Quantification of the Health Effects of Exposure to Air Pollution

Report of a WHO Working Group

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ABSTRACT

Quantifying the impact of air pollution on the public’s health has become an increasingly critical component in policy discussion. Those responsible for any health impact assessment must address important methodological issues related to both its design and conduct. A WHO Working Group examined several of these issues as they applied specifically to assessments of air pollution. The Group concluded that the most complete estimates of both attributable numbers of deaths and average reductions in life-span associated with exposure to air pollution are those based on cohort studies. Time-series studies would continue to contribute to scientific understanding of exposure–response relationships. The Group identified sensitivity analysis as an intrinsic part of impact estimation that is critical for quantifying the uncertainty of the estimates. Such analysis should consider deviations of the conditions in the target population from those in the assessed population, which would plausibly affect estimated pollution effects.

Keywords

AIR POLLUTION – adverse effects
ENVIRONMENTAL MONITORING – methods
ENVIRONMENTAL EXPOSURE
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1. Introduction

Over the past decade epidemiologic studies in Europe and worldwide have measured increases in mortality and morbidity associated with air pollution (1,2). As evidence of the accumulated health effects of air pollution has accumulated, WHO and European governments have begun to use data from these studies to inform environmental policies. Quantification of impact of air pollution on the public health has increasingly become a critical component in the policy discussion (e.g. 3–6). Although health impact assessments can provide important information for regulatory and public health decision-making, the results are often prone to misinterpretation, even when the assessment is done rigorously, and its multiple uncertainties are carefully presented and explained to decision-makers, the press, and the public.

Any health impact assessment of air pollution must address important methodologic issues relevant to both its design and conduct. Clarity in defining these issues is a prerequisite for proper interpretation of the results in the policy arena. An earlier WHO Guideline document, Evaluation and use of epidemiological evidence for environmental health risk assessment (7), examined the general methodology of the use of epidemiologic studies for health impact assessment. This report presents the conclusions and recommendations of a Working Group convened by WHO to examine several of these aspects as they apply specifically to air pollution health impact assessments.

The quality of estimates of health impacts of air pollution depends critically on the existing state of biomedical knowledge. And although gaps in scientific knowledge about the health effects of air pollution need not necessarily preclude action to protect the public health, our current assessments of impact would benefit from additional research. In addition to its evaluation of methods for health impact assessment, the Working Group made recommendations for additional research, including the effects of long-term exposure and factors that modify the effect of air pollution.

2. Scope and purpose

The overall objective of this consultation was to review the available methods for health impact assessment of air pollution and to agree upon common approaches. In general, the Working Group was charged to recommend methods of impact estimation, critically review their underlying assumptions, and recommend health impact estimators that would be the most informative for decision-making, and for use in integrated models of air pollution management. The Working Group was also asked to recommend approaches to the evaluation, interpretation, and presentation of uncertainties of health impact estimates. This report focuses on the use of epidemiologic methods and data for health impact assessment of air pollution. Although laboratory studies, both human and animal, have contributed to both hazard identification and risk assessment of air pollution (especially for certain carcinogenic substances), epidemiologic studies provide a rich source of information for impact assessment of the most common exposures and are a preferable basis for impact assessment.

Within this general framework, the Working Group was charged to pay particular attention to the interpretation and use of the wide range of possible outcome measures that could be used to quantify the impact of air pollution exposure.
Specifically, the Group was asked by WHO to consider:

- The relative merits for mortality impact assessment of estimating reduction in life expectancy versus the number of attributable deaths. In this context, the Working Group was asked to consider methodologic issues including displacement of time of death, possible harvesting effects, and the induction time (lag) for air pollution;
- The range of health outcomes (e.g. incidence and prevalence of diseases, symptoms, sub-clinical physiologic effects) that should be considered in health impact assessments of air pollution;
- The use of multiple pollutant-specific estimates of effect for a single outcome, and the use of multiple health outcomes in a single impact assessment of a given exposure;
- Which components of risk estimates made in one population can be transferred (generalized) to another? Despite the tremendous increase in research on the health effects of air pollution over the past decade, health impact assessments frequently must extrapolate the results of studies in one locale(s) to estimate impacts in another. Such assessments often apply exposure-response functions derived from studies on health effects of air pollution to estimates of ambient pollution concentrations in the locale of interest.

The Working Group was not requested to perform a critical review of the health risks due to air pollution, but rather to focus on methodology that could be applied when such review is completed according to the guidelines *Evaluation and use of epidemiological evidence for environmental health risk assessment*.

The Working Groups recommendations will be used in WHO programmes, and will also be made available to the national and international agencies using health risk assessment as a tool in the design of strategies to reduce air pollution and its impact on health. Furthermore, the results of this consultation will be used as input in a broader discussion on the economic valuation of the impacts of air pollution on health.

3. Process

The Working Group convened by the Bilthoven Division of WHO European Centre for Environment and Health, comprised experts who develop and apply methods for health risk analysis, and scientists involved in the communication of the results of the analysis to the public or decision-makers. It also included experts who conduct integrated assessment modelling for air pollution management and who use this work for decision-making (see Roster of Working Group members).

Prior to the meeting, the experts were invited to submit short working papers and/or to recommend background reading material. These were distributed to the Working Group members to provide input to the discussion at the meeting (see References).

Over a three-day period, (20–22 November, 2000), the Working Group held a series of plenary and small group discussions to develop their conclusions and recommendations. The Working Group selected Bert Brunekreef as its Chairperson, and Aaron Cohen as the Rapporteur. Two subgroups were formed to develop recommendations specifically addressing mortality and morbidity impact assessments, which were then discussed by the entire group at the conclusion of the meeting. Klea Katsouyanni and Ross Anderson chaired the subgroups, and Robert
Maynard and Irva Hertz-Picciotto acted as subgroups rapporteurs. The discussions and conclusions of the Working Group, revised according to the final plenary discussion, and eight specific recommendations derived from them, provide the major content of this report, and are presented in Sections 4–5, below.

