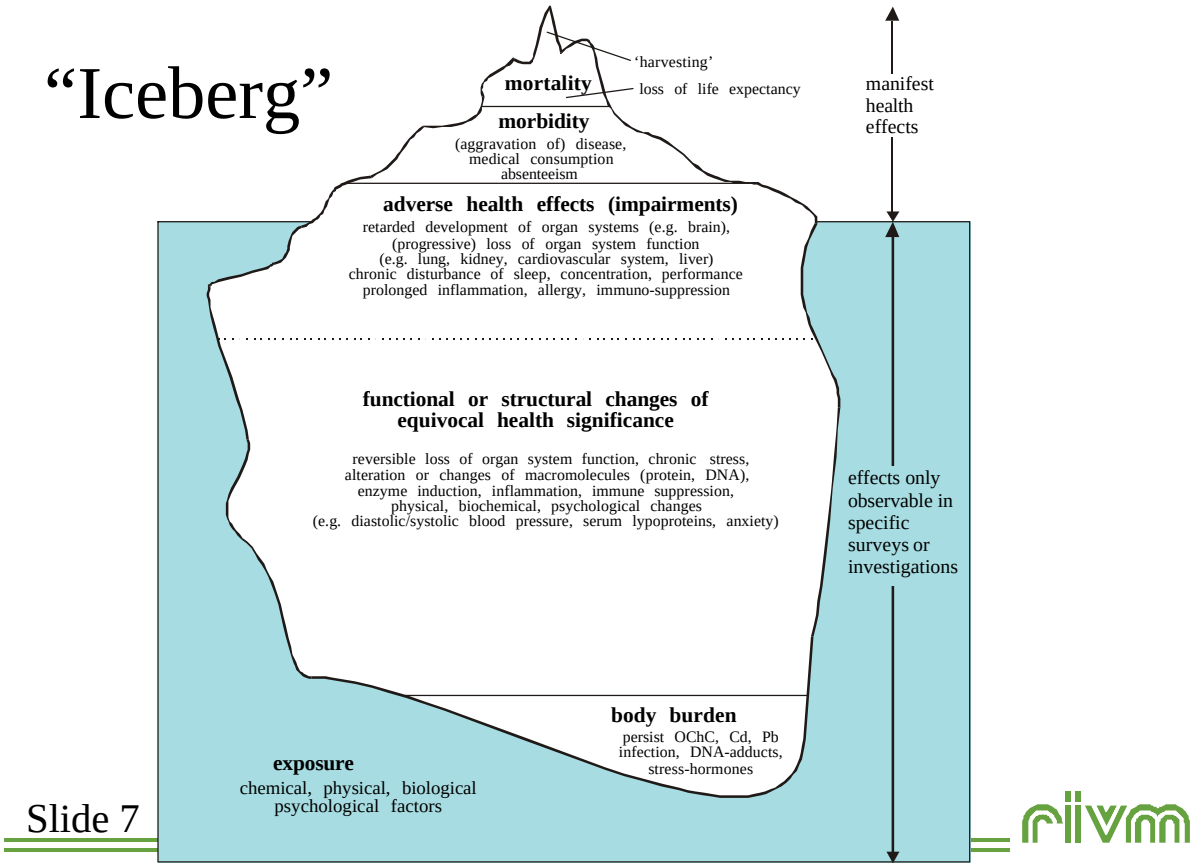
Pyramid model (ATS, 1989)



Slide 6

This pyramid model probably represents quite well the reality: The entire population is exposed (although large difference in personal exposure intensity may exist due to divergent time activity patterns, micro-environmental concentrations); physiological changes may affect most exposed, such as small, transient deficits of lung function, pulmonary inflammation; the more susceptible

people e.g. with preexisting respiratory disease may suffer from various disease outcomes. The measurement instruments are then randomly applied to parts of this pyramid, and we will find associations with air or noise pollution levels. We will, however, not really know what would be the effect on the total disease burden. A more detailed version of the pyramid is displayed in Slide 7.



- To interpret the huge toxicological data base the situation is probably even more difficult. Exposure to pesticides, persistent organic pollutants, and similar products may be have very important public health consequences. Toxicological indications for mutagenic, carcinogenic, immuno- reproductive toxic, hormone disrupting activity etc. are however very difficult to translate into real-life disease incidence.
- How do we deal with social-psychological responses such as annoyance, sleep disorders, disturbance of daily activities, small IQ deficits that don't have an ICD code but are still affecting quality of life? And where do we draw the line?
- How do we translate available epidemiological response indicators into disease states that can be used in the Global Burden of Disease context.

Some additional challenges are shortly listed in Slide 8.

An important challenge for this group would be how to deal with the issues addressed above.

Challenges 2

- Weighing ‘Health’ Responses
  - attributing weights (e.g. EuroQol 6D)
  - social versus clinical responses
  - health risk perceptions
- Dealing with uncertainty
  - Measurements, statistics etc.
  - Constructs, models
  - Assumptions

Slide 8 rivm

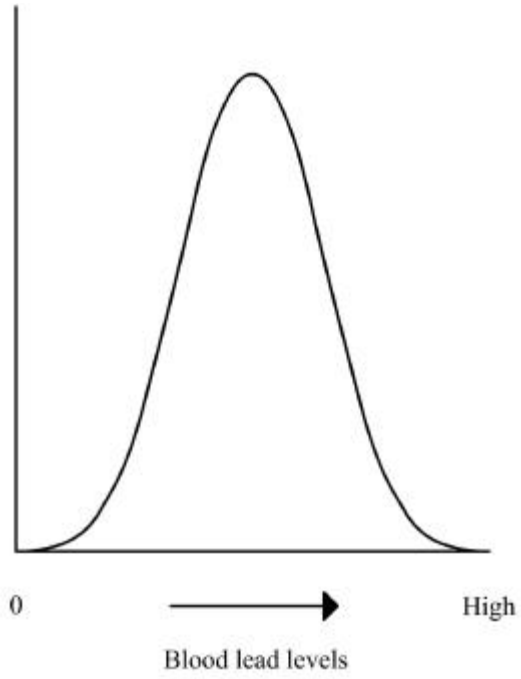
Annex 4.3: Burden of disease and selected conceptual issues: food for thought

Lorna Fewtrell
Centre for Research into Environment and Health, UK

To date, very little information has been gathered specifically to look at disease burden, especially at the global scale. For this reason a variety of approaches need to be utilised to make best use of what data are available. This presentation examines two approaches and focuses on some methodological considerations.

Lead – an exposure-based approach

There are numerous reports in the literature, from around the world, detailing the levels of lead in selected human populations. The most commonly assessed parameter is blood lead (BPb). Using a database of such references (prepared and undergoing development by CDC) it is proposed to establish exposure to lead on a regional basis for children and adults using a probability density function approach. In this way, $\log_{10}$ transformed mean values from individual studies are combined to producing an overall mean and standard deviation. These figures are used to form a probability density function representing blood lead levels as shown below.



Disease burden can be calculated by mapping the health effect thresholds onto the exposure curve, giving a series of 'slices'. For example, it is estimated in the ATSDR report that IQ effects occur at 10 μg/dl BPb. By inserting this cut off point and 'forcing' the curve to represent 1000 people, the area under the curve above the cut off line represents those affected by IQ deficit.

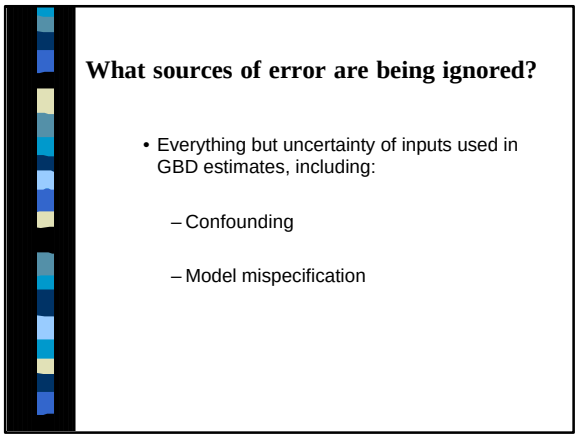
Water, sanitation and hygiene – creating a scene

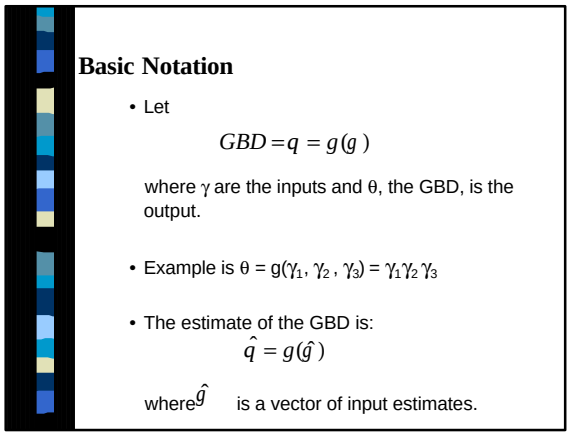
A scenario approach is proposed for determining the level of diarrhoea relating to WSH. Exposure scenarios are based upon access to basic or improved water supply and sanitation facilities and also approximate diarrhoea prevalence (high, medium or low). These categories will be combined to form a single, global, matrix. Relative risk values relating to each combination will be determined from the literature.

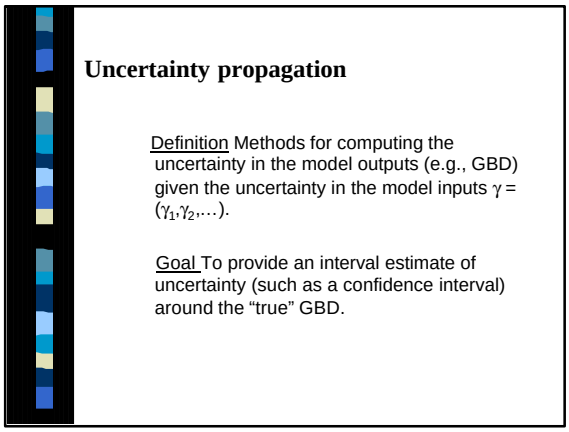
Annex 4.4: Statistical uncertainty in burden of disease estimates

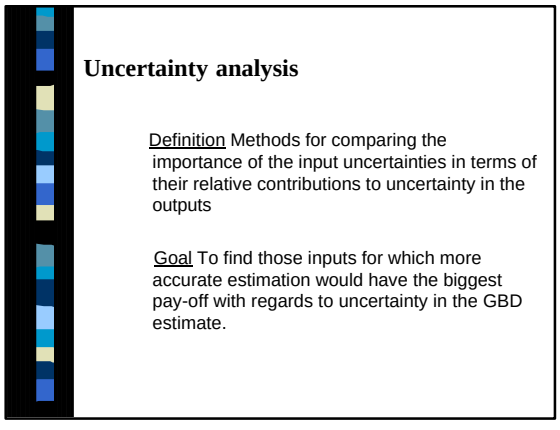
Alan Hubbard
University of California at Berkeley, School of Public Health, USA

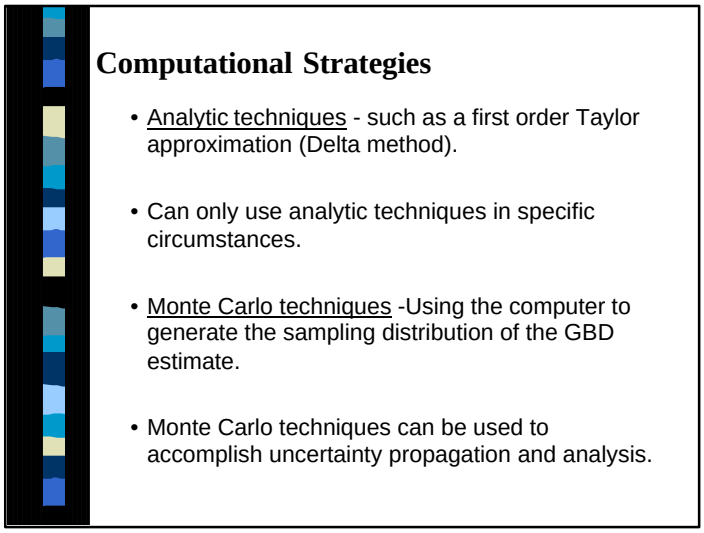
There are several sources of error that enter burden of disease estimates, including sources of bias (confounding, selection bias, etc.) and statistical error. Acknowledging that the other sources of error can dwarf the statistical uncertainty in burden of disease estimates, it is still of use to consider methods that can be used to quantify the statistical uncertainty. Disease burden estimates are somewhat complicated functions of other estimates (e.g., estimates of incidence, prevalence and case-fatality rates). A large body of literature exists on estimating statistical uncertainty of an estimate which is itself a function of existing estimates, for instance meta-analysis of epidemiological data. The risk assessment literature has several approachable guides to the characterization of uncertainty, particularly Finkel (1990) and Morgan and Hendrion (1990). Two issues will be discussed below: uncertainty propagation and uncertainty analysis.











Uncertainty propagation

Let $\hat{q} = g(\hat{\gamma})$, where $\hat{q}$ is the burden of disease estimate, $\hat{\gamma}$ is the vector of parameters and g is the function used to calculate $\hat{\gamma}$ and the hat(^) notation indicates that estimates of the parameters are being used.

Analytic techniques

The first step in deriving inference of the GBD estimate, such as confidence intervals for $\hat{q}$, is an estimate of the variance of $\hat{q}$. A Taylor approximation suggests,

$$\hat{s}^2 = \hat{\text{var}}(\hat{q}) = [g'(\hat{\gamma})]^T V\hat{C}(\hat{\gamma})[g'(\hat{\gamma})]$$

where g' represents the vector of first partial derivatives of g w.r.t g and $V\hat{C}(\hat{\gamma})$ is the estimated variance-covariance matrix of the vector $\hat{\gamma}$. If the estimates used to construct the GBD estimate are from independently drawn data, then one expects $V\hat{C}(\hat{\gamma})$ will be diagonal. Finally, if there is good reason to believe that $\hat{q}$ is normally distributed, for instance if *g(.)* is a linear function, then confidence intervals (CI's) for q are easily derived as:

$$(1-a)\,CI \text{ for } q \text{ is } \hat{q} \pm z_{1-a/2}\hat{s}$$

where $z_{1-a/2}$ is the 1-$a/2$ quantile of the standard normal distribution (note, that if log(g(.)) is a linear function of the inputs, then one could use this method to construct the confidence interval on the log scale) . However, if one can not assume that $\hat{q}$ is normally distributed, then the joint distribution of $\hat{\gamma}$ needs to be estimated. From this point, one can either derive the distribution of $\hat{q}$ by analytical (when possible) or numerical integration, or a Monte Carlo method can be used to estimate the distribution of $\hat{q}$.

Monte Carlo Estimation of Uncertainty

An attractive method that works more generally than the traditional method discussed above uses the computer to construct a set of new GDB estimates, say q^*_i, $i=1,...,M$, and investigate uncertainty in $\hat{q}$ by simple graphs or summary statistics (for examples see Hollander, et al., 1999; Nurminen, et al., 1999). The technique can be thought of as a generalization of calculating a GBD based on several scenarios, such as estimating a GBD for the minimum and maximum possible values of a risk factor. Specifically, 1) from the estimated joint distribution of $\hat{\gamma}$, the computer generates a random vector of g^*_i, 2) the computer calculates $q^*_i = g(g^*_i)$ and 3) repeats this M times. Then, the confidence interval for q can be derived from the empirical quantiles of the q^*_i. For instance, if M=1000 (1000 q^*_i are produced from a 1000 draws from the joint distribution of $\hat{\gamma}$), and the q^*_i are subsequently ranked from smallest to largest, then the 95% confidence interval would by the 25th and 975th of the ranked q^*_i.

Monte Carlo Technique

- Want to estimate the distribution of $\hat{q}$, $\text{dist}(\hat{q})$, in order to get statistical inference.
- However, depending on the complexity of g or the distribution of the estimated inputs, this will often be difficult or impossible to do analytically.
- However, one can use Monte Carlo (MC) techniques to generate samples from $\text{dist}(\hat{q})$.
- MC Can be thought of as a generalization of calculating a GBD for several scenarios, e.g., worst-case, best case, expected.

Monte Carlo Technique

Recipe

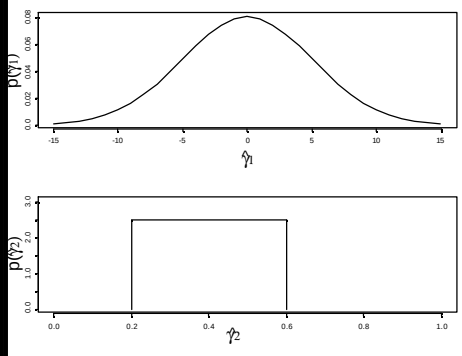
- Generate a set of new GBD estimates, say q_i^*, $i=1,...,M$ by randomly drawing from $P(\hat{g})$, the joint sampling distribution of the estimated input parameters.
- For each of the M repeated draws, calculated and record

$$q_i^* = g(g_i^*),$$

where g_i^* is a random draw from $P(\hat{g})$.

What does the joint sampling distribution of the inputs, $P(\hat{g})$, look like?

- Rarely will all the inputs consist of previous estimates with known sampling distributions.
- Typically, the information on the inputs will consist of estimates with reported standard errors and some educated guesses with ranges.
- Thus, $P(\hat{g})$ most likely will be expressed as product of marginal distributions which will be chosen to reflect the nature of the input estimates: $P(g) = P(g_1)P(g_2)\cdots P(g_p)$

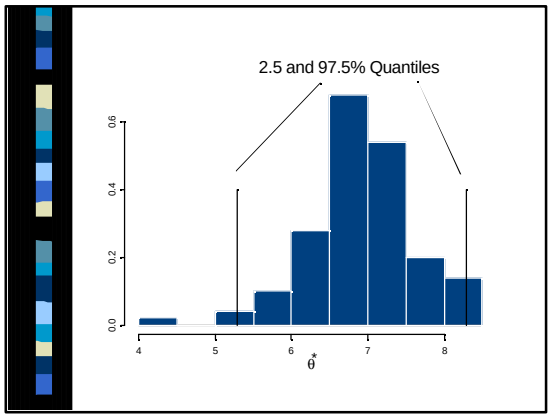


The above discussion assumes that the distribution of $\hat{\gamma}$ can be estimated. However, more often it will be the case that the information on the distribution of $\hat{\gamma}$ will be limited and consist of a mix of reported standard errors and simple regions of plausibility (e.g., the prevalence of a risk factor lies somewhere between 5 and 20%). The Monte Carlo technique can still be used, but the interpretation of the computer generate GBD estimates, q^*_i, will not be as a sample from the distribution of interest,

namely that of $\hat{q}$. However, at least this method provides evidence for the level of uncertainty and ranges of plausible values for q.

Uncertainty Propagation
Using Monte Carlo Simulations

- After generating the Monte Carlo sample, one can get qualitative feel for uncertainty in the GBD estimate by simply making histogram of computer generated GBD estimates, the q_i^*.
- If the inputs used are all estimates with "known" distributions, then one can interpret the q_i^* as random draws from the sampling distribution of GDB estimates and thus a confidence interval can be computed from the empirical quantiles.



Uncertainty Propagation, cont.

- Typically, the marginal distributions that make up the joint sampling distribution of g^* will consist of some input distributions that are not based on estimates from data.
- In this case, the quantiles of the distribution of the θ^*_i can not be interpreted as confidence intervals.
- Plausibility intervals?

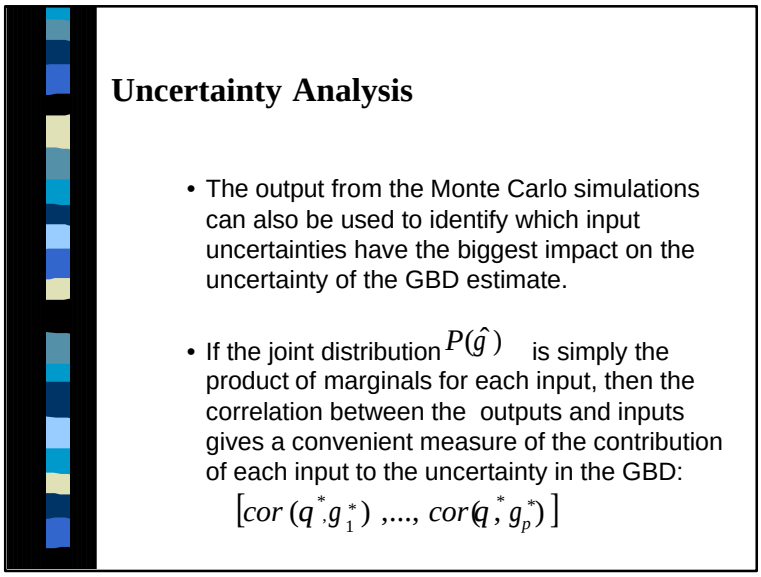
Uncertainty Analysis

Uncertainty analysis are methods for comparing the importance of the input uncertainties in terms of their relative contributions to the output uncertainty. The goal of such an analysis is to find those inputs for which more accurate estimation would have the biggest reward with regards to uncertainty in the GBD estimate. Fortunately, the output from the Monte Carlo simulations described above can also be used to explore which input uncertainties have the biggest impact on the uncertainty of the GBD estimate. Most simply, this can be done using the correlation between the outputs and,

$$\left[cor(q^*, g_1^*)\ ,\ldots,\ cor(q^*, g_p^*)\right]$$

where p is the number of input parameter estimates. If the correlation between the computer generated GBD estimates and a particular parameter estimate is very high, this implies the uncertainty in the GBD estimate will be very sensitive to the uncertainty in the particular parameter estimate. Conversely, if the correlation between the computer-generated GBD's and an input is small in magnitude, then one will gain little by reducing the uncertainty of the input. Performing both uncertainty

propagation and uncertainty analysis will give the researcher at least a qualitative feel for the uncertainty in the GBD estimate as well as some indication from where the uncertainty comes.



References

De Hollander, A.E.M., Melse, J.M., Lebret, E. and Kramers, P.G.N. 1999. An aggregate public health indicator to represent the impact of multiple environmental exposures. *Epidemiology* **10:** 606-617.

Finkel, A. 1990. *Confronting uncertainty in risk management: a guide for decision-makers.* Center for risk management resources for the future, Washington, D.C.

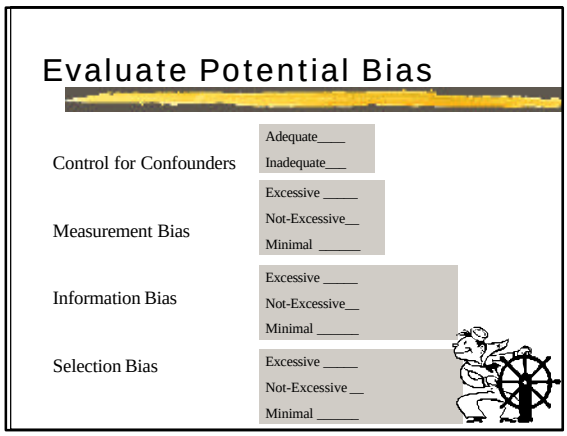
Morgan, M. and Hendrion, M. 1990. *Uncertainty: A guide to dealing with uncertainty in quantitative risk and policy analysis.* Cambridge University Press.

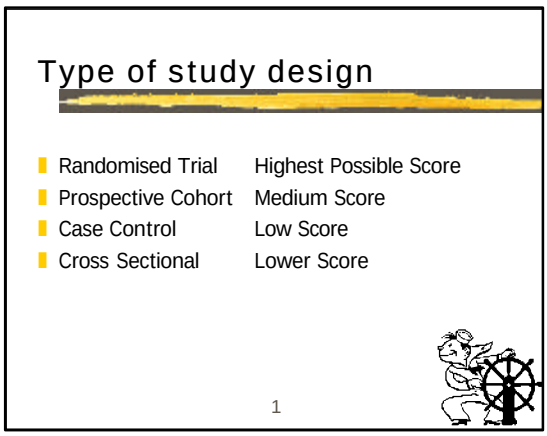
Nurminen, M., Nurminen, T. and Corvalán, C.F. 1999. Methodological issues in epidemiologic risk assessment. *Epidemiology* **10:** 585-593.

Annex 4.5: Determining the strength of evidence

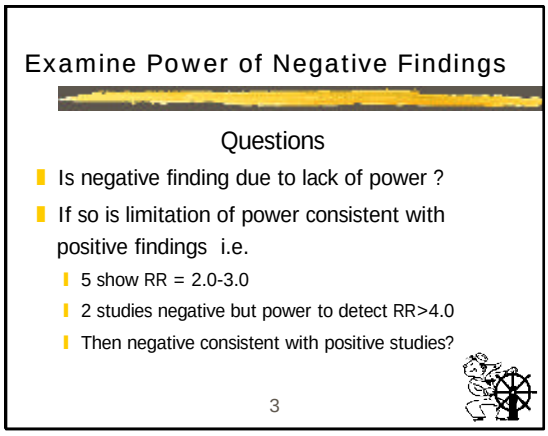
Jay M. Fleisher
Eastern Virginia Medical School, Norfolk, Virginia, USA

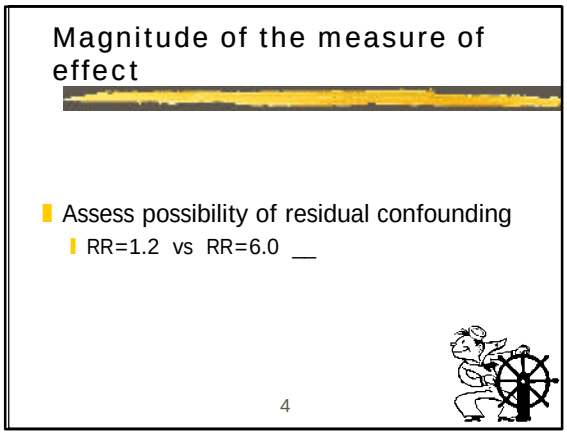
The strength of evidence between an exposure and its effect on health must be taken into account when deciding upon any action to be taken against environmental exposure. This effort, at times, tends to slow down remediation of an existing problem. It is, however, difficult to build up the evidence for a number of environmental cause-to-effect relationships is, because of low effects, difficulties in exposure or effect assessments, competing causes or complex interactions. Cause-to-effect relations which occur primarily in developing countries may also particularly lack of data, as efforts for studying these are usually much less intensive. Because of the different levels of evidence, it is important to provide information on the strength of the evidence when using exposure-effect relations for burden of disease estimates.





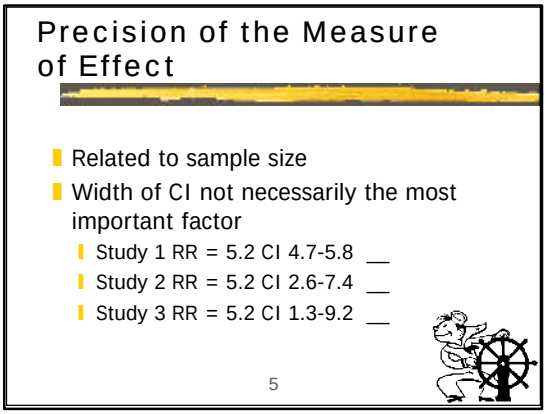
For an "objective" evaluation of the strength of evidence, a number of criteria, or ideally a sort of rating system should be used (some criteria which could be used are described in Slides 1 to 6). This would not mean that estimates based on less evidence would be less valuable, but simply indicate that they are based on a weaker evidence.

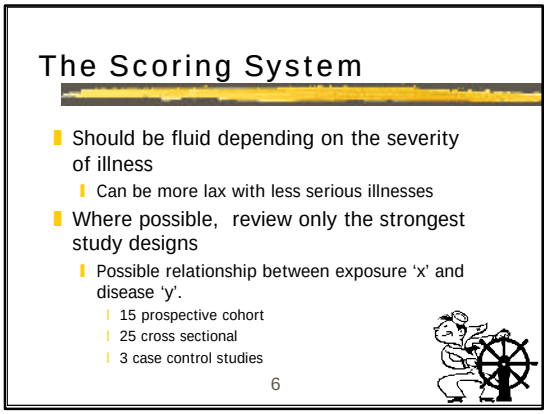




For most environmental issues, the existing literature should be used and graded in some way with reference to the accepted notion of Epidemiological Causality. In the less developed World, where there usually isn't much data available, the weight of the evidence still requires a

structured approach. All available knowledge of specific serious situations should be rigorously reviewed, and no single person should make the final determination on whether or not action should be taken, the type of action to be taken, or the immediacy of the necessary action to be taken.





Criteria for developing estimates although the underlying evidence is less than ideal could include the following: the number of people possibly impacted, strength of the evidence, cost vs. benefit, feasibility of a specific intervention, and other factors that would formulate a decision on whether to act and/or what form of action should be taken.

A practical, yet scientifically valid approach to assessing and considering to remediate environmental problems faced may be to take the available evidence at hand as the basis, in cases where the evidence is difficult to establish. The severity of threat should guide the scientific rigor applied to achieving a solution. One must however caution against an unscientific approach.

Annex 4.6: Climate change and uncertainty*:* Methods developed for intergovernmental panel on climate change

Third Assessment Report

Sari Kovats
London School of Hygiene and Tropical Medicine, UK

The assessment of health outcomes in relation to climate change is a complex task that must accommodate the multiple uncertainties that compound across those antecedent environmental and social changes. There are many different types of uncertainty relating to the health impacts of climate change.

Uncertainty relating to predicting futures changes in climate

The major source of uncertainty relates to the future emissions of greenhouse gases that will force the climate to change. These emissions are driven by complex factors such as population growth, economic growth, energy policy and so on.

Climate change is projected using computer simulations which model the physical processes in the global atmosphere and oceans. Major uncertainties within these global climate models include:

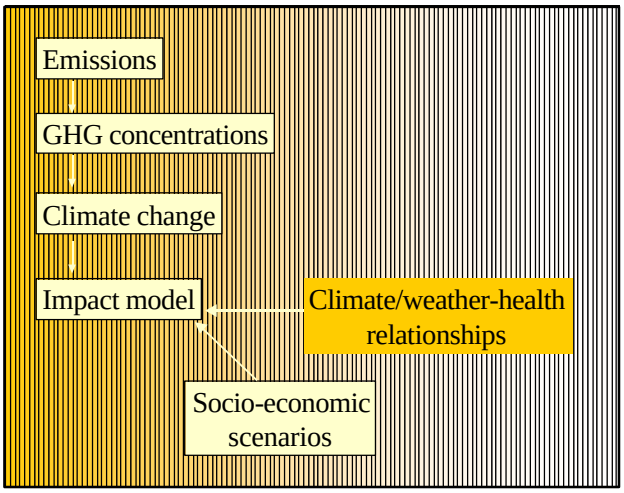
- Climate sensitivity
- Clouds, oceans, aerosols
- Natural climate variability
- Projections at regional or local scales

Global climate scenarios are generated by global climate models, i.e. global patterns of future climates up to 2100. The HadCM2 climate model was run four times with the initial conditions varied only slightly. The range of future climate described by the four experiments (the ensemble members) provide an estimate of the uncertainty in the structure of the climate model. The ensemble members also provide an indication of the natural variability of climate that is described within the model. Ideally, the climate models should be run many times but it far to expensive to do this.

Scenario-based assessment of futures health impacts

The approach that is traditionally used in climate impact assessment is to answer the question, "*if climate changes like this, then what will be the effect on specific health outcomes?*" A variety of "*off the shelf*" climate scenarios are available that can be applied directly to impact models (see figure 1). The use of climate scenarios removes the need for exposure assessment.

Figure 1



The uncertainties relating to impact models (e.g. malaria models, food crop yield models) include:

- The climate-health relationship (dose-response or biological model)
- Initial conditions (including baseline health data)
- Parameter values

Confidence intervals are used in classical empirical epidemiology but it may not be possible to apply these to the results of scenario-based health risk assessment, except where the impacts are derived from empirical statistical models. However, it is important to specify the likely range of uncertainties and the magnitude and direction of errors.

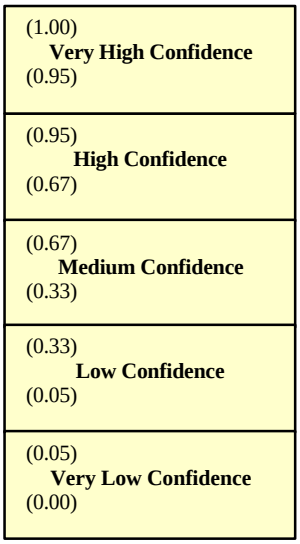
Many other factors affect health (e.g. access to health services, drug development, equity, sustainable development). How these factors will change in the future is another major source of uncertainty.

IPCC

Scientists within the United Nation's Intergovernmental Panel on Climate Change (IPCC) comprehensively review the scientific literature on climate change and its impacts. For the Third Assessment Report (due to be published early 2001), the IPCC has developed formal methods to look at uncertainty in order to improve communication across disciplines and between decision-makers, the public and scientists.

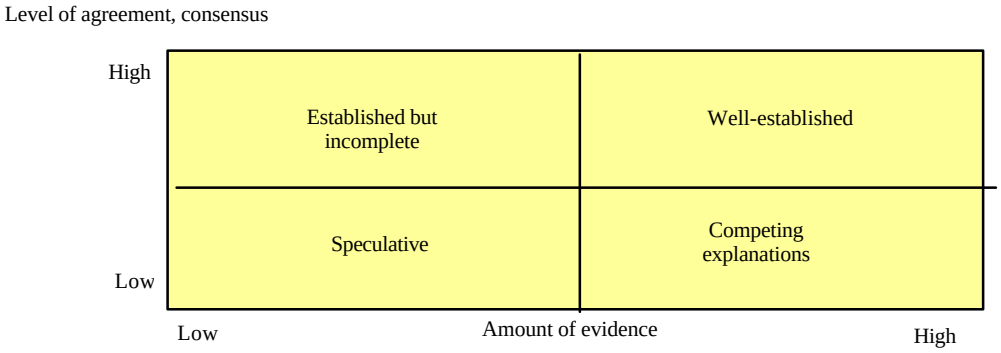
The IPCC has defined levels of confidence that are applied to all the major conclusions in the report. This is used consistently across all chapters that address impacts by region (health, ecosystems, industry, etc.) and region (Africa, Latin America, etc).

Figure 2



The IPCC also addresses qualitatively the state of knowledge. This allows readers to understand where conclusions are based on little information and where there is information but the experts cannot agree.

Figure 3



Annex 5.1: Report of the working group on air pollution

Participants:

Erik Lebret, Chair
Keith Florig, Rapporteur
Rebecca Calderon
Dafina Dalbokova
Majid Ezzati
Sumi Mehta
Paulina Pino
Francesca Racioppi
Isabelle Romieu
John Vena

1. Categorization of Risk Factors

Currently, the global burden of disease exercise categorizes air pollution risks into indoor and outdoor categories at the topmost level. Indoor air pollution is further broken down by source into solid fuels and radon. Outdoor air pollution is sub-categorized by pollutant specie. The rationale for this scheme is based on routes for risk management. Indoor air pollution is managed by controlling sources. Outdoor air pollution is managed by species-specific ambient air quality standards and emissions standards.