4. Methodologic issues: summary of Working Group discussions

The Working Group, after considering WHO’s charge as presented in Section 2 (above), identified six methodologic issues that should be considered in the planning of a health impact assessment of air pollution, and offered specific recommendations for addressing them (see Section 6). These reflect closely the recommendations of an earlier WHO guideline document, Evaluation and Use of Epidemiological Evidence for Environmental Health Risk Assessment (and its Annex 3.2). Within a general framework set by that document, the Working Group considered issues specifically related to air pollution.

The Working Group focused its attention mainly on the choice of health outcomes for use in health impact assessments, and on how epidemiologic estimates of the effects of air pollution should be used in such assessments (Sections 4.1–4.3, below). The characterization of air pollution exposure and sources of uncertainty in health impact assessments (Sections 4.4–4.6, below) were not discussed in comparable depth, though the Working Group did offer general recommendations in each case. These issues were also addressed in the earlier WHO Guidelines cited above.

While the general points and conclusions of the discussion will apply in a variety of populations, the recommendations focus on the conditions pertinent to the European Region of WHO. Therefore, any extrapolation to the other regions should be made with consideration of possible differences in social, health and environmental conditions possibly influencing health impact assessment procedures in those populations.

4.1 Which health outcomes should be considered in a health impact assessment of air pollution?

Exposure to outdoor air pollution is associated with a broad spectrum of acute and chronic health effects ranging from irritant effects to death (8,9). According to the WHO definition of health, all these outcomes are potentially relevant for health impact assessment (10). Recently, a committee of the American Thoracic Society identified a broad range of respiratory health effects associated with air pollution that should be considered “adverse”, spanning outcomes from death from respiratory diseases to reduced quality of life, and including some irreversible changes in physiologic function (11). In general, the frequency of occurrence of the health outcome is inversely related to its severity (Fig. 1). This suggests that the total impact is likely to exceed that contributed by the less frequent, more severe outcomes, and, in some cases, may be dominated by the less severe, but more frequent, ones.

Among the broad categories of mortality and morbidity there are a wide variety of specific outcomes that could be assessed, and should be considered for health impact assessment. With regard to morbidity, both acute and chronic conditions were deemed pertinent. As discussed in the earlier WHO guideline document, and also below, the choice of health outcome will ultimately depend on the objective of the health impact assessment. For example, some assessments focused on mortality only (12), and others on several indicators, both mortality and morbidity, for a number of cardio-pulmonary diseases (3).
As an individual’s sensitivity to pollutant exposure increases so the severity of the response will increase for a given pollutant exposure. In other words, a response resulting in a specific outcome (e.g. hospital admission) will occur at a lower concentration in a more sensitive individual. Fig. 2 illustrates this model for two hypothetical individuals with differing sensitivities. We can infer that the average response in a population will depend on the population distribution of sensitivities, and, therefore, on this basis alone, effects estimated at identical ambient concentrations may be expected to differ among populations.

4.1.1 Mortality

The Working Group considered the relative contributions to health impact assessment of time-series studies of daily mortality versus cohort studies of mortality over extended periods, and concluded that both designs could contribute useful, albeit different, information.

- Time-series studies of daily mortality measure the proportional increase in the daily death rate attributable to recent exposure to air pollution. Their estimates are robust with regard to measurement error in exposure classification, and potential confounding from a wide range of mortality risk factors (13). In all likelihood, many deaths caused by air pollution occur among those who are frail due to either chronic disease, or to some transient condition. Their deaths have presumably been advanced (i.e. are “premature”) to some degree, and, therefore, time-series studies can provide estimates of counts of premature deaths due to recent exposure. However, because chronic effects of long-term exposure cannot be fully quantified in such studies, some deaths attributable to air pollution will be missed and the extent to which air pollution advances the time of death cannot be quantified (14,15). For this reason, the use of risk estimates from time series studies of daily mortality will in most cases underestimate the impact of air pollution exposure on both attributable numbers and average lifespan in a given population. Recent advances in the analysis of time-series data (so-called “harvesting resistant estimators and distributed lag models”, provide evidence that short-term increases in air pollution exposure advance the average time of death beyond a few days or weeks (the relative risks appear to be increased at longer time scales for total and cardiovascular mortality), but still do not allow the accurate quantification of average reductions in life expectancy (16,17).

- Time-series studies of daily mortality will continue to be valuable for:
  - demonstrating and documenting the adverse effects of air pollution in specific locales;
  - evaluating the toxic components of the air pollution mixture as more detailed monitoring data become more widely available;
  - quantifying the effects of short-term variation of pollution, including air pollution episodes;
  - serving as the basis for air pollution alert systems;
  - periodic assessments of the health effects of air pollution over time;
  - providing indirect evidence of the plausibility of a longer term effect on health;
  - providing insight on factors (e.g. characteristics of the air pollution mixture, population, climate) that may modify the effect of air pollution on mortality.

- Cohort studies, in which large populations are followed for years and their mortality ascertained, can provide the most complete estimates of both attributable numbers of deaths and average reductions in lifespan attributable to air pollution. Such studies include not only those whose deaths were advanced by recent exposure to air pollution, but also those who died from chronic disease caused by long-term exposure (15,18). The relative risks of mortality from cohort studies of air pollution can be applied to population life-
tables to derive estimates of average reductions in lifespan associated with air pollution \((5,12,19,20)\). Annex 1 provides a discussion of the life-table method for health impact estimation, and an illustration of its application to data from the United Kingdom.

- Because cohort studies provide a more comprehensive estimate of the effect of air pollution on mortality than the time-series studies, their results are to be preferred for health impact assessment. Currently, only three US studies \((21–23)\) provide such estimates, and have been extensively used for impact assessment. The generalizability of the cohort study estimates to populations in Europe or other regions is a concern, and research needs in this area are discussed below.