Clearly, however, there are many other ways of categorizing air pollution risk factors. A more complete list of alternatives would include categorizing air pollution risk factors by the following:

- Economic sector (industrial, residential etc)
- Source type (boilers, cookstove)
- Health outcome (Chronic obstructive pulmonary disease, asthma, respiratory infection etc.)
- Government authority responsible (Ministries of Environment, Energy, Agriculture, Health)
- Pollutant specie (Pariculate matter, SO_2, etc.)
- Affected population (urban/rural, child/adult)

Each of these alternatives would have use in a particular policy context. Industry lobbyists might want to categorize by economic sector to compare impacts of industry-created air pollution to impacts from residential, natural, transportation, and other sources of air pollution. Health officials interested in the relative contributions of air pollution to various diseases would want to create categories based on health outcomes. Officials of an Environment Ministry would want to create air pollution categories that are consistent with their internal bureaucratic structure (e.g. large

stationary, mobile, radon, household fuels). UNICEF would want to compare air pollution impacts on children to the impacts of other risk factors in childhood. **We conclude that, if disease burden studies are to be useful, the choice of categories for risk factors should be driven by the policy context of the analysis.**

2. Alternative Exposure Scenarios

Like the choice of risk factors to be analyzed, **the choice of alternative exposure scenario should be driven by the policy context.** In the table below, we show several policy goals, the alternative exposure distributions they imply, and the analytical tasks that use those alternative exposure distributions.

Policy goal	Alternative exposure	Analytical task
Allocate research funds to diseases that create the largest burden	Theoretical minimum, e.g. zero	Rank risk factors by total disease burden
Reduce risk for those at greatest risk	Shift those above threshold of acceptable risk to exposures below threshold of acceptable risk	Rank risk factors by disease burden above some threshold of acceptable risk
Reduce population risk in the most cost-effective way	Marginal exposure reduction	Rank risk factors by most cost-effective opportunities for intervention.

3. Strength of Evidence

A number of national and international expert bodies have recently prepared assessments of the strength of the evidence for a number of air pollution risk factors.

A scoring system for strength of evidence in the air pollution context would make it easier to convey uncertainties to users of global burden assessments.

Extrapolation from developed to developing countries is uncertain.

4. Recommendations

- Framing of analysis should be based on needs of policy setting.
- Sensitivity/uncertainty analysis is important to convey strengths and weaknesses of the analysis.
- Analysis should fold in public values where appropriate by considering dimensions that the community considers to be important, e.g. odor, soot. A new multi-attribute impact measure could be defined that incorporates DALYs as well as non-mortality/non-morbidity dimensions.
- When epidemiologists define health outcomes to study, they should consider to collect data that are meaningful to policymakers, such as the duration of asthma symptoms or numbers of school-days missed.

- Epidemiologic results based on exposure, rather than dose, cannot be used to determine the chronic exposure effects on the incidence of either chronic (e.g. COPD incidence) or acute conditions (e.g. daily deaths). Substantial uncertainties remain concerning these chronic components. Epidemiology and policy both need to move toward a “dose-response” rather than and “exposure-response” paradigm for air pollutants.

Annex 5.2: Report of the working group on chemical exposures

Participants:

W. Jedrychowski
A. Koppikar
H. Hicks
S. West
G. de Hollander
C. Corvalán
H. Pastides
V. Bencko
S. Grosse
S. Tarkowski

List of Chemicals

The chemical exposures work group identified four groups of chemical risk factors that can serve as the subject of environmental health assessments: metals, pesticides, other organochlorines and related compounds, and solvents and volatile organic compounds (VOCs). The group chose not to address physical agents such as asbestos or ozone, radionucleides, or naturally-occurring food contaminants such as aflatoxins. Naturally-occurring chemical contaminants in water, air and food should be considered in medium-specific risk assessments.

Priority-setting

Criteria for setting priorities regarding which chemicals should be the subject of health assessments include: the availability of data indicating significant human exposures, the strength of evidence and magnitude of health effects observed in humans, the quality of animal data demonstrating toxicity and biological mechanisms, and the prevalence of the exposure as a public health problem. Additional criteria include persistence in the environment and bio-accumulation. Finally, relevance of the chemical exposure to policy-makers and regions must be taken into account.

Estimating exposures

An exposure-based approach to assessment of chemical risk factors requires the availability of reliable exposure data. In general, the most reliable indicator of actual human exposure is a biological measure of body burden. Likely exposure can also be calculated for many chemicals on the basis of data on industrial emissions and ambient concentrations from environmental monitoring, although a number of factors may intervene between these listed factors and actual exposure, including human behaviours.

Several models of collection of chemical exposure data were discussed. One is the analysis of blood samples from a large, nationally-representative sample of the U.S. population for scores of toxic chemicals. This project is currently being undertaken by the CDC. A more focused project was the analysis of breast milk samples from 19

European countries for dioxin and PCBs, which allowed estimation of national-level population exposures. Where feasible, national monitoring of exposures is ideal.

Most population studies of chemical exposures and health effects have focused on specific regional populations and sets of chemicals. One example is the Great Lakes Study by the U.S. Agency for Toxic Substances and Disease Registry, focusing on exposure to organochlorines through consumption of fish. Another is the U.S. Agricultural Health Study, which collected both environmental and biological exposure data.

A model of the use of industrial exposure data is the long-term study of arsenic exposures and health effects in a district in Slovakia conducted by the Charles University.

Health effects-strength of evidence

The health effects of chemicals can be categorised into cancer, chronic diseases and other non-cancer outcomes, including reproductive, developmental, and neurological outcomes.

The totality of all types of data, human and animal, can be used to categorise the strength of evidence. For heavy metals, there is a strong evidence of adverse health effects, even at low levels of exposure. Strong evidence links arsenic exposure to lung and skin cancer and liver damage, cadmium exposure to kidney and lung cancer, hexavalent chromium to lung cancer, lead exposure to neurodevelopmental behavioural and hematologic disorders and hypertension, and organic mercury exposure to brain and central nervous system impairments. Other metals with adverse effects include nickle and berylium.

Strong evidence exists that high levels of exposure to organochlorines, notably dioxin, are associated with elevated risk of cancer in humans. Evidence on lower levels of exposure is weaker. Several studies provide strong evidence of an association of pre-natal dioxin and PCB exposures with modest neurodevelopmental outcomes in offspring. *(including GEMS and HEAL)*

Pesticides when used improperly can be toxic, and cases of neurologic effects from acute exposures are often reported. There is weak data to quantify the burden of disease resulting from chronic exposure to pesticides. Nonetheless, data from poison control centres may be used to monitor pesticide safety.

Among solvents there is strong evidence that benzene causes cancer and CNS effects, although not at background levels characteristic of most populations. For TCE, there is weak evidence of carcinogenicity.

Alternative Scenarios

The work group suggests that when defining alternate scenarios of reduced exposures that these be based on groups of proposed interventions. Interventions can take the form of source reduction or risk management, including modifying behaviours. On the basis of proposed interventions, it is possible to project decreased population exposures.

General comments and recommendations

The work group addressed specific chemicals but recognises that mixtures of chemicals pose a complication. Further study is needed to address the health effects of interactions among these chemicals.

There is a need to monitor ongoing research on the health effects of chemicals. An example is of compounds suspected of acting as endocrine disruptors.

Future studies may examine immunotoxic and genotoxic markers of long-term health effects. It is difficult to relate exposures to cancers occurring decades later, and these types of markers can strengthen the ability to relate exposures to estimates of future burden of disease.

More research is needed to quantify the burden of chronic disease from chemical exposures, e.g. cadmium in relation to osteoporosis and hip fractures.

Finally, the group recognises a need to develop better approaches to quantify neurodevelopmental and other subtle effects of exposures. Without appropriate severity weights for these conditions, the negative effects of these exposures on public health may be understated.

Slide 1.

Chemical Exposures

Category of risk factors to investigate:
1. Pesticides
2. Metals
3. Solvents & VOCs
4. Other Organochlorines

**physical agents could also be included

Hierarchical considerations
(criteria for setting priorities)

1. Human data availability
2. Strength of human effects
3. Good toxicologic animal & mechanistic data
4. Persistence
5. Bioaccumulation
6. Relevancy to policymakers
7. How prevalent is the problem
8. Relevancy to region

Slide 2

Strength of Evidence

Exposure:
1. How available is exposure data from:
   - Industrial emissions
   - Ambient levels
   - Body burden
2. How reliable is exposure data?

Examples of types of exposure data that have been collected:

Organochlorines
- European Breast Milk Study
- ATSDR Great Lakes Study

Pesticides
- US Agricultural Health Study

Metals
- Arsenic in Slovakia

Solvents
- Long Island Breast Cancer Study
- Overall
- US Nat'l Exposure Report Card (NHANES)

Slide 3.

Strength of Evidence

Health Effects (strength of evidence today)
- Cancer
- Chronic diseases
- Reproductive/Developmental/Neurological (Non-cancer)

(based on totality of all data)

Onganochlorines
- Strong evidence for cancer at high exposure
- Strong evidence of a modest association for reproductive/developmental/neurological effects

Pesticides
- Cases of neurologic effects from acute exposure
- Weak data to quantify chronic burden of disease

Metals – strong evidence
- Arsenic → lung/skin cancer, liver damage
- Lead → neurodev. effects & hypertension
- 6+ chromium → lung cancer
- cadmium → kidney & lung cancer
- mercury → brain & CNS

Solvents
- Bensene — strong evidence for carcinogenicity
- TCE — weak evidence for cancer

Slide 4.

Geographical Resolution

1. National monitoring of exposures is ideal
2. Regional monitoring may be appropriate
3. Availability of data is quite variable

Alternative Scenarios

Assumed reduction in exposures should be based on proposed interventions (tech/science based and behavioural modifications)

General comments & Recommendations

1. Need to address mixtures as next step
2. Need to monitor ongoing research on chemicals, especially regarding endo disrupters
3. Markers of future effects should be considered (genotoxicity & immunotox)
4. Need to quantify burden of chronic disease from chemical exposure., e.g.cadmium in relation to osteoporosis and hip fractures
5. Develop better approaches to quantify neurodev & other subtel effects

Annex 5.3: Report of the working group on global environmental change

Participants:

Roberto Bertollini
Diarmid Campbell-Lendrum (Rapporteur)
Carlos Corvalan
Kris Ebi
Simon Hales
Sari Kovats
Tord Kjellstrom (Chairman)
Bettina Menne
Tony McMichael
Harris Pastides
Shilu Tong

Several key points were raised under each of the suggested headings. Discussion covered both the task of producing the estimates required by the WHO GBD exercise, and the broader picture of identifying the most important questions and approaches for future research. For clarity, the discussions related to these two themes are summarized separately.

1) DEFINITION/CLASSIFICATION OF THE RISK FACTOR

- **Current climate and/or climate change?**

  - Within the GBD assessment: We propose to assess climate change (rather than baseline climate) as a risk factor that may itself be altered.

  - Outside of the GBD assessment: An assessment should be carried out on GBD attributable to climate variation over time, (e.g. seasonal and extreme events), and with geography. Although climate itself may not be altered, adaptations may reduce exposure, e.g. flood defences, or air-conditioning for heatwaves.

- **Climate change scenarios are in the middle of the causal chain, and may act on health through other CRA risk factors (Table).**

  - Within the GBD assessment: For each health outcome, relative risks will be estimated under each climate change scenario. These will be used to adjust estimates from other risk factors.

  - Outside of the GBD assessment: We recommend future assessments higher up the causal chain, e.g. transport and energy policies. Such an approach would facilitate the inclusion of secondary benefits of changes in emissions.

-

Table: Classification of climate change according to the DPSEE model:

Drivers	Pressure	State	Exposure	Effect	Actions
Population growth Development Energy policy	GHG emissions	Climate	Heatwaves, windstorms, floods Food-, water-, vector–borne infection Food shortage* Indoor / outdoor air pollution* Occupation* Physical activity* Socioeconomic status* Water / sanitation*	Cardiovascular, Respiratory diseases Malnutrition Drownings/ Accidents Various infectious diseases +mental health, ability to work**	National & Global monitoring and BOD assessment National & International agency mitigation and adaptation strategies Kyoto protocol

*Other risk factors within the GBD.
**No GBD or ICD code

2) ALTERNATIVE SCENARIOS (FOR COMPARISON WITH THE REFERENCE SCENARIO, THAT NOTHING IS DONE TO MITIGATE GREENHOUSE GAS EMISSIONS)

- **Which alternative exposure scenarios should be used?**
  - Within the GBD assessment: in addition to the reference scenario of unmitigated emissions, the Intergovernmental Panel on Climate Change (IPCC) describes two possible future trajectories for stabilization of greenhouse gas emissions at 750 and 550ppm CO_2 equivalent. These have in turn been applied to global climate models. We will use the resulting predictions of future climate, as alternative exposure scenarios, in addition to a hypothetical scenario of no change from the baseline climate for 1961-1990.
  - Outside of the GBD assessment: We recommend future exploration of IPCC SRES scenarios, which incorporate socioeconomic as well as climate predictions. If we were to make a future assessment of the effects of current climate, alternative adaptation scenarios would need to be defined.

- **What time frame should we adopt?**
  - Within the GBD assessment: Estimate effects in 2020s, 2050s. In the final report, it will be important to emphasise the extremely long term + persistent nature of climate change effects, - i.e. low risk reversibility.
  - Outside of the GBD assessment: Further consideration needs to be given to how the long-term nature of climate change effects are accounted: for example whether DALY estimates should be projected forward beyond the range of the 2020s and 2050s, and whether they should be discounted for future generations.

- **In contrast to other risk factors, our intervention scenarios relate not to a reduction in burden, but to making the burden 'less bad' than it would be without climate change.**
  - Within the GBD assessment: We will express climate change effects as proportional changes in incidence of specific health impacts. This will allow our estimates to be integrated with predicted changes in incidence through other mechanisms: e.g. reduction in water-borne disease transmission through improved sanitation.
  - We will also present results for optimistic and pessimistic scenarios of changes in vulnerability, such as changes in socioeconomic conditions.
  - In addition to health burdens of climate change, we will also include health benefits (reduced winter mortality in temperate regions, beneficial effects on food production in some regions).
  - Outside of the GBD assessment: Future assessments should include consideration of short-term benefits of reduction in GHG emissions, from lower pollution levels.

3) STRENGTH OF EVIDENCE:

- **There is little doubt that climate *variability* affects each of the health impacts listed above (unless adaptation measures are implemented): there is less certainty that climate *change* will affect health.**

Both during the GBD, and in the future, we need to communicate strength of evidence for:
1) likelihood of change in hazard: We will use the IPCC range estimates for changes in specific hazards (e.g. averages/extremes of weather).
2) likelihood of resulting change in health impact: Use IPCC estimates of uncertainty (i.e. low/medium/high probability).
3) strength of dose-response relationship: assessment will be based on model validation; e.g. ability of the model to explain the relationship between geographical variation in climate and health in the present, or temporal relationships in the past.

4) GEOGRAPHICAL RESOLUTION:

- **Although climate scenarios include relatively high resolution geographic distribution of climate variables, impact assessments are usually aggregated to regions (9 by IPCC, variable for impact specific models). These do not necessarily correspond to 14 GBD regions.**

  - Within the GBD assessment: Wherever possible, we will disaggregate model outputs to national level and repackage into the 14 GBD regions.

  - Outside of the GBD assessment: In order to gather better data for estimation of burden of disease, and to make detailed recommendations on how to adapt to climate change, it is important to collect monitoring data and generate predictions at higher spatial and temporal resolution (e.g. national or sub-national level, divided into rural/urban etc.). This is especially important for regional and national assessments.

5) RECOMMENDATIONS FOR FUTURE WORK:

- Consideration of health outcomes without well-established climate-response relationships, or DALY weightings: e.g. effects on mental health, ability to work.

- Sectorial analyses: moving upstream to examine all effects of population growth and development, particularly energy, transport and agriculture policies.

- More formal consideration of interactions between climate change and other risk factors, such as socioeconomic status.

- More formal consideration of feedbacks (e.g. the positive and negative health effects of adaptation measures in response to climate change)

- New meeting to discuss changes in the protocol and theoretical framework for future assessments.

Annex 5.4: Summary of the working group on water quality and sanitation

Participants:

J. Eisenberg
L. Fewtrell
P. Bermejo
L. Galvão
P. Murphy
A. Hubbard
X. Bonnefoy
J. Fleisher
D. Kay

The working group on water and sanitation was charged with the following tasks in the water sector:

1 Define the categories of causal agents/risk factors and produce a listing (Table 1)
2 Consider alternative scenarios and recommend appropriate scenarios
3 Consider the strength of evidence
4 Consider appropriate geographical resolution for EBD estimation
5 Make appropriate recommendations on methodology

The group first developed a list of the important water quality related causal agents (Table 1). Disease burden can be structured in terms of specific risk factors (drinking water, recreational water, eating raw fish, lack of hygiene, inadequate sanitation, inadequate reuse of wastewater for irrigation etc.), or vehicle of transmission (water, food etc.). A qualitative assessment of the strength of evidence, and the availability of data at appropriate geographical scales (task 4) was made between the factor and health (Y-yes, N-no) is presented in Table 1.

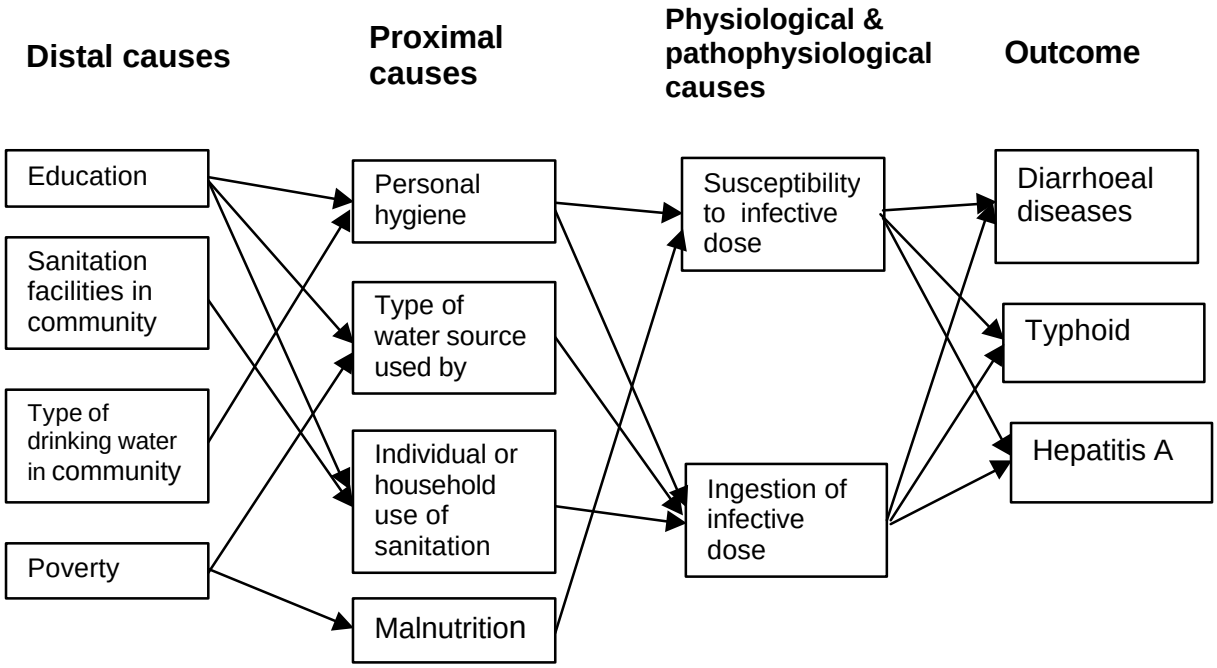
Table 1: Causal agents

	Strength(3)	Geodata(4)
Bacteria	Y	Y
Viruses	Y	-
Parasites	Y	Y
Nitrate	Y	Y
Arsenic	Y	Y
Pesticides	N	N
Chromium	Y	Y
Organoleptic	-	-
Lead	Y	Y
Fluoride	Y	Y

In defining appropriate scenarios (task2) the group was firmly of the view that scenario development and analysis should be in the form of a causal web (an example of causal web is represented in Figure 1). In each case this should cover the whole *water and sanitation* sector. This is an important conceptual point which the group felt was essential if EBD estimates are to inform potential remediation strategies. Thus, the methodology (task 5) would be causal web construction covering the water

and sanitation sector, importantly, using the drainage basin as the most appropriate spatial scale. This approach also has policy resonance with new instruments such as the EU Framework Directive on the water environment.

Figure 1: Causal web for faecal-oral transmission



Annex 6.1:

12th Annual Meeting of the International Society for Environmental Epidemiology (ISEE 2000)

Session on Environmental Burden of Disease

Programme – 22 August 2000

Chair: Carlos Corvalán, World Health Organization

Introduction and background to environmental burden of disease assessment, Carlos Corvalán, Protection of the Human Environment, World Health Organization, Geneva, Switzerland

Methodological approaches to environmental burden of disease assessment, Annette Pruess, Protection of Human Environment, World Health Organization, Geneva, Switzerland

Assessing environmental disease burden: examples from the Netherlands, Hollander AEM de, Kempen EEA, Staatsen BA, Center for Chronic Disease and Environmental Epidemiology, National Institute of Public Health and the Environment, Bilthoven, Netherlands

Global burden of disease from exposure to indoor air pollution, Sumi Mehta, Kirk Smith, School of Public Health, University of California, Berkeley, USA

Approach for burden of disease estimation for exposure to lead, Lorna Fewtrell, Centre for Research into Environment and Health, Crewe, UK

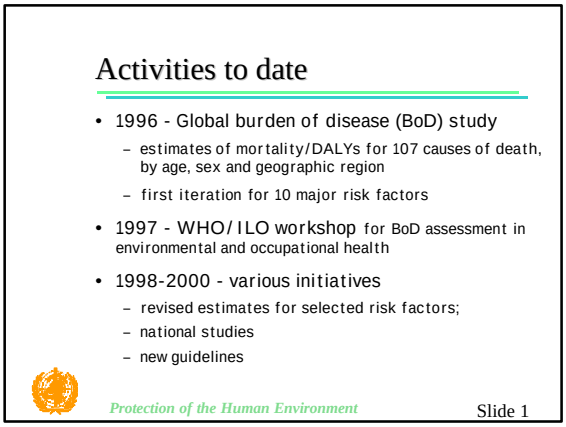
Assessing the global burden of disease attributable to climate, Tony McMichael, Department of Epidemiology and Population Health, London School of Hygiene and Tropical Medicine, London, UK

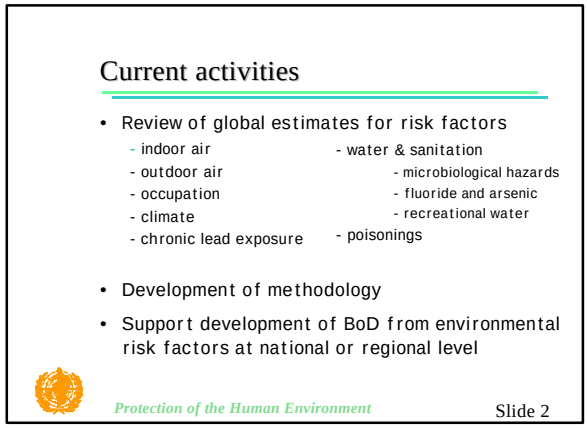
Discussion

Annex 6.2: *Environmental burden of disease* - Background and rationale

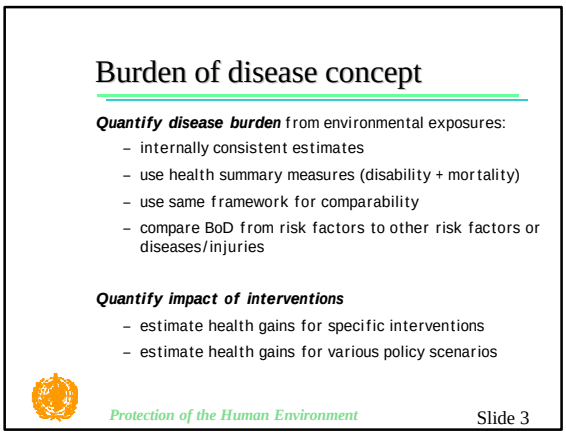
Carlos Corvalán
Protection of the Human Environment, World Health Organization

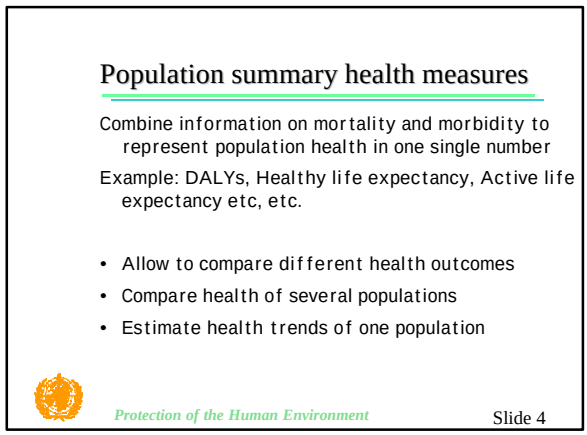
Information about the impact of environmental risk factors on human health, at different levels (village, city, province or country), is necessary in order to support management and the decision-making process for environmental health protection. Decision-makers need this information in order to develop preventive strategies, to compare the potential effects of different decisions and choices and to assess the impacts of their decisions. The development of a scientifically sound methodology and estimates of the environmental burden of disease is, however, a major challenge. WHO has been developing activities supporting such initiatives for several years (slide 1). Particular efforts are currently under way to develop methodologies for country and regional level assessments. In parallel, disease burden for selected risk factors is being estimated at global level (slide 2).





To introduce the presentations in this special session on environmental burden of disease, we need to briefly address the basic concepts of burden of disease (slide 3) and summary measures of population health used to assess it (slide 4); the term Disability Adjusted Life Years (slide 5), and the main results of the burden of disease study by Murray & Lopez (slide 6).





Disability-Adjusted Life Years

- **DALY = YLL + YLD**

  years of life lost because of premature death (YLLs)

  years of life lived with disability (YLDs)

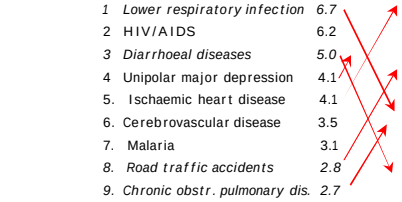
Burden = Mortality + Disability

- one DALY = one lost year of healthy life
  - Death of a male at 50 = 30 DALYs
  - Schizophrenia at 20 = 30 DALYs

Protection of the Human Environment Slide 5

Top ten: 1999 and trends to 2020

Rank	Cause	%DALY total
1	*Lower respiratory infection*	6.7
2	HIV/AIDS	6.2
3	*Diarrhoeal diseases*	5.0
4	Unipolar major depression	4.1
5.	Ischaemic heart disease	4.1
6.	Cerebrovascular disease	3.5
7.	Malaria	3.1
8.	*Road traffic accidents*	2.8
9.	*Chronic obstr. pulmonary dis.*	2.7
10.	Congenital abnormalities	2.5



Protection of the Human Environment Slide 6

The rationale for generating environmental burden of disease estimates at national and international level are summarized in slides 7 and 8. The presentations to follow in this symposium will address the methodological framework in environmental burden of disease, examples of current studies and applications in specific settings.

Aims of GBD project: national/regional level

- To provide a tool for quantifying BoD from major environmental risk factors

Uses:

- Provides information on burden of disease and preventable part
- Together with cost-effectiveness of interventions and social and ethical framework provides rational basis for priority setting in research, implementation and policy development
- Monitor progress
- Points to vulnerable population subgroups
- Compares environmental health to other areas

Protection of the Human Environment Slide 7

Aims of GBD: international level

- Provide a worldwide picture of disease burden due to environmental risk factors

Uses:

- Provides information for major policy directions / international efforts
- Highlights main problems at global level
- Provides information to donors
- Points to countries in greatest needs for support on selected issues

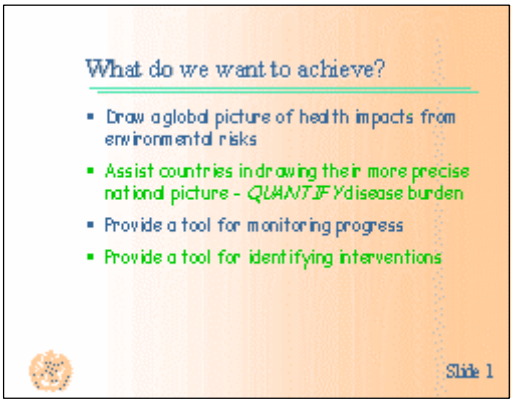
Protection of the Human Environment Slide 8

Annex 6.3: *Environmental burden of disease-* Methodological approaches

Annette Prüss
Protection of the Human Environment, World Health Organization

Countries are increasingly interested in looking at causative life-style, social or physical factors and wish to quantify the disease burden they cause. Environmental health factors are at the origin of a large part of the disease burden world wide. WHO is intensifying its effort to provide support in the assessment of environmental burden of diseases. The main emphasis is on national or regional assessments, as decision-making is usually taking place at that level and typically relies on national and regional assessments (besides issues with of global impacts, such as climate change).

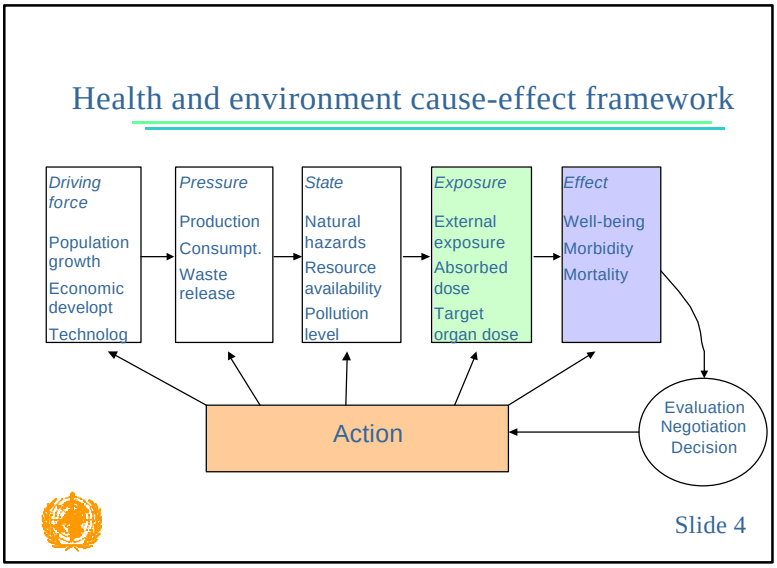
Planned activities in the assessment of environmental burden of disease are summarized in Slide 1. Slide 2 shows the additional type of information which the burden of disease assessment can feed into the policy debate.

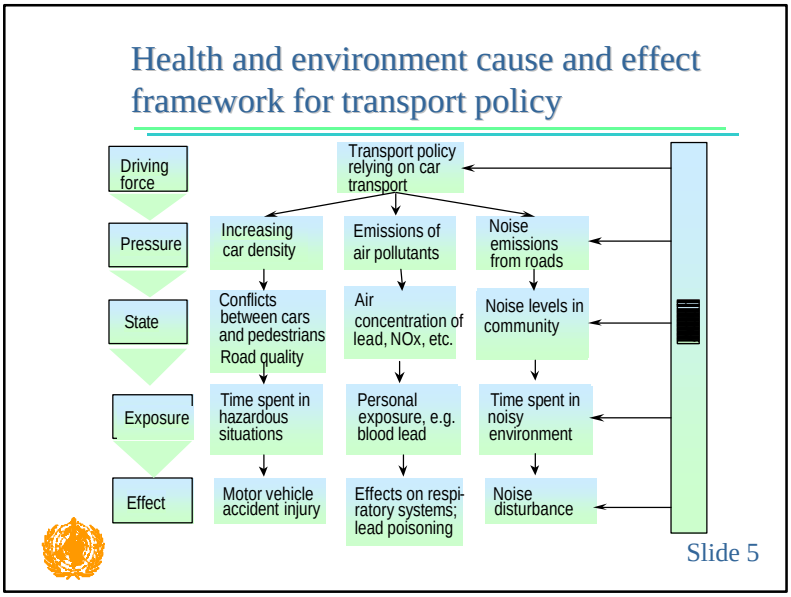


For example, a study performed in the Netherlands and the USA on the positive and negative consequences of adding disinfection products to drinking water has compared potential health outcomes in terms of disease burden. Potential burden of microbiological disease due to lower disinfection levels were compared to the potential disease burden from cancers suspected to be associated with disinfection by-products.

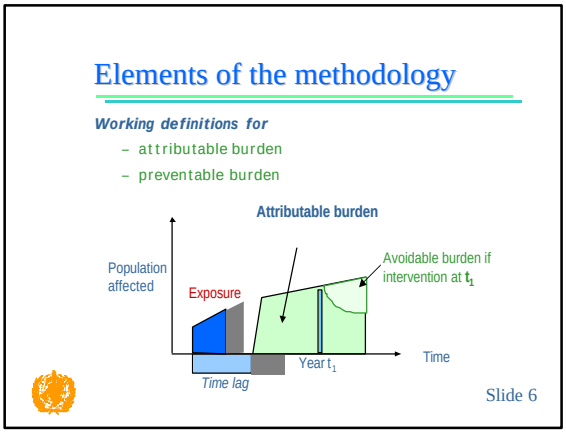
For comparability of results between disease outcomes and risk factors, some common features or methodologies are needed when estimating environmental disease burden, which is yet to be developed (Slide 3).

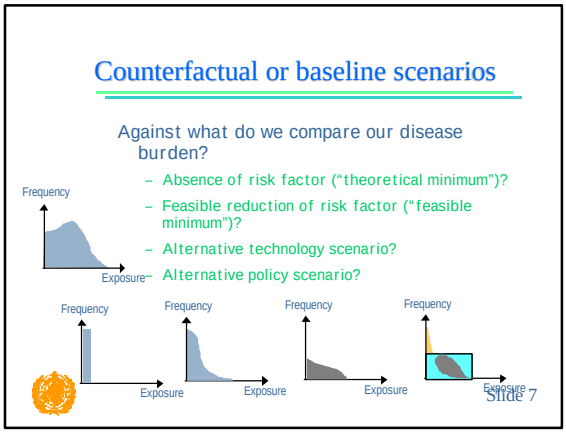
The health and environment cause-effect framework (Slide 4), links measurable indicators to environmentally caused diseases and relates distal and proximal causes in a global perspective. It could be expanded to include the analytical aspects and consideration of interactions between causal parameters, which is necessary for quantification of the disease burden, in particular when interactions between risk factors and disease outcomes are complex. Its application to transport policy is outlined in Slide 5. A more analytical version of such frameworks is needed to support the estimation of environmental disease burden assessments.



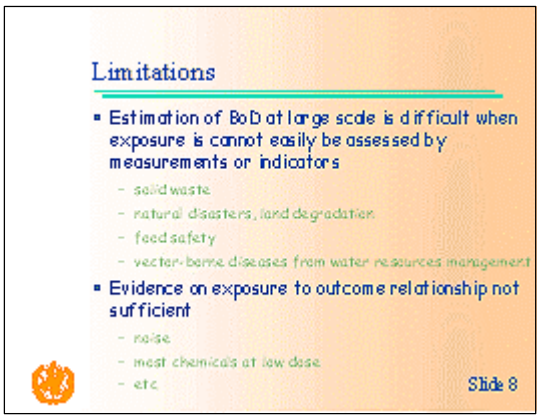


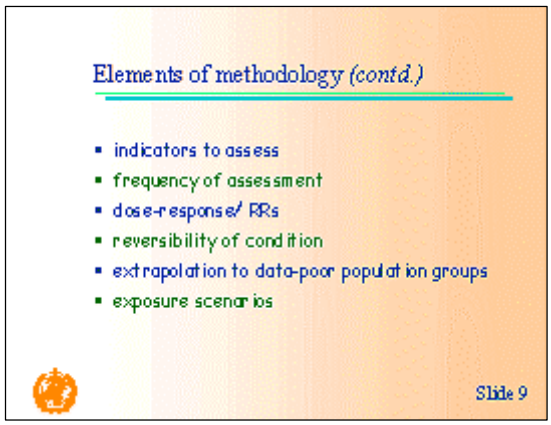
Main issues which will need to be addressed to support initiatives in environmental burden of disease are described in Slide 6. Working definitions will need to be established, and alternative (or counterfactual) scenarios will need to be defined (Slides 7 and 8).