The Working Group considered the mortality rates that should be used for impact assessments and concluded that they should include, to the extent possible, rates of:

- **Total deaths from non-external all-causes.** The Working Group noted that data on all-cause mortality were almost invariably more reliable than data on cause-specific mortality with respect to both classification and registration. Moreover, there may be causes of death that are related to air pollution that have not been identified. Therefore, risk estimates for all-cause mortality should always be used when available. One important caveat, however, concerns transferring total mortality risk estimates to target populations in which causes of mortality might differ from those in the evidentiary population \((24)\). While, arguably, this may not be a major problem when transferring estimates between United States or western European populations, it could be a considerable problem when the extrapolation is made to developing countries.

- **Cause specific deaths.** The Working Group recommended that, where data are available, the impact of air pollution on cause-specific mortality be estimated for several specific causes of death for which there is evidence that rates have increased due to air pollution exposure.

- **Cardiovascular disease.**

- **Chronic non-malignant respiratory disease.** It is well appreciated that deaths from chronic non-malignant respiratory disease are often misclassified as deaths from cardiovascular disease in death certificate data.

- Investigators have attempted to circumvent this problem by grouping them together as “cardio-respiratory deaths” \((22)\). However, even in the presence of acknowledged biases in their measurement, impact assessments using cause-specific mortality rates for cardiovascular and respiratory diseases may provide results for a biologically plausible subset of deaths, if the biases are well-understood and can be quantified.

When using cause-specific mortality relative risk estimates, competing causes of death need to be taken into account using life-table methods.

- **Lung cancer.** Lung cancer is greatly feared and may, therefore, play a significant role in health impact assessment of air pollution. Although lung cancer mortality may be accurately ascertained in many populations, risk estimates with regard to air pollution may

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1 The recent HEI reanalysis \((27)\) of the ACS and 6-Cities studies study \((2,22)\) disaggregated these deaths, and did not observe effects of air pollution on deaths from respiratory disease per se, but rather on deaths attributed to cardiovascular causes. The Working Group saw no reason to question these results, but found them difficult to understand none the less.
be more subject to random error (due to a small number of expected cases) and to
confounding by cigarette smoking.

- **Age-specific deaths.** Health impact assessments should consider separately age-specific
effects where possible. The Working Group recommended estimation of mortality impacts
separately for younger and older sub-populations, given that current evidence suggests that
the elderly are particularly at risk. The Working Group noted that recent papers have
estimated increased risk of infant and childhood mortality associated with exposure to air
pollution (25,26). Though such effects might not have a large impact in terms of actuarial
calculations in developed countries, (the number of very young children dying is per se
small), the impact on society’s attitude to reducing levels of air pollutants could be large.

The Working Group stressed the need for better estimates of the effects of air pollution on
mortality in population subgroups considered to be at particularly high risk, in light of recent
results that suggest that socioeconomic status may modify the relative effects of air pollution
(27).

### 4.1.2 Morbidity

The recommendations of the Working Group concerning the choice of health endpoints to be
considered in health impact assessments is based on a natural history of disease model in which
physiologic changes precede the development of physical symptoms, reduced function, or even
death. The disease process may have attendant consequences such as reduced quality of life,
restricted activity, and increased use of medical and social services. Air pollution could
conceivably affect any stage in the development of clinical disease and impact any attendant
consequences. Consistent with the ATS statement (11) morbidity indicators can be at the level of
physiologic function (e.g. lung function), symptoms, or consequences for daily living.

The Working Group developed a list of health outcomes that comprise both acute and chronic
conditions plausibly associated with air pollution, and therefore potentially of interest for health
impact assessment (Box 1). In general, these outcomes are consistent with those considered
adverse by the ATS. Box 1 reflects that although there are relatively few categories of
pathologies, there are numerous ways to measure ill health, each of which may contribute to
both the public health and economic impact of air pollution. All of these should at least be
considered in the planning of health impact assessments, without undue concern for the fact that
individuals may (in fact, probably will) experience several of these outcomes. The objectives of
impact assessment may determine which of the outcomes will be included in the final analysis.
Where possible, impacts on these outcomes should be calculated based on age and sex-specific
rates.

A variety of epidemiologic study designs have been successfully applied to study the diverse
range of morbidity outcomes and provide potentially useful estimates of the effects of air
pollution exposure. These designs include cohort studies on the incidence of chronic respiratory
diseases and time series or panel studies of incidence of acute symptoms or diseases.

Some known or suspected effects of air pollution concern constituents other than the commonly
measured gases and particle indices (sometimes referred to as air toxics or hazardous air
pollutants). For this reason, health impact assessments should also consider, where appropriate,
such health problems as neurologic outcomes related to lead exposure, leukemia and non-
Hodgkins lymphoma from benzene exposure, and lung cancer from exposure to PAHs and
metals, and hematopoetic cancer related to butadiene.
Proximity to sources of pollution may create other stresses, e.g. the psychological stress of living near factories due to risk perception, or noise from vehicular traffic. Such effects have been addressed in recent health risk assessments (28) but the Working Group did not address these issues further.

4.2 Which indicators of impact should be estimated?

Various estimators of the health impact of air pollution have been employed in recent health impact assessments. Some assessments have used indices such as the attributable risk (AR), or measures derived from it, such as the number of attributable cases, to quantify the burden of disease or death in a given population (29). The impact of increases in the mortality rate due to air pollution has also been quantified in terms of the average reduction of lifespan produced in a given population (5,12,30). Still other assessments combine impacts on morbidity and mortality, using estimators such as disability- or quality-adjusted life-years (DALYs or QALYS, respectively) (31). Such assessments combine various health outcomes using explicit weighting schemes. The construction of these weights and the estimation of the summary indicators were beyond the scope of the Working Group discussion.

The choice of estimator(s) used in a given assessment should anticipate the use to which the impact assessment will be put. The Working Group appreciated that the policy-setting process must integrate information from science-based impact assessment with the values of the public. Therefore health impact assessments should present their estimates in sufficient detail with regard to various health endpoints, population strata (e.g. age, sex, race, social class), and pollutants to provide the evidence to policy analysts, with an indication of the level of

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Box 1. HEALTH OUTCOMES POTENTIALLY RELEVANT FOR HEALTH IMPACT ASSESSMENT OF AIR POLLUTION

**Acute outcomes**
- Daily mortality
- Respiratory hospital admissions
- Cardiovascular hospital admissions
- Emergency room visits for respiratory and cardiac problems
- Primary care visits for respiratory and cardiac conditions
- Use of respiratory and cardiovascular medications
- Days of restricted activity
- Work absenteeism
- School days missed
- Self-medication
- Avoidance behaviour
- Acute symptoms
- Physiologic changes, e.g. in lung function

**Chronic disease outcomes**
- Mortality (in infants and adults) from chronic cardio-respiratory disease
- Chronic respiratory disease incidence and prevalence (including asthma, COPD, chronic pathological changes)
- Chronic change in physiologic function
- Lung cancer
- Chronic CVD

**Reproductive outcomes**
- Pregnancy complications (including fetal death)
- Low birth weight
- Pre-term delivery
uncertainty (e.g. expressed in terms of full sampling or posterior distributions of the impact estimates), in order to apply them to regulatory decision-making.

Various indices can be derived from the application of mortality risk coefficients from cohort studies to population life-tables (32). They include:

- changes in life expectancy/average years of life lost (presumably decreasing as pollutant levels fall);
- expected decrease in deaths over a given period;
- expected increase in people reaching a given age (e.g. 65 or 75 years).

The choice among indices such as those listed above will depend, in part, on their value for subsequent cost–benefit analyses, which attempt to monetize the value of reductions in ambient air pollution. For example, some analyses use data on peoples willingness-to-pay for specific health improvements (or changes in risk) to rank the predicted benefits (33). In order to use data on years of life lost in such analyses, information about people’s preferences regarding mortality risk and longevity must be elicited and weighted.

As noted above, a wide range of morbidities has been associated with air pollution exposure. Some recent impact assessments estimated the increase in the incidence of certain acute or chronic diseases due to air pollution (3). However, the Working Group considered that impact measures that integrate various clinical manifestations of a disease, and provide estimates of the effects on quality of life are to be preferred. Such measures focus on the end consequences of pollution related illness rather than on the pathological or clinical aspects. Restricted activity days, which include operational concepts such as missed work or school days, as well as reduced physical activities, are concrete, quantifiable and easily communicated. However, more research is needed to quantify the relation of these measures with air pollution exposure, as there have been few studies using this type of outcome. Furthermore there are substantial issues related to transferability between different populations, e.g. different countries or cultures.

The proper use of impact estimates for economic valuation requires close collaboration of health professionals with economists: two groups which, at present, speak different languages. Such collaboration is needed to ensure that economists appreciate the strengths and limitations of the available epidemiological data, and that epidemiologists appreciate the uses to which the estimates may be put and design them appropriately.

4.3 Which components of risk estimates made in one population can be transferred (generalized) to another?

Health impact assessments usually apply air pollution effect estimates (e.g. regression coefficients) derived from a study in one population (the evidentiary population), to estimate impacts in another (the target population). Such assessments assume that the effect estimates in the evidentiary population are transferable, or generalizable, to the target population. The validity of this assumption implicitly requires that the two populations be similar with regard to factors that influence the magnitude of the effect estimates. For example, as noted in Section 4.1, care must be taken when transferring the estimates for total mortality if one cannot assume that the contribution of various causes of death is not similar. Further factors to be considered include the mixture of pollutants, the baseline population health status. Such factors may vary over space and time. Recent analyses have begun to explore how such factors may explain the variation in air pollution effect estimates observed among locations in Europe and the United States.
(2,27,34,35). They suggest the presence of significant and real heterogeneity in location-specific estimates that may need to be taken into account in health impact assessments. However, at present knowledge about effect modifiers is quite limited (see Section 5 below). Until we have a more complete understanding of these factors, their value for health impact assessment will also be limited. Additional research on modifiers of the health risks of air pollution exposure, and how they distribute among populations, is necessary. Further understanding of the sources of heterogeneity will require distinguishing between those due to stochastic variability and real differences between the populations. In addition, exposure measurement error may induce heterogeneity in effect estimates across locations (see Section 5 below).

Health impact assessments should exercise great care when the evidentiary and target populations differ. In practice this means that:

- those designing the health impact assessment, should consult with local experts in the relevant subject matter areas, and with those who conducted the research from which the effect estimates are derived, to assess whether key assumptions are tenable;
- underlying assumptions that justify transferability of effect estimates should be made explicit, and thoroughly discussed in all published reports;
- uncertainties in impact estimates resulting from possible violations of assumptions about transferability should be quantified if possible (see below).

In general, the most precise valid effect estimate should be used for impact assessment. In some cases, that may be the estimate from the target population itself. However, in some, perhaps many, cases where an effect estimate exists for the target population, that estimate may not be the most precise (or valid) estimate, due to random error or epidemiologic bias. Therefore, health impact assessments in specific locales should consider using risk estimates from multi-site studies or meta-analytic summary estimates in the absence of compelling evidence that the target population differs from the aggregate vis-à-vis its response to air pollution.

When compelling evidence of modification of the relative risk does exist, impact assessments should use the most specific relative risk estimates available. It might be more appropriate for example, for an impact assessment of PM and daily mortality in eastern Europe to use the mortality coefficient from eastern European cities, rather than the pan-European coefficient.

The transferability of the mortality effect estimates from the US cohort studies to other, non-US, target populations can be justified on the basis that: (1) these estimates are the only ones that currently exist; (2) they are the only ones which are theoretically justifiable (see Section 4.1.1). None the less, some non-US scientists and government agencies have been reluctant to apply them to European populations because it is not clear how such estimates would be expected to differ, though such differences might be expected “a priori”. Ideally, application of these estimates to other target populations should incorporate information on factors that influence the magnitude of the mortality coefficients and cause them to differ among populations. Unfortunately, lack of knowledge all but precludes this at present. Specifically:

- Although recent reanalysis of the current US cohort studies identified level of educational attainment as a modifier of the air pollution mortality relative risk, the educational level-specific relative risks should not be used for impact assessment in other target populations (27). The role of educational attainment vis-à-vis health effects of air pollution is not well

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2 Such coefficients are not currently available but could be calculated from the APHEA II database.
understood, and it is by no means clear that it should be expected to modify air pollution relative risks in the same way in Europe or especially other, non-western, populations in a similar fashion. Some indication of applicability may be provided by observation of similar short-term effects in Europe.