The limited data availability in environmental health, and the weakness of the evidence in some areas results in important limitations in many applications in this area, and should be noted (Slide 8). A recapitulation of activities planned in the framework of this project are outlined in Slide 9.





Other issues outlined during this presentation are described in the Background document, in Annex 1 of this document.

Annex 6.4: Assessing environmental disease burden
the example of noise in the Netherlands

Augustinus EM de Hollander, Elise EMM van Kempen, Rudolf T Hoogenveen
National Institute of Public Health and the Environment (RIVM)

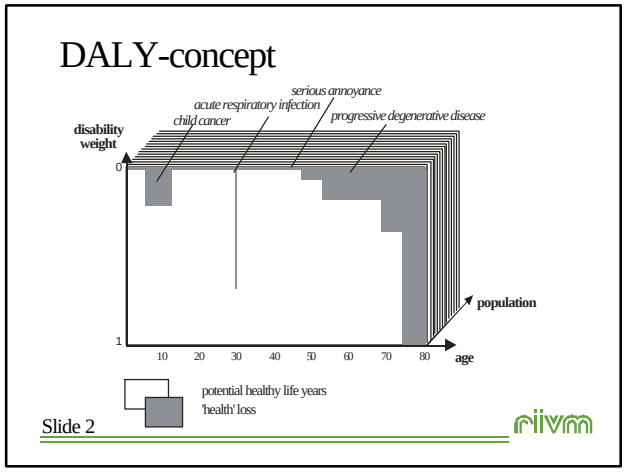
The RIVM produces National Environmental Outlooks (NEO) every 3 or 4 years to support environmental policy making by the government. The first one was produced in 1987, and now we are about to publish number 5.

Basically we try to assess the current as well as the future state of the environment using different scenarios for the future. In the fifth NEO we try to look 30 years ahead. Indicators are used from one end of the causal chain, driving forces such as demography, economy, public, health, pressure, state and impact: for instance ecological and human capital.

From the public health perspective it is necessary to assess the health loss to environmental exposures, as there are indications that the perception of environmental health risks may be somewhat distorted in our society.

To do so one has to apply a public health currency unit that encompasses the very diverse responses that may be associated with environmental pollution. That may range from slight aggravation of respiratory disease all the way up to the loss of many potentially healthy life years due to premature mortality. Ergo: this measure had to comprise important aspects of health such as quantity of life, quality of life and number of people involved. Inspired by the Global burden of disease project we applied a concept very close to the disability adjusted life years DALYs (Slide 1).

Slide 2 represents a simplified diagram of the basic idea behind DALYs. At birth we all have eighty years of potentially healthy life ahead. Unfortunately most of us will suffer from diseases, due to our genetic program, our unhealthy life styles, dietary, occupational, environmental factors or just bad luck. The aim here is to estimate the loss of DALYs that can be attributed to environmental exposures.

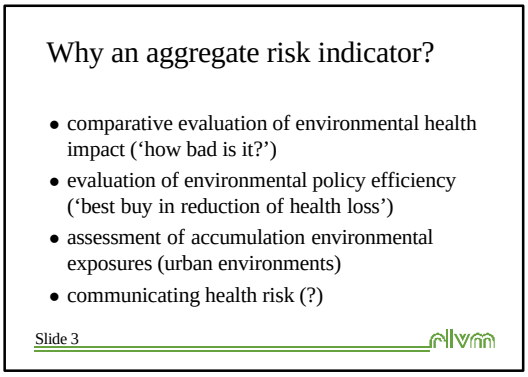


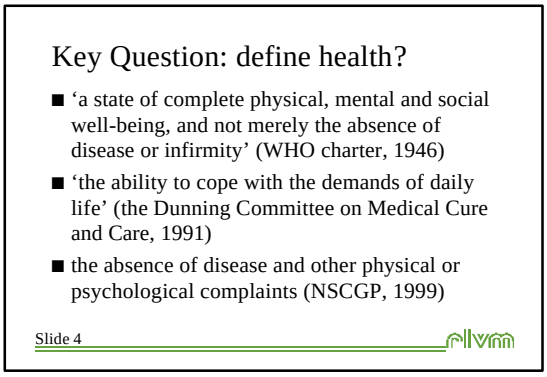
The reasons for applying an aggregate health impact indicator include the following (Slide 3):

- To compare the significance of exposures with other environmental exposures or life style factors. Most common risk measures are non informative (probabilistic, death, non-fatal health outcomes): PM versus noise.
- To evaluate the most effective policy options in terms of health gain (classical example chlorination drinking water, acute infectious disease compared to cancer). Should we concentrate on carcinogenic air pollution or would the abatement of noise exposure provide better returns. Or is particulate matter the only thing that really matters?
- In the NL there is significant spatial accumulation of environmental stress, especially in urban areas. Environmental DALYs may help us to compare one situation to another.

In public health terms, one should remember that there is more to good risk communication than finding the right impact measure.

Before going any further, on might have a look at the health definition according to the WHO-charter; this definition is quite close to the definition of happiness; others would prefer to only consider responses that can be clearly defined by medical doctors (Slide 4).

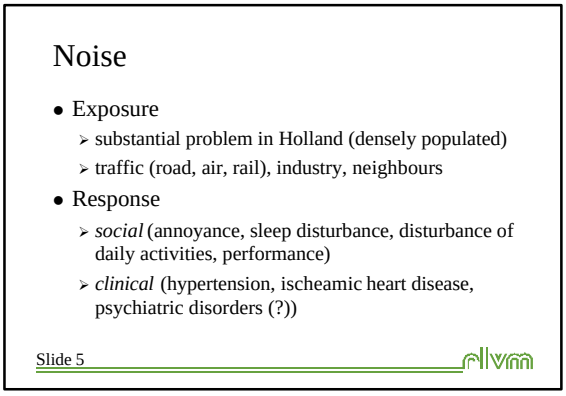


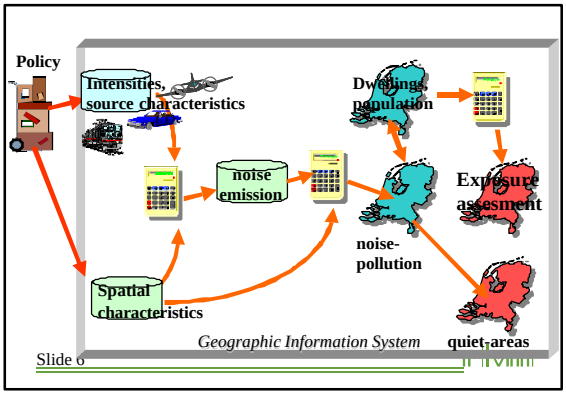


In our very densely populated country environmental noise really is a major problem. Cities are built in a very compact way; there is a lot of traffic congestion; and last but not least we want to operate a relatively large airport in the most densely populated area of the Netherlands: Schiphol. 27% of the Dutch population reports themselves to be severely annoyed by traffic noise, for air traffic noise this percentage is 17.

An interesting feature of the health effects of noise is that one might distinguish social and clinical responses, depending on the definition of health one is using. (uncertainty of health responses: annoyance no problem, cardiovascular disease inconclusive, borderline significant), Slide 5.

The Netherlands have the advantage to have relatively good data on noise emissions and exposure. These are processed by quite sophisticated models to assess the effectiveness of policy measures, using geographic information systems. These encompass mobile source characteristics (cars, planes road surface characteristics, large noise shields), spatial characteristics (such as how residential areas and traffic roads are organized), Slide 6.

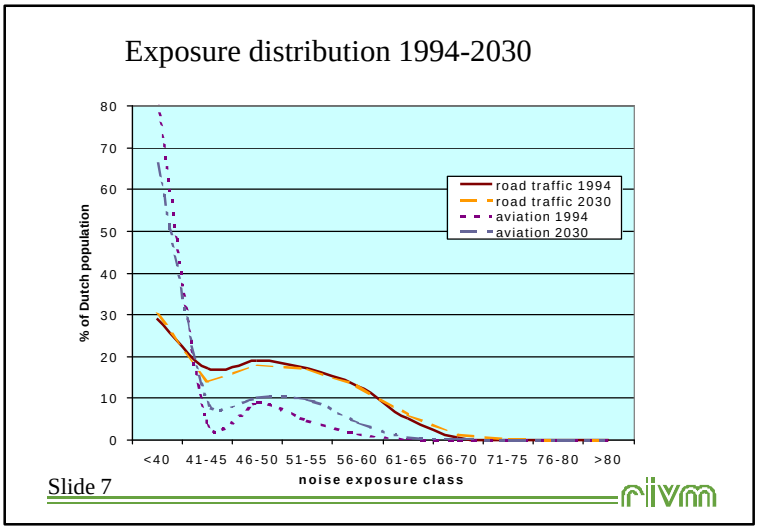




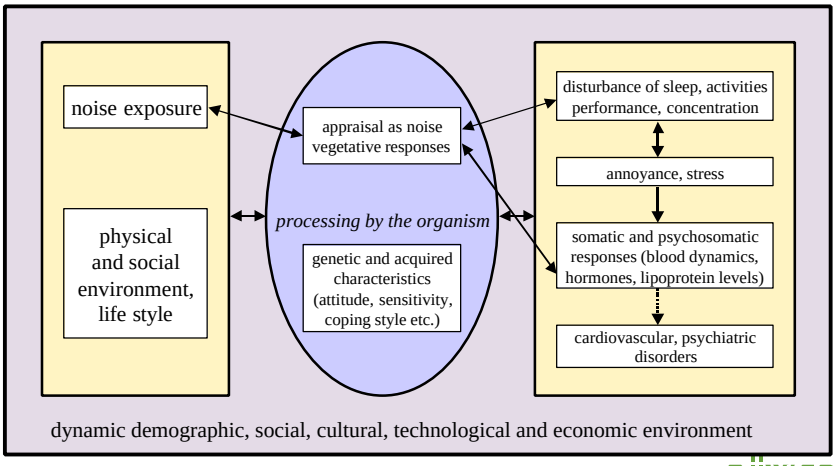
Slide 7 shows a crude output of this national model for road traffic and air traffic in 1994 and projections for 2030. Traffic noise exposure roughly stabilizes, while exposure to airplane noise significantly increases given the expansion Schiphol airport.

A conceptual model describing the impact of noise is represented in Slide 8. Response are determined by noise levels and characteristics of course, but may be modified by social and endogenous factors such as attitude, coping style etc. Noise induces disturbance of sleep and daily activities, annoyance, stress which may lead to various intermediate responses, such as hypertension, increased stress hormone levels, shifts in cholesterol composition etc. In turn these may affect the risk of cardiovascular disease. This model is still controversial; there is mechanistic evidence from clinical studies, and there are epidemiological indications for an association between noise exposure and cardiovascular endpoints, be it still inconclusive and controversial.

To assess what would be the public health significance of noise exposure for cardiovascular disease, if the association was causal, we used the results of a comprehensive meta-analyses of all published studies to assess the noise attributable cardiovascular disease burden. Relative risk estimates were combined with exposure distributions and Dutch prevalence and incidence data on cardiovascular disease. These are preliminary estimates, keeping in mind that some of the estimates were far from statistical significant.



Conceptual model (HCN, 1999)

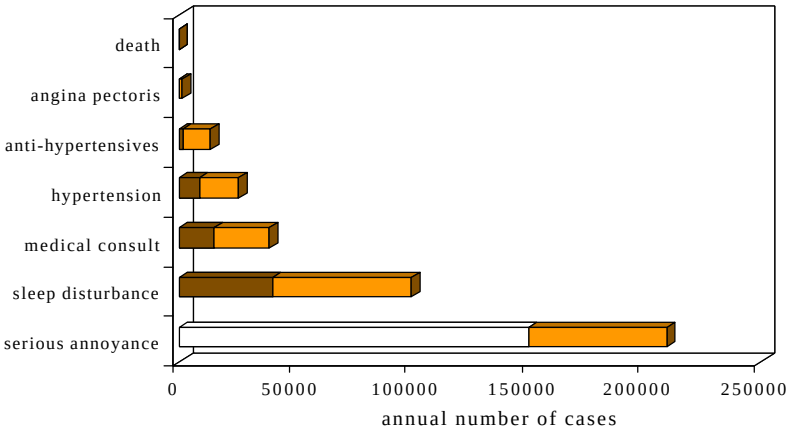


Slide 8

Slide 9 shows the results for road traffic exposure, which display a pyramid shape: Many people suffering from mild effects such as annoyance or sleep disturbance, relatively few people having serious cardiovascular symptoms. We are still in the process of refining the calculations especially with respect to uncertainty analyses (Monte Carlo).

- severe annoyance 1 500 000-2 000 000
- sleep disturbance 400 000-1 000 000
- GP consult 15000-40000
- hypertension 9000-25000
- anti-hypertensives 1500-13000
- Angina pectoris 0-1100
- death 0-21

Disease burden road traffic noise

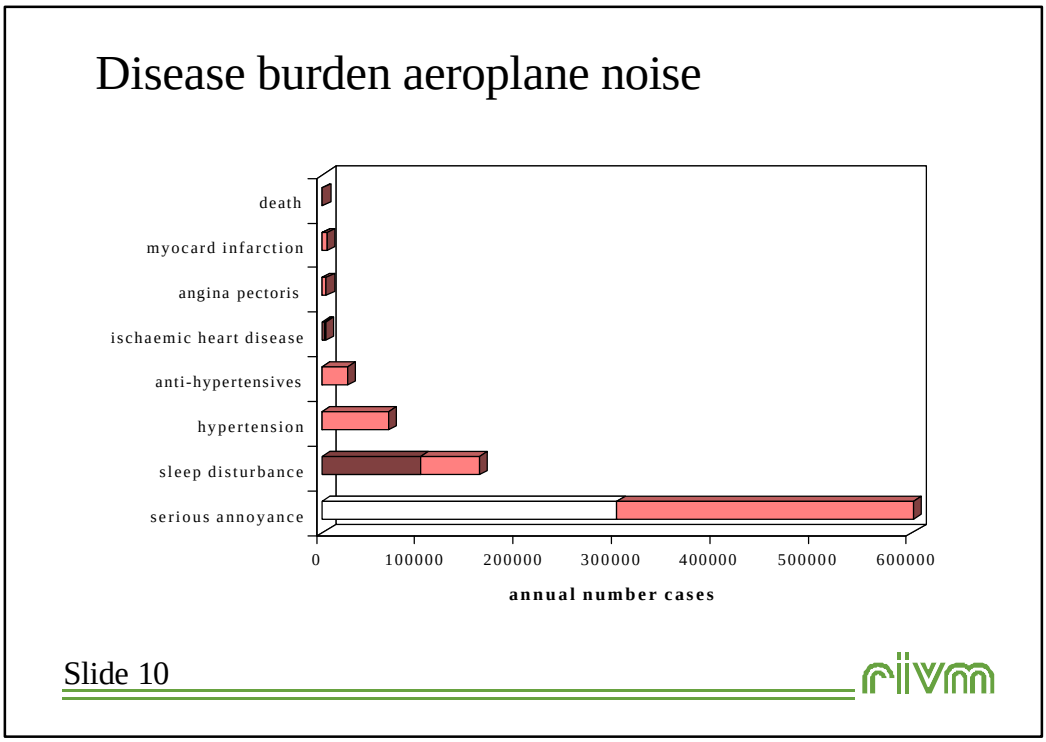


Slide 9

Cardiovascular health end-points associated from air traffic noise show a similar pattern (Slide 10). Some of these end-points have a lower limit of zero, reflecting non-significant meta-analysis results.

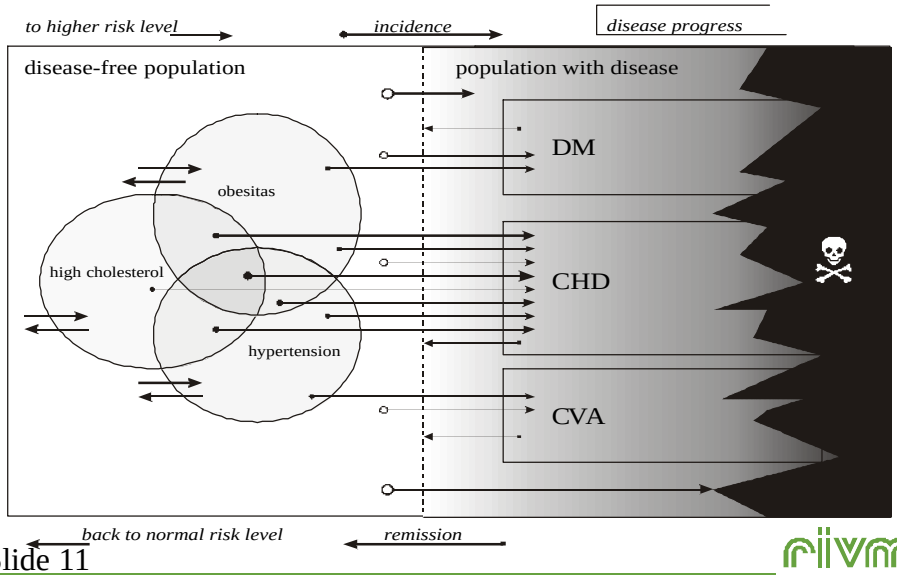
- annoyance 300 000-600 000
- sleep disturbance 100 000-160 000
- hypertension 0-68 000
- anti-hypertensives 0-25 500
- Ischaemic heart disease 1 400-3 000
- Angina Pectoris 0-3 700
- Myocard infarction 150-5 000
- death 0-82

Sleep disturbance is measured sleep logs and diaries, actimeters (watchlike instruments recording nocturnal movements: subjective sleep quality measurements, and number of awakenings during sleep period time. A good test model is urgently needed.