- Recent multi-site studies and meta-analyses (2,34,35) have identified factors that may modify the effect of air pollution on daily mortality and may partly account for its geographic variability. This knowledge may help guide efforts to apply the results of US cohort mortality studies to other locations, although, fundamental differences between processes assessed by time-series and cohort studies, discussed above (see Section 4.1.1) will need to be addressed.

Transferability of baseline mortality and morbidity rates among European populations cannot be implicitly assumed for purposes of impact assessment. With regard to mortality, population-specific rates, compiled using relatively standardized approaches, are widely available. They should, of course, be used in this context. Differences in recording and classification of cause-specific morbidity among countries lead to non-comparability of baseline rates. Better data on the baseline rates of key morbidity outcomes is a priority for strengthening the capability to perform health impact assessments (see Section 5 below).

Finally, the validity of the statistical model form is an important issue. For example, if a log-linear model is not correct, then differences in baseline risk and typical exposure levels between evidentiary and target populations will produce erroneous impact estimates.

In summary, the transferability of the evidence for impact assessment requires clear formulation of the assumptions made, their comparison with the available data related to the target population and a scientific judgment, supported by sensitivity analysis to assess if the extrapolations made are valid.

4.4 How should exposure to air pollution be characterized for the purpose of a health impact assessment?

Although it is common to refer to the results of epidemiologic studies of air pollution as providing estimates of the exposure-response relation, most epidemiologic studies actually measure the relation between ambient concentration and response. However, in time series studies, we generally interpret these estimates as measuring the effects of daily average exposures of the entire population (or broad strata of it) across broad geographic areas. Use of these broad measures of exposure results in misclassification of exposure for any given individual. Such misclassification of exposure would, under most realistic scenarios, cause an underestimate of the true effect (13), which adds to the uncertainty of impact assessments, which use effect estimates from time-series studies.

A strength of the time-series studies of daily morbidity and mortality is that their effect estimates are calculated using daily concentrations that are widely, consistently and, for the most part, completely recorded. However, health impact assessments of exposure to air pollution from specific sources, e.g. vehicular traffic, should be based on air pollution measurements specifically designed for that purpose. Recent research has considerably advanced the state of the art, by providing new methods, based on GIS and measurement of chemical composition of the pollution (36,37). The usual estimates from time-series studies of daily mortality cannot estimate the effects of relatively brief excursions of exposure of certain individuals, such as exposure to
traffic-related pollution at street level, if such exist. However, certain specialized designs, such as case cross-over studies, may be able to ascertain the effects of such situations (38,39).

Interpretation of the coefficients from the existing cohort studies as reflecting the effects of long-term exposure depends on the assumption that averages of relatively recent pollutant concentrations are indeed indices of long-term exposure during the relevant time window (27). Impact assessments that use the coefficients from the existing US cohort studies should apply them to multi-year concentration data for pollution in the target locale. In any case, the lack of knowledge about the timing of air pollution effects (e.g. critical ages, duration of exposure and persistence of effects) will add uncertainty to the impact assessment of chronic effects.

When the evidentiary and target populations differ, health impact assessments should strive to characterize exposure in the target population to mirror as closely as possible exposure in the study providing the effect estimate. In particular, health impact assessments should:

- Use caution in extrapolating beyond the range of the pollutant concentrations reported in the evidentiary studies. In practice, this constraint applies more to the cohort studies than to the time-series studies: in the latter the observed ambient concentrations generally span a wider range. In particular, one can use sensitivity analysis to test influence on impact estimates of various assumptions used for the extrapolation of exposure-response curve.
- Carefully evaluate the similarity of the sources of air pollution as well as the pollution mix and its variation in time and space in the target and evidentiary locations. If they differ then the ability to transfer effect estimates may be limited. Consultation with experts concerning local conditions will likely be important to fully address these technical questions.
- Consider how cities may differ in their placement of monitors and in determinants of population average exposure (i.e. time outdoors, use of air conditioning, exercise and work habits). A given city's reported levels of pollutants may depend critically on the placing of the monitors during the measurements. In general, data from source-oriented monitoring does not provide reliable evidence for population exposure.

Recent analyses suggest that there is no discernable threshold for the effects of particulate air pollution on daily or longer-term average mortality from cardio-respiratory disease (7,27,40), though for other pollutants, such as ozone, the evidence is not as clear (32). Although this provides some theoretical justification for calculating impacts based on exposure levels down to and even including so-called “background” (possibly non-anthropogenic) levels, the Working Group recommended that in most cases impacts should be calculated for a range of population exposure levels that reflect realistic policy options. Estimation and presentation of the entire exposure – response function facilitates the decisions about the range of exposures used for impact assessment and related risks (40). Depending on the pollutant, those options might include an ambient concentration of zero, some non-zero “clean” concentration, or a concentration mandated by an air quality standard. The desirability of considering separately anthropogenic and non-anthropogenic pollutants will depend on the questions being asked by the policy makers.

In practice, mortality impact estimates have been sensitive to the values chosen for the range of population exposure (3). This sensitivity should be quantified by calculating and reporting the estimates obtained under various assumptions concerning exposure levels.
4.5 How should health impact assessments address the issue of exposure to the multi-pollutant mixture?

The Working Group appreciated that the specific pollutants whose effects are estimated in epidemiologic analyses are best viewed as surrogates for mixtures of pollutants emitted by particular sources. This view suggests that:

- Impact assessments should not simply add estimates of effects of individual pollutants derived from single-pollutant statistical models. However, multi-pollutant models may produce unstable estimates, as the number of pollutants they include increases (41). Adding pollutant-specific effects may be justified when levels of the specific pollutants are clearly not correlated. For example, the overall impact of pollution in some locations in Europe might be estimated by summing the impacts of particles and ozone. This should be done cautiously, because in some cities PM and ozone levels may well be correlated and because the possibility for a synergy (or antagonism) of pollutants cannot be excluded with confidence.