To estimate the actual health loss associated with noise exposure in terms of disability adjusted life years, we used a chronic disease model developed at our institute (Slide 11). Basically this model can be regarded as a sophisticated life-table. Applying a demographic module and trends in (common) risk factor prevalence it simulates annual changes in disease-specific morbidity as a result of incidence, recovery, disease progression or death. By using noise attributable changes in hypertension prevalence as input we were able to calculate attributable morbidity and excess mortality rates (incidence, initial prevalence and mortality were derived from Dutch health data collected in the framework of our Public Health Status and Forecast Report. By combining years of life lost and years spent with disease we were able to calculate the loss of DALYs due to noise exposure).

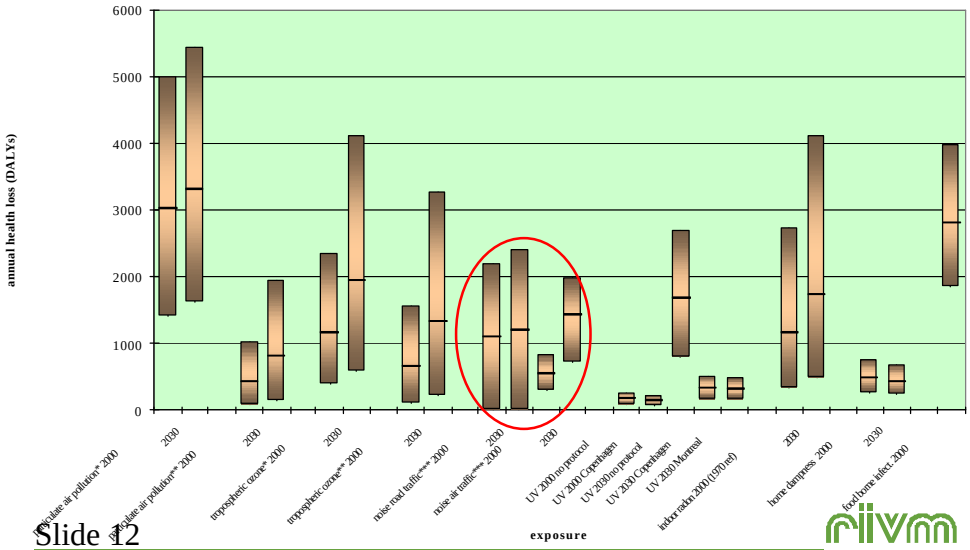
Chronic Disease Model (RIVM 1997)



Slide 11

Slide 12 provides some provisional results compared to disease burden estimates for a number of other environmental exposures for a 2030 scenario.

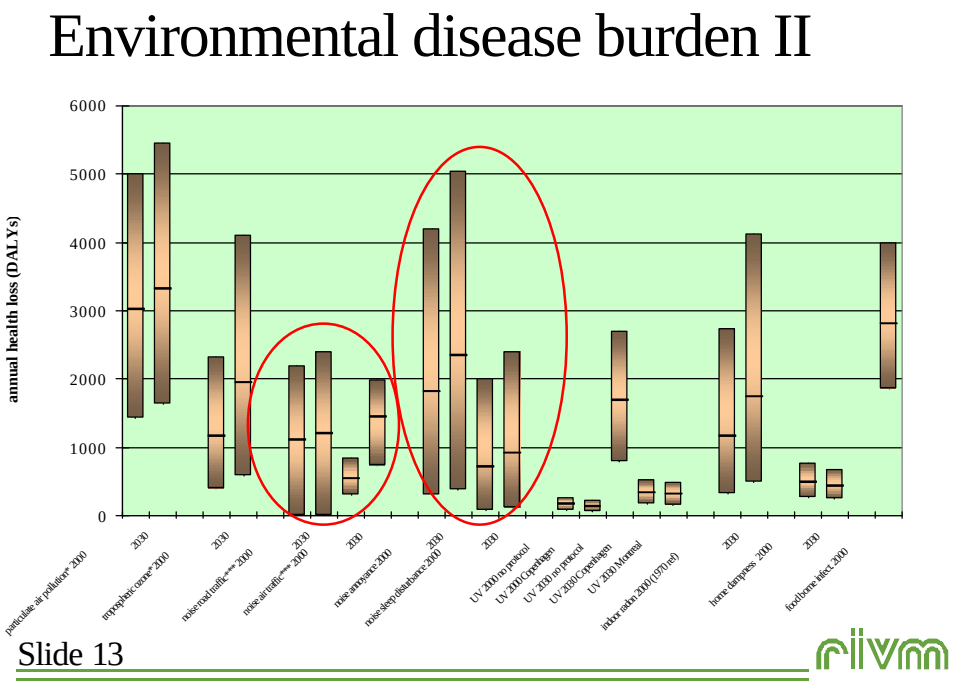
Environmental disease burden I



Slide 13

Slide 13 represents disease burden in the hypothesis that social responses such as annoyance and sleep disturbance are considered as a genuine health effect (cumulative not source specific). In fact annoyance and sleep disturbance was included in our formal exercises to attribute severity weights to health states by panels of physicians. Very few

of the panel members objected to giving weight to these states for not being a health end-point. Although the weights were very low in general, due to the large number of cases the resulting health burden was very substantial. It is disputable whether these end points can be evaluated in the same league.



A number of critical points to conclude:

The epidemiological evidence with respect to noise and cardiovascular disease is relatively poor and inconclusive, especially the exposure assessment is often very poor, furthermore most studies are of a cross-sectional design. Substantial confounding due to social-economic status is suspected, which makes it difficult to detect the small attributable risk due to noise.

The discussion on what to consider as health effect is interesting. Healthy life expectancy in postmodern society has remarkably increased and quality of life issues are increasingly dominating the discussion.

The application of severity weights, although formally derived in a relatively sophisticated way, introduces a subjective aspect into the model, which is sometimes disputed. These severity weights only seem to be critical with respect to mild response with a substantial prevalence.

In these types of integrated assessments many substantial uncertainties are accumulating. Despite available methods to describe and quantify uncertainty, it will be difficult to convey the right message to policy makers and the public. Uncertainties may even regard the constructs we use.

Annex 6.5: Estimating the global burden of disease from indoor air pollution

Kirk R. Smith and Sumi Mehta

University of California at Berkeley

Human exposure to air pollution is dominated by the indoor environment. Here, we address indoor exposures from indoor sources. A significant amount of indoor air pollution comes from outdoor sources, and vice-versa, depending on the exposure scenario. However, here we do not address indoor exposures resulting from outdoor sources, nor do we address how indoor sources can affect outdoor pollution levels. Sources of indoor air pollution in the household environment are described in Slide 1 below:

IAP Sources in the Household Environment

Pollutant	Source
Particles	Solid fuel combustion, smoking, cleaning
Combustion Byproducts	Fuel combustion, smoking
Volatile Organic Compounds (VOCs)	Furnishings, household products, smoking, solid fuel combustion
Biological Pollutants	Furnishings, ventilation, moist areas in home
Pesticides	Household products, outdoor dust
Radon	Ground beneath structure, ventilation

Slide 1

We focus on the household environment, as the largest fraction of time spent indoors occurs at home. Other key indoor environments include schools, vehicles, and the workplace. However, there is a lack of exposure-response studies in schools and vehicles, and workplaces exposures are diverse and better dealt with separately.

This project focuses on three major indoor air pollution exposures, as detailed below (Slide 2):

3 Major IAP Exposures

1. Largest traditional source of exposure:
   Cooking and heating with solid fuels (wood, coal, dung, charcoal, agricultural residues)
2. Largest modern source of exposure:
   Environmental tobacco smoke (ETS)
3. Potentially large source of exposure:
   Radon

Slide 2

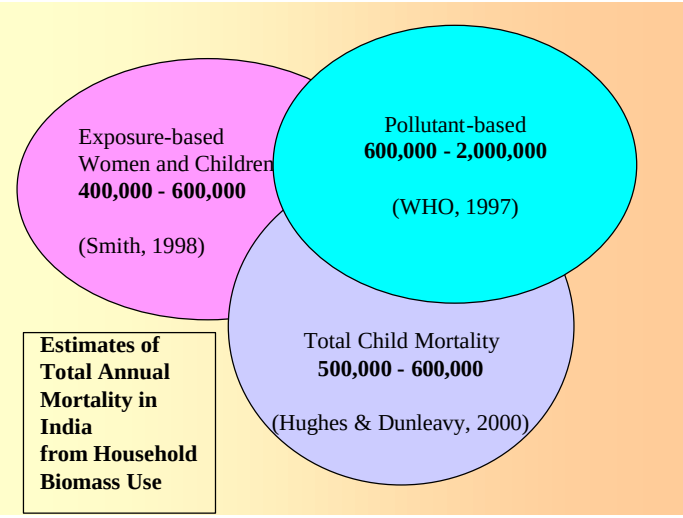
Four major approaches have been used to estimate the GBD from IAP (Slide 3). Each approach uses different types of data and methodology. It should be noted that the exposure-based approach, which involves a disease-by-disease summation of associated health effects, is the only method likely to result in an underestimate of GBD.

Four Approaches to Estimating the GBD from IAP

Approach	Method	Likely Bias
Pollutant-based	Exposure-response extrapolation	Overestimate
Child Survival	Survival analysis	Overestimate
Cross-National	Regression	Overestimate
Exposure-based	Disease by disease summation	Underestimate

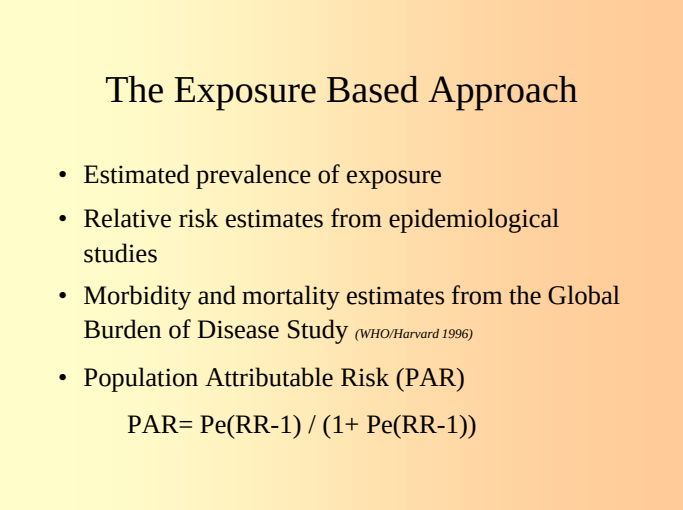
Slide 3

The Slide below (Slide 4) demonstrates how estimates of annual total mortality from indoor air pollution from household biomass use in India differ depending on the approach used.



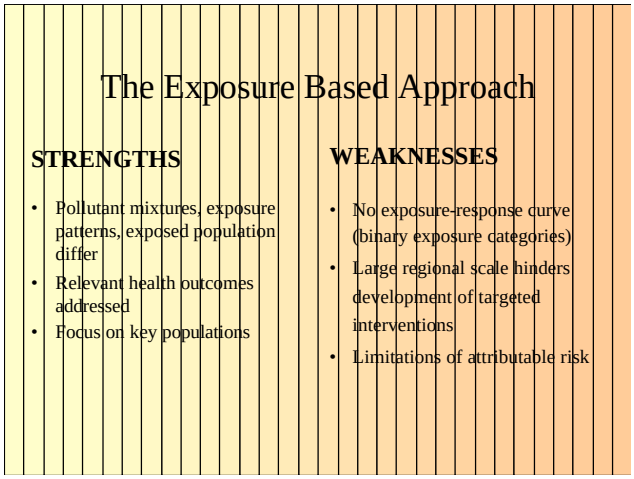
Slide 4

This project uses the exposure-based approach to quantify the global burden of disease (GBD) from household sources of indoor air pollution. A description of the methodology used in this approach is provided in Slide 5 below.



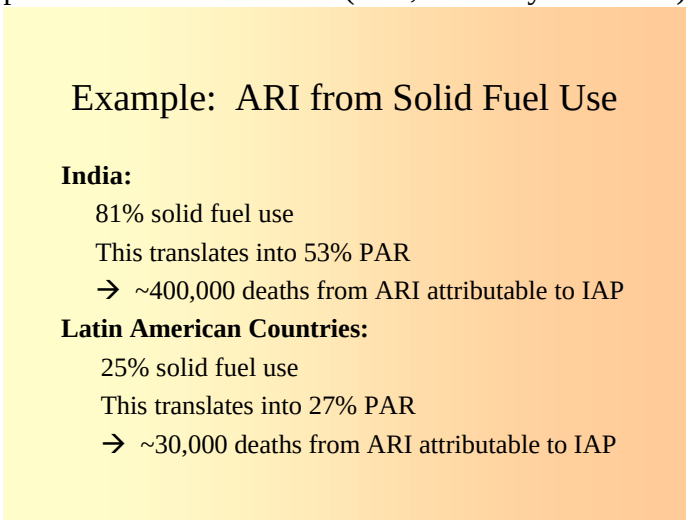
Slide 5

As with all approaches, the exposure based approach has strengths and limitations (Slide 6).



Slide 6

An application of the attributable risk calculation is demonstrated for acute respiratory infections (ARI) associated with solid fuel use in Slide 7 below. India and the Latin American / Caribbean region have very different patterns of solid fuel use, resulting in very different percentages of population attributable risk (PAR) even when the same relative risk estimate is used. When these PAR are used in conjunction with the different incidences of ARI in the two regions, very different patterns of disease burden (here, mortality from ARI) emerge.



Slide 7

Indoor Air Pollution from Solid Fuel Use

Slide 8 details the health outcomes are addressed in the solid fuel use section, and their resulting burden of disease. For health outcomes with strong epidemiological evidence, the geometric mean of the low and high relative risk estimates were used. For health outcomes with moderate or limited evidence, the low relative risk estimate was utilized. It should be noted that 'moderate' and 'limited' do not refer to inconclusive findings. Rather, they suggest that additional, carefully conducted studies are needed to strengthen the evidence base.

GBD from Solid Fuel Use:
Health Outcomes Addressed*

Illness	Population	Evidence
Acute Respiratory Illness (ARI)	Children <5	Strong
Chronic Obstructive Pulmonary Disease (COPD)	Women ≥15	Strong
Lung Cancer (coal only)	Women ≥15	Strong
Tuberculosis	Women ≥15	Moderate
Blindness (Cataracts)	Women ≥15	Moderate
Asthma	Women ≥15	Moderate
Ischaemic Heart Disease	Women ≥15	Limited

** Insufficient evidence to address other potential impacts, including low birth weight and other adverse pregnancy outcomes*

Slide 8

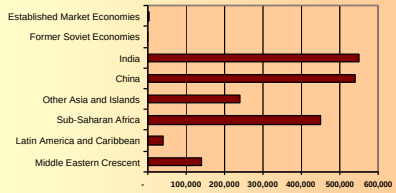
The following four slides (Slides 9 – 12) provide a brief description of our findings. Solid fuel use is associated with nearly 2 million deaths in 1990. Over 1.2 million of these deaths are attributable to ARI in children under five years of age, with India and Sub-Saharan Africa bear the largest burden of these deaths. Solid fuel use accounts for around 4.9% of deaths and 4.4% of DALYs in developing countries. When compared to other major risk factors in developing countries quantified in the original burden of disease study, this ranks below malnutrition (14.9% of deaths, 18% of DALYs) and water / sanitation (6.7% deaths, 7.6% DALYs), but much higher than outdoor air pollution (0.7% deaths and 0.4% DALYs). It should be noted, however, that all of these other risk factors are currently being re-evaluated, so their ranking are likely to change.

GBD from Solid Fuel Use, 1990

	Deaths	DALYs
ARI	1,230,000	43,264,000
Asthma	9,000	511,000
Blindness	400	642,000
COPD	417,000	5,243,000
Ischaemic Heart Disease	98,000	785,000
Lung Cancer	31,000	296,000
Tuberculosis	185,000	3,598,000
TOTAL	1,970,400	54,339,000

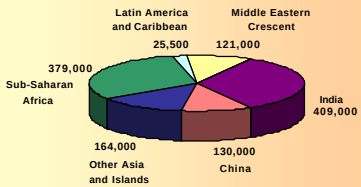
Slide 9

Nearly Two Million Deaths from Solid Fuel Use in 1990



Slide 10

Over 1.2 Million Deaths from ARI from Solid Fuel Use in 1990



Slide 11

How does solid fuel use compare with other major risk factors in developing countries?