- Despite growing evidence from toxicologic and epidemiologic research that particulate air pollution per se is harmful, other pollutants (e.g. SO₂) should not be ignored. They may, in some settings, be better surrogates for specific sources than some indices of PM (e.g. CO or NO₂ for mobile sources, or SO₂ for the combustion of home heating oil). In some cities their impact on health may be substantial as well. More attention will need to be paid to the analysis of multi-city data to derive reliable coefficients for these pollutants.

- The health impact of air pollution in a given city may depend on the mixture of pollutants. There may be merit in adjusting a given city’s effect estimate for PM₁₀, for example, according to the local concentrations of other pollutants that have been identified in multi-site studies (2,34,35) as effect modifiers for the effect of particles, e.g. NO₂. This needs further development and research.

4.6 How should health impact assessments quantify and express the uncertainty of their estimates?

Health impact assessments should address the uncertainties in their estimates of impact in as explicit and quantitative a manner as possible. They should indicate how deviations from key assumptions would be expected to affect the results of the assessment and their application in policy analyses. The specific content of the uncertainty analysis will, therefore, depend on its purpose (e.g. in consideration of various policy options, or in scientific investigation). The uncertainties in such assessments include those of the effect estimates (random error, bias, and confounding), as well as those associated with generalizing those estimates to target populations. Therefore, the standard measures of statistical precision of epidemiologic estimates (p-values, confidence intervals) alone are not sufficient.

Vigorous sensitivity analyses should be planned as part of any health impact assessment of air pollution. These analyses should be designed to measure the effect on impact estimates of changes in the choice of statistical models for exposure-response relations, population exposure distribution, and baseline mortality and morbidity rates.

Some sources of uncertainty in health impact assessments using the results of time series studies can be identified and, to some extent quantified. For example, the use of a meta-analytic summary estimate of relative risk from the APHEA II study to estimate impacts on daily mortality in a single European city might result in impact estimates that differ by up to 3–4 times
from estimates based on the city-specific relative risks (although, formally, partitioning the variance of the summary risk estimate might reduce this variability and noted above in Section 4.3).

5. Where is more research needed to improve the quality of health impact assessments of air pollution?

Health impact assessment of air pollution is currently limited by knowledge gaps in the following areas:

- **Effects of long-term exposure on morbidity and mortality.** The lack of European studies on the chronic effects of long-term exposure to air pollution, including mortality and the incidence of chronic non-malignant respiratory and cardiovascular disease, is a major research gap. Although the validity of the US cohort studies has recently been corroborated by reanalysis, their generalizability to European situations is not established. Moreover, the United States’ studies do not address key aspects of the exposure response relation, such as induction time (27). In addition, a better understanding of the mechanisms of the chronic effects of air pollution exposure would strengthen the case for transferability.

- **Causes of heterogeneity in the time-series studies.** Recent meta-analyses and analyses of multi-site studies in Europe and the United States suggest that the magnitude of the effect of air pollution on daily morbidity and mortality varies among locations, and that factors such as the nature and level of air pollution, as well as the health status of the population may determine the extent of that variability (2,27,34,35). Analyses of effect modification in time-series studies may well provide important insights into factors that modify the effects of long-term exposure on chronic effects, as well. However, we need to understand this variability and its determinants in considerably greater detail before we can begin to directly apply this knowledge to health impact assessment.

- **Determinants/indicators of the (increased) susceptibility to air pollution.** As discussed in Section 4.1, the distribution of the susceptibility in a given population may in part determine the nature and severity of the observed health effects. Better knowledge of determinants of susceptibility and their frequency in the target population could also help in designing efficient approaches to risk reduction in the face of constraints on ability to immediately reduce exposure.

- **Key indicators of morbidity impacts.** There has been little empiric research on the effects of air pollution on broader health indicators, such as restricted activity days. This is the major factor limiting their more widespread use in health impact assessment. We also need to better understand relations between various indicators and how to interpret them, e.g. how do changes in hospital admissions reflect burden of disease.

- **Improved data for the calculation of quality- and disability-adjusted life-years.** Current time-series studies say little about the health status of those dying due to exposure to air pollutants. Although such data are now becoming available from studies by Goldberg et al. in Montreal (42) and Prescott et al. in Edinburgh (43), these studies need to be replicated in multiple locations.

- **Baseline data on disease frequency throughout Europe.** Improved surveillance and registration of key acute and chronic diseases associated with air pollution would allow health impact assessments to more accurately quantify potential impacts, which now require questionable assumptions about the transferability of baseline rates. Standardized
surveys, such as the ECRHS and ISAAC are available but these are not designed specifically for HIA.

6. Recommendations

These recommendations recapitulate the major conclusions of the Working Group, as summarized above.

- The most complete estimates of both attributable numbers of deaths and average reductions in lifespan associated with exposure to air pollution are those based on cohort studies. Until the risk estimates from the European studies are available, impact assessment will need to rely on the results of currently available United States’ studies. Additional cohort studies, in Europe and elsewhere, and confirmation of the transferability of United States’ results to European populations are critical research needs.

- Time-series studies of daily mortality, which are likely to provide a lower bound on the number of attributable deaths, and which can be conducted relatively easily in diverse locations, will continue to be valuable for: demonstrating and documenting the adverse effects of air pollution in specific locales; quantifying the effects of short-term variation of air pollution (including air pollution episodes); and serving as the basis for air pollution alert systems. They will also likely continue to contribute to scientific understanding by identifying factors that modify the effects of air pollution on mortality and morbidity, toxic components of the air pollution mixture, and high-risk subgroups, and by furthering understanding of exposure-response relationships.

- All indicators of disease and health-related quality of life plausibly related to the exposures of interest should be included in the planning of health impact assessments of air pollution, though not necessarily included in them per se. When available, indicators measuring the actual effect on quality of life (e.g. reduced activity days) should be included. The possibility of “double-counting” of health-related events affecting the same individuals should be considered. The objectives of a particular impact assessment will determine the acceptability, and scope, of “double counting” of health-related events affecting the same individual.