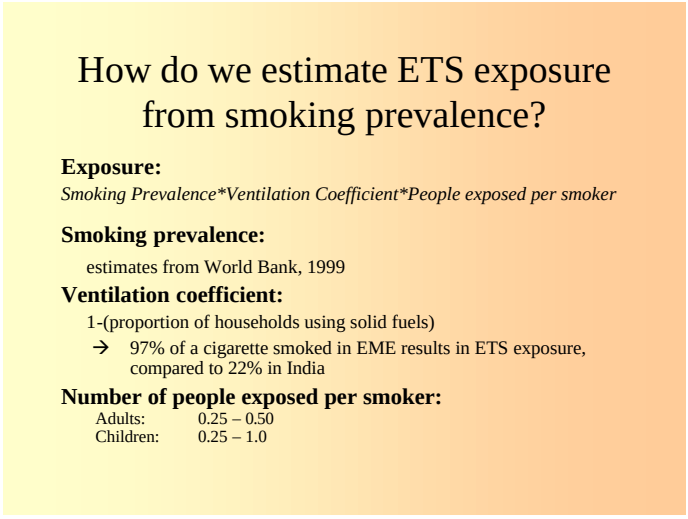
Risk Factor	Percent of Total LDC Deaths	Percent of Total LDC DALYs
Malnutrition	14.9%	18%
Water/Hygiene/Sanitation	6.7%	7.6%
Solid Fuel Use	**4.9%**	**4.4%**
Unsafe Sex/Unwanted Pregnancies	2.5%	3.7%
Alcohol	1.6%	2.7%
Occupation	2.3%	2.5%
Traffic Accidents	1.8%	2.2%
Tobacco	3.7%	1.4%
Hypertension	3.8%	0.9%
Illicit Drugs	0.2%	0.4%
Outdoor Air Pollution	0.7%	0.4%

*Estimates for other risk factors from *The Global Burden of Disease*, WHO/Harvard 1996

Slide 12

Indoor Air Pollution from Environmental Tobacco Smoke (ETS)

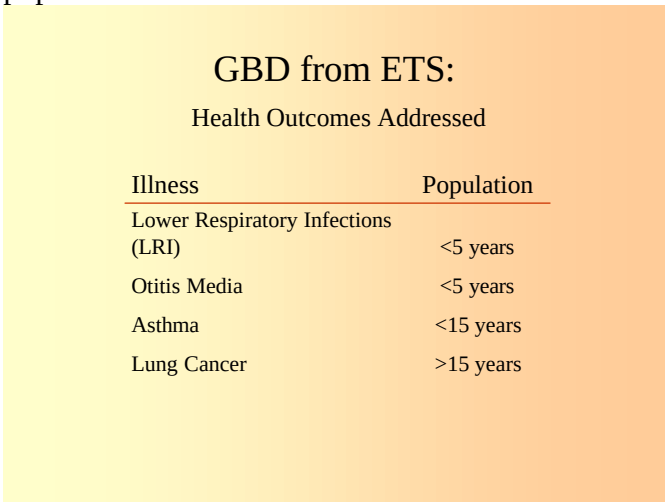
The biggest challenge in quantifying the burden of disease from ETS comes with determining how to estimate ETS exposure from information on smoking prevalence. Slide 13 below details the assumptions used in determining exposure to ETS for each region, and includes information on each of the three components (smoking prevalence, ventilation, and number of people exposed per smoker) that affect the exposure estimate.



Slide 13

The ventilation co-efficient was used to estimate the effective ETS exposure resulting from smoking indoors. A cigarette smoked in a tightly sealed house in EME would result in much greater indoor exposure to ETS than a cigarette smoked in a hut with a thatched roof and open doorway. In general, there seems to be a trend in household ventilation that is inverse to the energy ladder, so that shifts up the rungs of the energy ladder are associated with decreased 'openness' of homes (i.e. less open doors and windows). In the absence of regional differences in household ventilation, the ventilation coefficient was estimated to be 1-(proportion of households using solid fuels) in each region. For example, 97% of a cigarette smoked in EME could result in ETS exposure, compared to 22% in India.

Slide 14 lists the health outcomes addressed by this project, and the relevant populations to which the relative risk estimates were applied.



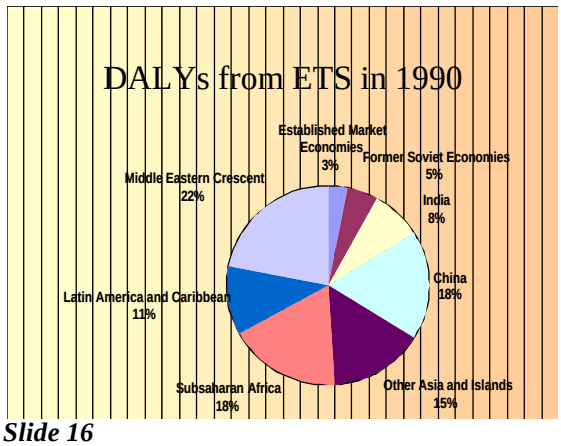
Slide 14

Slides 15 and 16 present our working estimates of the burden of disease from ETS exposure. While ETS is generally regarded as a developed country exposure, these findings suggest that the Middle Eastern Crescent, China, and Sub-Saharan Africa bear a large proportion of the burden of disease from ETS. In addition, most of the deaths attributable to ETS exposure are occurring in young children from lower respiratory infections. While reliable information on smoking prevalence trends are not currently available for many regions of the world, the certain increase in smoking prevalence that is taking place in developing countries is likely to result in an even greater disease burden in the future.

GBD from ETS

	Deaths	Episodes	DALYs
LRI	61,000	6,146,000	2,141,000
Otitis Media	400	3,510,000	16,000
Asthma	140	201,000	69,000
Lung Cancer	5,000	6,000	48,000
TOTAL	67,000	9,863,000	2,274,000

Slide 15



Slide 16

Indoor Air Pollution from Radon

Estimates of mortality from lung cancer associated with radon exposure are only reliable for the U.S., where there is information available on residential radon exposures. Attributable risks from the NAS Beir VI report were applied to 1990 lung cancer mortality for the U.S from the National Center for Health Statistics to estimate the deaths and YLL from lung cancer in the U.S.

As these attributable risks are based on U.S. levels of residential radon exposure and smoking prevalence (due to the strong interaction between radon exposure and smoking), they are not directly generalizable to other regions of the world. However, as Slide 17 suggests, these results suggest a potentially large global burden of disease.

Lung Cancer from Radon in The United States, 1990

	DEATHS	YLL
Male	11,000	78,000
Female	6,500	47,000
TOTAL	17,500	125,000

Slide 17

Discussion

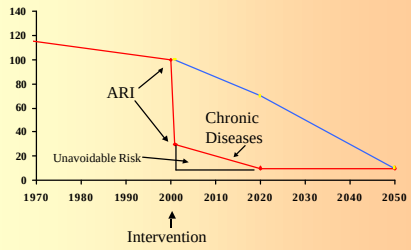
Slide 18 lists some of the limitations of attributable risk, and then continues by addressing the problem of determining avoidable burdens. There is a fundamental difference between attributable and avoidable risk, which is demonstrated here by comparing ARI, an acute health outcome influenced by recent exposures, with chronic diseases such as COPD, which are influenced by an accumulation of exposures over time. As this Slide 19 suggests, an intervention put in place today could vastly affect the incidence of ARI in the future. However, the incidence of chronic diseases will decline over time, as illness in the future can still be attributed to accumulated past exposures.

Discussion

- Limitations of attributable risk
  - How can we deal with interaction between different risk factors and health outcomes?
  - How can we calculate attributable risk when we have multiple risk factors for the same health outcome?
- Determining avoidable burdens
  - Lack of trend information for fuel use, smoking
  - What should be the counterfactual level of exposure?

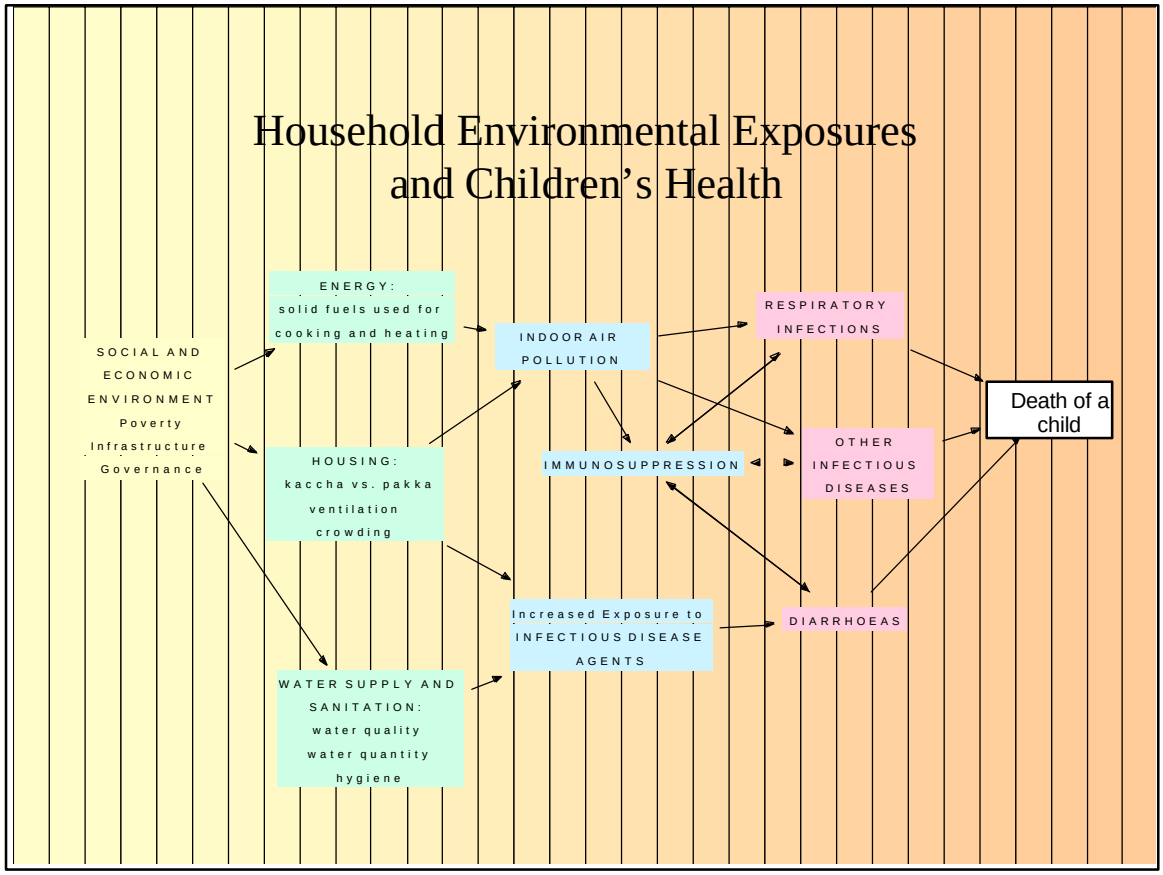
Slide 18

Attributable vs. Avoidable Risk



Slide 19

Finally, it is important to underscore the fact that attributable risk only looks at one class of exposure and outcome at a time. In reality, there are a complex set of interactions between multiple risk factors and health outcomes, which cannot be addressed by this framework. To demonstrate this, Slide 20 provides a schematic representation of a 'causal web' of household environmental exposures and children's health. Indoor air pollution is clearly an important risk factor in and of itself. However, when located within the context of the household environment, the complexities involved with characterizing the health effects of interrelated risk factors becomes apparent.



Slide 20

Annex 6.6: Estimating the global burden of disease from environmental exposure to lead

Lorna Fewtrell
Centre for Research into Environment and Health (CREH)

Lead is a normal constituent of the earth's crust. It is also abundant, easy to mine and has a number of uses. Unfortunately for man it is also highly toxic and doesn't degrade in the environment. Lead has been implicated in a number of health effects, ranging from severe encephalopathy and death to subtle effects on IQ. For the purposes of the initial estimate of the global burden of disease relating to lead a small number of effects have been selected. In children these include:

- IQ loss
- Colic
- Anaemia
- Nephropathy
- Encephalopathy
- Death

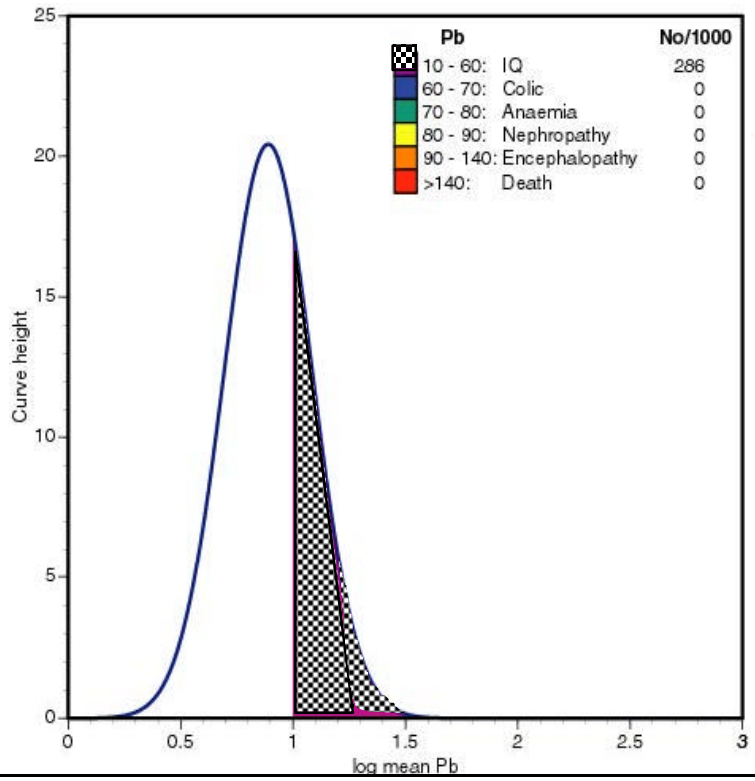
Because of its range of uses, people are exposed to lead through air, water and food. Exposure leads to a measurable burden of lead within the body, which is most often assessed as blood lead level.

CREH has been fortunate to obtain a draft copy of the 'Lead Information' database that is currently under development by CDC. This is serving as the primary source of information on lead exposure. The database contains over 700 references reporting human lead levels, over which, over 85% of the studies report blood lead level.

The approach for determining exposure involves examining the blood lead levels in the database on a regional basis (driven by the 14 regions defined by the World Health Organization). Results from individual countries within any one Region are examined statistically before being pooled. Data from children are being analysed separately from adults, and where there are sufficient data it is hoped to examine children under the age of five as an additional group. The mean data (derived from the individual studies reported in the database) appear to be log normally distributed, therefore the mean and standard deviation of the pooled studies can be used to determine a probability density function. Health effects can then be superimposed onto the exposure distribution (pdf) to determine the number of people affected and to what extent.

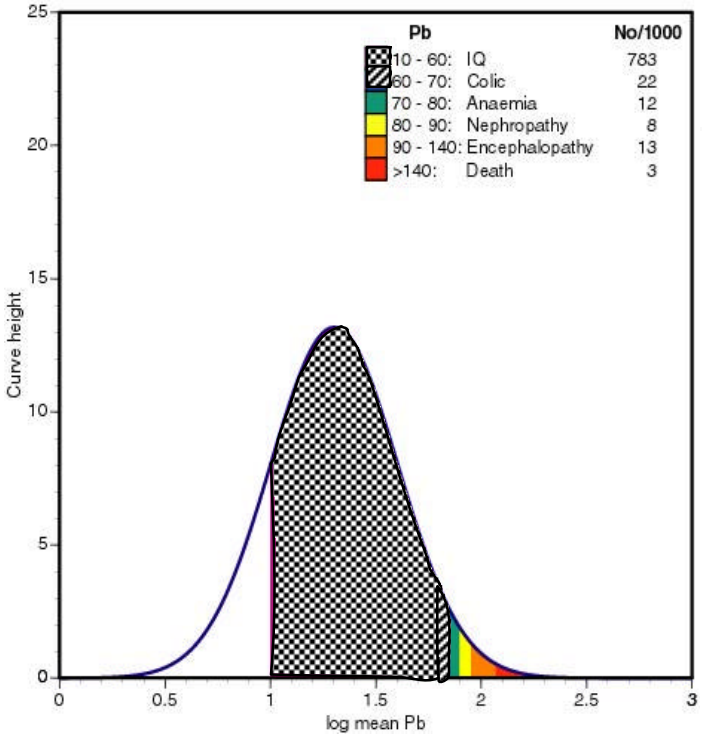
Slide 1 slide shows the pdf derived from data from Canadian children (from studies conducted between 1984 – 1992), with the bands representing health effects, determined from cut off points. This results in an estimate of almost 300 children/1000 affected by IQ reduction. With IQ reduction being the only health effect seen.

Canadian exposure and health effects



Slide 1

Amr B exposure and health effects



Slide 2

The situation (from studies conducted between 1980 – 1996) is rather different in the Amr B region where there is a far greater burden of disease in children due to lead (Slide 2). The complete spectrum of health effects can be seen, including an estimate of three deaths/1000 population.

The last stage, in terms of the global burden of disease is to convert these figures to Disability Adjusted Life Years (DALYs) using a severity weighting.

The use of the blood lead level data, to derive probability density functions, is not without its problems.

- Many studies in the database concentrate on high-risk groups, such as occupationally exposed adults or children living close to a lead smelter. Groups can be split into 'controls' and 'exposed' but then there is the additional problem of ascribing population figures to each group.

- Blood lead level is not the ideal marker. It can be fraught with contamination problems, especially if capillary samples are taken, and it indexes recent, rather than long-term, exposure.

- Many of the studies do not report their quality control measures, so it is not possible to determine if, for example, lead free sampling kit and reagents have been used.

- The database covers studies ranging over a number of years. Many countries have implemented lead reduction programmes, which have had a significant effect on lead exposure; the dates, measures taken and the effectiveness of these programs vary from country to country.

Overall, the use of probability density functions provides a simple and transparent way of describing lead exposure. Their use allows easy visual comparison between areas. With further refinements, to account for some of the problems outlined above, they represent a useful way forward in terms of describing exposure to environmental contaminants.

Annex 6.7: Comparative risk assessment of the health effects of climate change

Tony McMichael, Diarmid Campbell-Lendrum, Sari Kovats
London School of Hygiene and Tropical Medicine

Many aspects of human health are highly sensitive to temporal and geographic variations in climate. It is clear that the global climate has changed significantly over the last century, characterised principally by an increase in average temperatures. There is accumulating evidence both that this change is largely due to anthropogenic emission of greenhouse gases (GHGs) (IPCC 1996), and that the resulting climate change is likely to have significant, mainly adverse, affects on human health (McMichael et al. 1996, Patz et al. 2000). Climate change caused by GHG emissions can be considered an environmental risk factor for health, and a risk factor that may be altered by human intervention. WHO has therefore requested an assessment of the human health benefits of amelioration of climate change through reduction in GHG emissions, using the comparative risk assessment (CRA) framework.

PROPOSED METHODS:

Due to the long-term nature of the relationship between human actions, GHG emissions and climate, actions taken to reduce climate change now are likely to result in avoidance of future, rather than present, health burdens. Estimation of climate change effects on health is therefore a predictive exercise, comparing the expected health consequences of the future climate scenarios that are predicted to result from different, more or less feasible, changes to GHG emissions trajectories (Slide 1). Following CRA terminology, we propose to use the following definitions for a comparison of the possible future health effects of climate change.

Risk factor:
Future changes in global climate attributable to increasing atmospheric concentrations of greenhouse gases (GHGs).

Units of "exposure":
Discrete climate scenarios derived from alternative future trajectories of GHG emissions, as defined by the Intergovernmental Panel on Climate Change (IPCC) in 1995.

Reference scenario:
Business as usual (BAU), i.e. unmitigated current emissions trends (reference scenario)

Alternative or counterfactual scenarios for comparison:

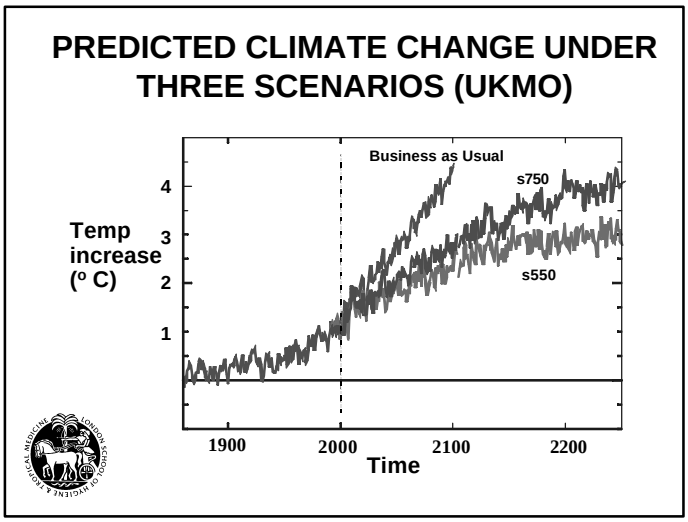
1) Stabilization at 750 ppm CO_2-equivalent (can be considered the *feasible* minimum)

2) Stabilization at 550 ppm CO_2-equivalent (*plausible* minimum)

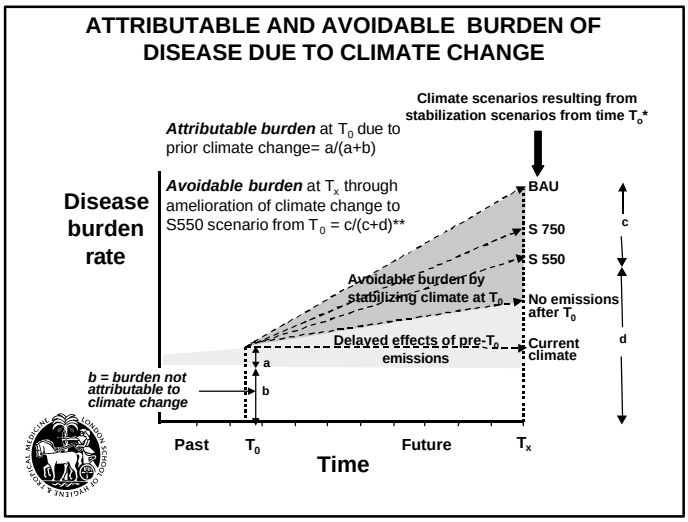
3) 1961-1990 levels of GHGs and associated climate, (the World Meteorological Office definition of baseline climate, which can be considered the *theoretical* minimum).

Time slices for estimation:
Averages from 30 year time-windows, centred on the 2020s and 2050s.

SLIDE 1

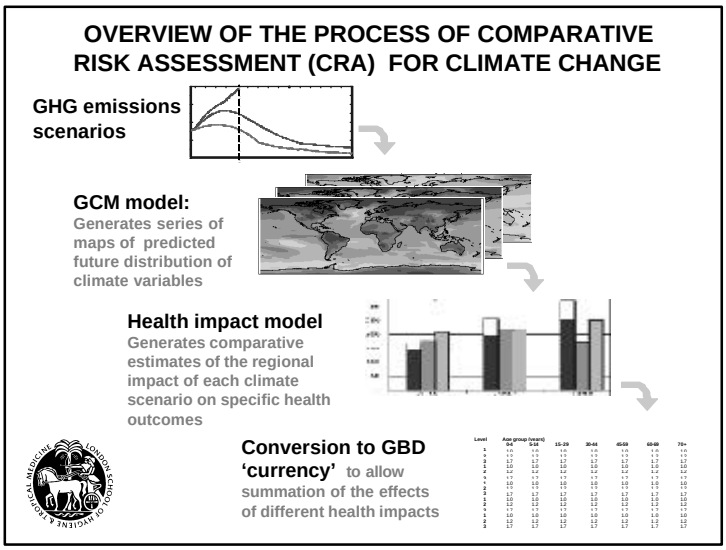


SLIDE 2



Estimation of the attributable and avoidable burdens of disease (Slide 2) may be generated by integrated assessment modelling, summarised in Slide 3. This consists of linking predictive models describing the chain from GHG emissions to climate, to impacts on health-related outcomes, to health outcomes recognised under the GBD system (i.e. which have either ICD or GBD codes).

SLIDE 3



This preliminary assessment will be based on existing models for specific health impacts, rather than new analyses. Although such modelling is in its infancy and remains subject to multiple uncertainties, some form of quantitative predictive model is available for a range of health impacts.

a) Outcomes which can be estimated directly or (often very) indirectly from existing models.

Direct impacts of heat and cold:		GBD code
Incidence of deaths due to	Cardiovascular diseases	(G089)
	Respiratory diseases	(G094)
Incidence of	non-specific hospital admissions	(G136)
Food and water-borne disease:		
Incidence of episodes of	Diarrhoea	(G009)
Vector-borne disease:		
Incidence of cases of	Malaria	(G018)
	Dengue	(G027)
	Schistosomiasis	(G022)
	Trypanosomiasis	(G020)
	Onchocerciasis	(G025)
	Leishmaniasis	(G023)
	Chagas disease	(G021)
	Lymphatic filariasis	(G024)
Natural disasters:		
Incidence of deaths due to	Drowning	(G129)
	other unintentional injuries	(G131)
Incidence of	other unintentional injuries (non-fatal)	(G131)
Risk of malnutrition		
Prevalence of	deficiencies in recommended calorie intake	(G048)
Lack of water		
Incidence of death/diseases	attributable to water shortages	(G136)

b) Health impacts for which no quantitative models exist, which may therefore have to be assessed qualitatively.

Health impacts of population displacement due to natural disasters, crop failure, water shortages
Possible outcomes include all health impacts of refugee status, increased risk of conflicts.

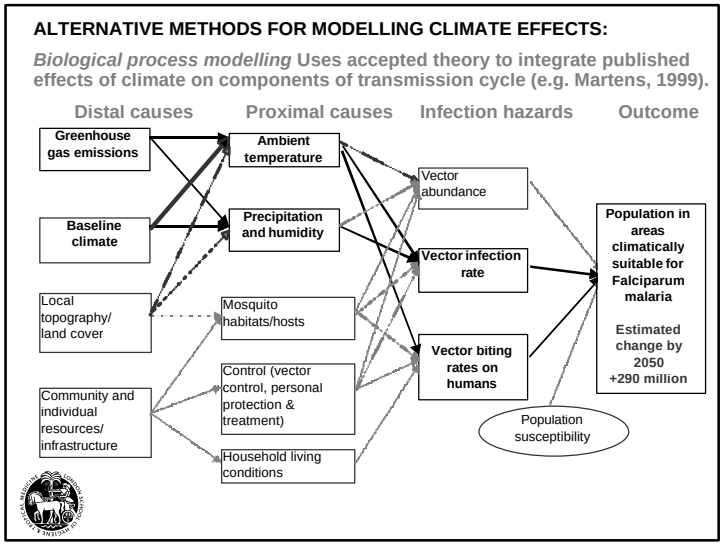
Health effects of reduction in biodiversity and ecological stability
Increased risk of outbreaks of new or previously rare infectious diseases.

EXAMPLE OF QUANTITATIVE IMPACT ASSESSMENT MODELLING:

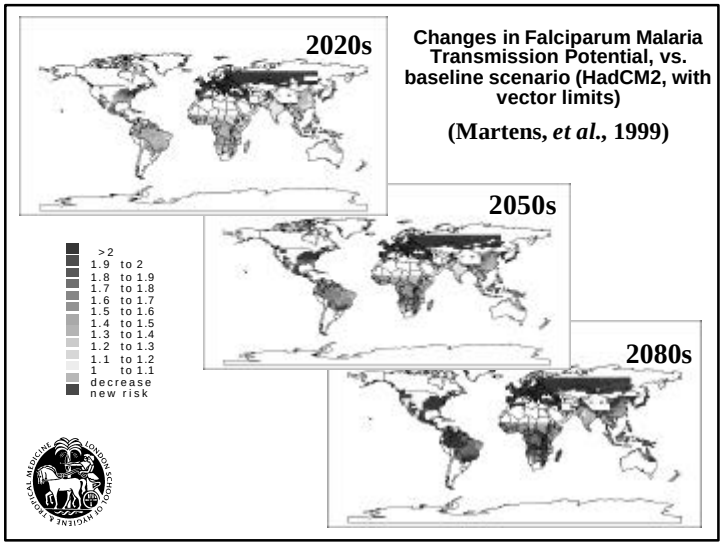
Substantial research effort has been directed towards estimating the potential effect of future climate change on malaria transmission. Martens et al. (1999) have integrated published estimates of the effects of temperature on the main components of vectorial capacity (slide 4), in order to estimate the potential effect of future climate change on the geographic distribution of malaria (slide 5), and hence the potential change in the future population at risk of the disease.

Such models are flexible, and may be applied to alternative scenarios describing future climate and other consequences of population growth and development. For example, new alternative scenarios defined by IPCC (SRES scenarios) include not only future changes in climate, but associated changes in population and development (slide 6). When these are applied to the malaria model, they result in slightly different estimates of the number of people at risk of malaria, although substantial increases are still predicted under each scenario (slide 7). Changes in the proportion of people at risk are less dramatic, but still significant (slide 8).

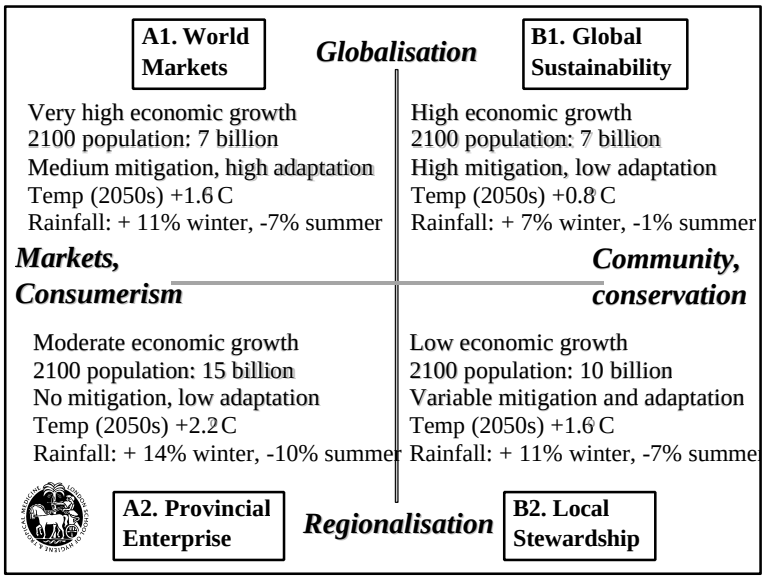
SLIDE 4



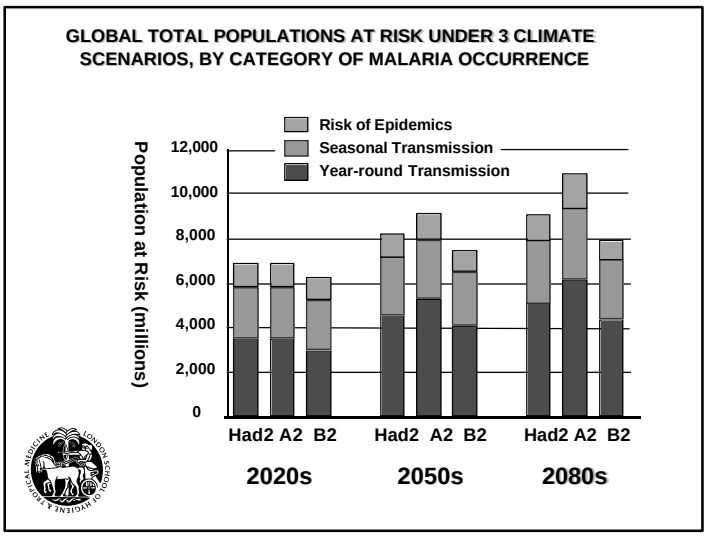
SLIDE 5



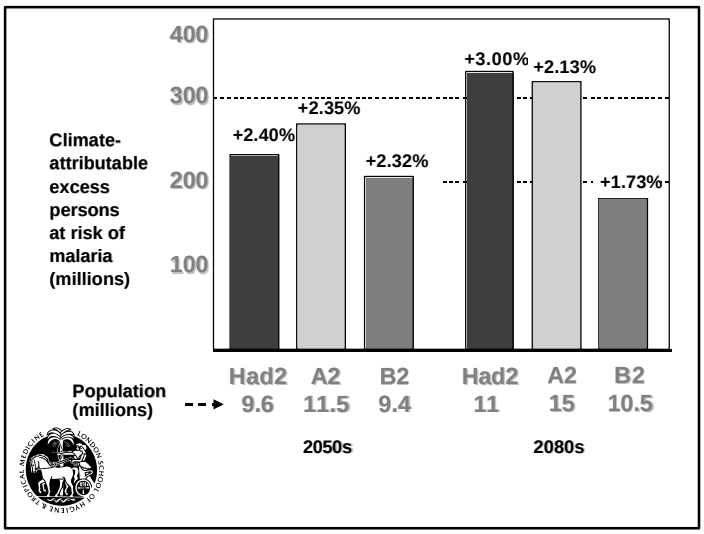
SLIDE 6



SLIDE 7



SLIDE 8



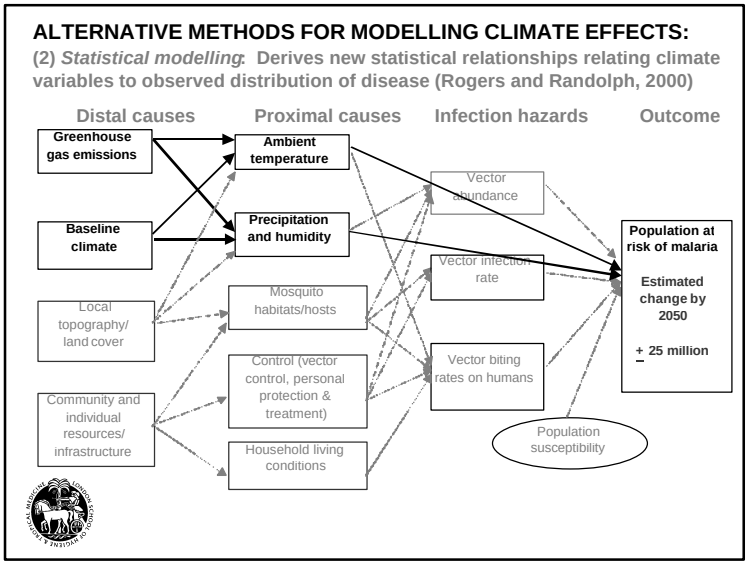
UNCERTAINTIES AND KNOWLEDGE GAPS:

There are considerable uncertainties in predicting the effects of future climate change on health. The most important of these relate to:

- Future emissions of greenhouse gases (based on population and economic growth etc.).
- Effects of simplifying assumptions and choice of initial conditions and parameter values within global climate models.
- Natural variability of climate.
- Effects of simplifying assumptions and choice of initial conditions and parameter values within health impact models.
- Levels and effects of non-climate determinants of health in the future - particularly socio-economic aspects that determine "vulnerability".
- Limited opportunity for directly assessing the accuracy of predicted health outcomes.

Some of these will be addressed as more baseline data is collected, as the field of impact assessment modelling expands and improves, and as alternative approaches are compared. For example, Rogers and Randolph (in press) describes direct statistical correlations between climate variables and the current distribution of malaria (rather than attempting to model individual components of the transmission cycle) and links these derived relationships to climate prediction models (Slide 9).

SLIDE 9



Although the resulting predictions of changes in the number of people at risk are much lower than previous estimates, it is not yet clear how much the discrepancies are due to the different modelling approaches employed, or differences in definition of the outcome predicted: populations living in areas climatically suitable for malaria vs. living in areas where malaria is actually predicted to occur. It should be noted that due neither model directly estimates the most important outcome for this exercise; proportional changes in numbers of malaria cases.

CONCLUSIONS:

The primary objective of the CRA exercise is to generate the best estimates that can currently be made of the net health effects of future climate change. Perhaps more importantly, the CRA

should also stimulate testing and improvement of existing models, generation of new models for health impacts which have not yet been investigated, and help to focus future modelling efforts on the questions of greatest relevance to policy.

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