- The choice of estimator(s) used in a given assessment should, if possible, anticipate the use to which the impact assessment will be put. Health impact assessments should present their estimates in sufficient detail with regard to various health endpoints, population strata (e.g. age, sex, race, social class), and pollutants to allow policy analysts maximum latitude and flexibility in applying them to regulatory decision-making. The choice among impact indices will depend, in part, on their usefulness for subsequent valuation analyses.

- Health impact assessments should exercise great care when the evidentiary and target populations differ. In general, the most precise, valid and specific effect estimate should be used for impact assessment. The deviations of the conditions in the target population from those in the evidentiary population which would plausibly affect estimated pollution effects must be made explicit and, whenever possible, should be included in the uncertainty analysis.

- Health impact assessments should design exposure characterization in the target population to mirror as nearly as possible exposure in the study providing the effect estimate. Impact assessments should avoid adding estimates of effects of individual pollutants derived from
single-pollutant statistical models unless there is a good reason to assume that various pollutants from air pollution mixture affect health independently.

- Sensitivity analysis is an intrinsic part of impact estimation and is critical for quantifying the uncertainty of the estimates. Such analysis should focus on the assumptions and input parameters which are the most important determinants of the magnitude of the estimated impacts.

- Research to quantify chronic effects of pollution, to identify the determinants of variation in health response to an exposure between various populations, as well as to quantify the impacts of air pollution on disease burden are the most needed to improve the scope and reliability of health impact analysis. The research should be specific to target populations and provide support for generalization of the studies to wider target populations.
References


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42. HEALTH EFFECTS INSTITUTE. *HEI Report 97: Identifying subgroups of the general population that may be susceptible to short-term increases in particulate air pollution: a time-series study in Montreal*. HEI, Quebec, October 2000.

Fig. 1. Air pollution health effects pyramid (adapted from ATS 2000)

Fig. 2. Severity of health response to air pollutant in relation to subject’s sensitivity
Annex 1

Life-table methods for predicting and quantifying long-term impacts on mortality

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Introduction

This note presents a framework, based on the well established statistical method of life-tables, within which impact predictions may be made and summarized. The author has used this framework for a number of quantitative impact assessments for air pollution.

Representing mortality risks

The probability that an individual will die at a certain age depends both on him/her not dying before that age, and on a probability (or risk) that in adults increases with age. We can observe differences in age-related differences in a “life-table” such as Table 1. This example tabulates the mid-year population sizes by sex and one-year age groups (from census data), along with numbers of deaths at these ages (from the death registration system). The data are for England and Wales, 1995. (These were the most recently available when we did the work. The current availability of more recent data does not alter the principles involved.) Dividing deaths by mid-year populations produces annual death rates. To save space, Table 1 shows rates summarized in five-year age groups. However, Fig. A1 shows the rates for all ages. The rates for ages above 90 were estimated from rates for a combined age group, by log-linear extrapolation.

Statistical theory for mortality risks can be based on the concept of a hazard rate, which can be described as an instantaneous age-specific death rate. Observed mortality rates such as those in Fig. 1 provide estimates of the underlying hazard rates. We refer to these below as observed hazard rates.

If we know the hazard rates appropriate to a group of individuals, then we can predict the probabilities of their survival to different ages. The two graphs in Fig. A2 show survival curves for males and females derived in this way. In each graph, the curve depicted by a solid line is based on the observed hazard rates in Fig. A1, that is from data for England and Wales, 1995. Note however that an interpretation of this curve as a prediction of survival in a single birth cohort makes the strong assumption that the cohort will, as they age, experience in the future the same age-specific hazards as were observed in 1995.

The life-table calculation of survival probabilities takes into account that deaths take place throughout a year. Without precise dates of each death, the usual (“actuarial”) convention is that about half the deaths in a year take place in each half of the year. So, if there are d deaths in a year in a group whose mid-year population is m, then the observed hazard h is calculated simply as

\[ h = \frac{d}{m}. \]

Because half the deaths have occurred by mid-year, the size e of the population at the start of the year was

\[ e = m + \frac{d}{2} \]

The probability s of surviving to the end of the year (conditional on being alive at the start) is

\[ s = \frac{e - d}{e} \]

and can be re-expressed in terms of the hazard

\[ s = \frac{2 - h}{2 + h} \]
which relationship inverts as

\[ h = \frac{2(1 - s)}{1 + s} \]

Thus we have a simple mechanism for converting from hazard rates to survival probabilities (and vice versa). For an individual to survive several periods, he/she must independently survive each period. Thus the chain rule for multiplying independent probabilities allows the generation of the whole survival curve by cumulative multiplication of the period-specific survival.

For a birth cohort of a given size, the survival curve can be rescaled from % to numbers, simply by multiplying by the initial size of the cohort. Number of deaths in a period can then be predicted from the drop in numbers surviving over the period.

For summarizing mortality experience, a useful concept is the life-year (or person-year). Here we distinguish between an individual who survives a year, thus providing exactly a whole life-year; and one who dies during the year, providing only a partial life year. If we do not have exact dates of death, we can continue with the assumption that half have occurred by mid-year. (Then we can easily see that the total life-years for a given age-group and year has exactly the same value as the size of the mid-year population. If both are calculated from exact dates of death, this equality still holds true.)

The survival curve for a birth cohort predicts the temporal pattern of deaths in the cohort. Expected length of life from birth can be calculated easily by summing the life-years over all periods and dividing by the size of the starting population. Conditional expectation of life, given achieving a certain age, can also be calculated by summing the years of life at that age and later, and dividing by the number achieving that age. Some example results are shown in Table 2, which also shows that the results may be summarized as percentage reaching a stated age.

**Quantifying differences in mortality risks**

As well as summarizing the survival in a population experiencing the age-specific hazards in England and Wales (solid line), which we may treat here as a reference group, Fig. 2 also shows the survival curves generated by two other sets of hazard rates. The longer dashes in each graph trace out the survival for hypothetical male and female groups whose annual hazards are twice those of the reference group, while the shorter dashes are for groups whose hazards are half those of the reference group. It is notable that even twofold differences in hazards produce quite similar curves.

There are a number of ways to characterize the difference between two survival curves; and the choice may be driven by the context in which the question is asked. We may compare the difference in the total life-years experienced (which is equivalent to comparing the area under the two curves); we may compare the average expectation of life; and we may compare the position of specific points on the curve, e.g. what proportion survive to a particular age, as in Table 2. Because every member of a cohort dies exactly once, it is not useful to attempt to summarize the total difference between two survival curves for the same population as a difference in the number of deaths, which will be identically equal.

**Application to impact assessment**

For a typical impact assessment, say of a change in air pollution concentration, we need first to predict how a change in concentrations will affect future hazards, then quantify the ensuing change in predicted mortality, using measures such as life-years.

It is important to distinguish clearly between calendar age and calendar time. Although they both increase synchronously, they are two separate dimensions. At the time some intervention affects mortality hazards, the extant population has a distribution of ages, and expectation of remaining life is age-dependent. Therefore, in quantification, it is an advantage to arrange the calculations in a two-dimensional array such as Table 3. This is a schematic representation of the hazard rates each age-specific cohort will experience in each year of theoretical follow-up, separating out the dimensions of age and the passage of calendar

\[ h = \frac{2(1 - s)}{1 + s} \]
time. For any such matrix filled with projected hazard rates, we may combine those down any diagonal to calculate cumulative survival probabilities and life years, as described above.

The second and third columns of Table 3 are easily completed using the available published data, but subsequent columns represent the unknown future. In our assessments to date we have assumed that in future years the hazards will be the same as in 1995. We emphasize that this is only one of many possible assumptions, but that any projection into the future must be based on some assumptions, which need to be stated explicitly.

Once the table of hazards is completed, we may perform the life-table calculations down each diagonal. From this we calculate the number of deaths and the total life-years in each cell, as in Table 4. We can do this separately for each of the sexes.

These calculations are designed to quantify the mortality implied by a set of predicted hazard rates. Impact assessment requires quantification of the impact of a change in hazard rates. But we may treat the calculations done so far as representing a baseline scenario; then, we may alter the hazard matrix in Table 2 to reflect the impact in which we are interested, representing an alternative future scenario; and quantify the predicted impact on mortality by comparing the outputs of Table 4 for baseline and alternative scenarios.

Because we may control the ways in which the hazards are altered for the alternative scenario, we may set up any pattern we desire in the alternative hazard rates. Thus impacts can be restricted to particular age groups, or differ by age; and impacts may follow an intervention immediately, or phase in gradually. Choices will be guided by the assumptions that appear plausible in a particular application.

**Quantifying and summarizing the impact**

Once more, the matrix layout of Table 4 allows for great flexibility to answer a variety of questions. As an example, we might envisage a change taking place which would affect mortality hazards from the year 2000 onwards, and ask what would be the impact on the population alive at the start of 2000. Their mortality experience will lie within the grey triangle in Table 4. As noted above, the total number of deaths must always equal the size of the population at the start of 2000; but the temporal pattern of the deaths depends if the hazards are changed, and the total number of life years will change. Thus one way to quantify the impact is as the difference between baseline and alternative scenarios, in the life years experienced, totalled over the grey triangle. We might, alternatively, ask about the predicted change in life years for everyone over a given time period, and include part-life contributions from cohorts born in 2000 and later, summarizing over a rectangular area of Table 4 rather than a triangle.

It is also possible to apply weights to the elements of Table 4 before we summarize, and the weights may also vary across the age and/or dimensions of the matrix. For example, we may wish to give less weight to years lived at older ages because quality of life may be reduced. If a summary in terms of economic value is desired, the weights could be economic values attached to a life year, and we may wish to apply lower values per life year at older ages. We may also wish to apply discounting (at a fixed rate per year, and akin to compound interest) which will reduce the current value of future life-years, and place more emphasis on changes in life years in the immediate future.

**Summary**

The calculations described above provide a method for quantifying the effects on survival patterns of altering a set of hazards. The method is purely arithmetic, and requires no functional assumptions about the distributions of the hazard rates or any of the population age distributions. The patterns of the alterations across the two-way matrix of can be as complex as desired, depending on the assumed mechanisms of impact. The principal steps involved are:

- obtain information on current mortality (hazard) rates;
• predict future mortality taking current rates (or some adaptation) as a baseline;
• create an alternative scenario by manipulating projected future mortality rates according to some risk model of assumed pollution change;
• compare predicted life expectancy (or other quantitative summaries of mortality) between the baseline and alternative scenarios;
• (optionally) apply economic valuation or other weighting to the difference in mortality patterns between scenarios;
• summarize the output appropriately.

**Example results**

Table 5 shows the results of some sample calculations of this sort described in this Annex. These are shown as an example, and no claim is made that the particular set of assumptions adopted are optimal; other assumptions would produce different predictions.

From the 1995 data for England and Wales, an estimated start-of-year population for 1995 was derived. Age-specific baseline hazard rates from 1996 onwards were assumed equal to those for 1995, and the mortality patterns implied by those baseline patterns were calculated.

For the alternative scenarios, the hazard rates were reduced uniformly by 1%, from the year 2000 onwards. (In the context of air pollution reduction, the results of US cohort studies may be taken to suggest that a reduction of 2.5 µg.m⁻³ in ambient PM₁₀ concentration would be associated with about a 1% reduction in hazard; gains in expectation of life can be scaled linearly for other hazard reductions or equivalent amounts of pollution reduction.). Additional alternative scenarios applied the 1% reduction after delays of various lengths, so that the hazard rates remained unaltered until 2005, 2010, 2020, 2030, after which they were reduced by 1%. Mortality patterns were calculated for each alternative scenario.

Separate calculations were carried out for men and women, but the gains from a 1% change in hazard were very similar, and have been combined here in a single total. The results are shown in Table 5, for the impact on the population estimated alive at the beginning of 2000. These calculations do not include any effects of hazard reduction in populations born in 2001 and later. Table 5 shows both the total impact of the change, and the equivalent Fig. scaled per 100 000 population, which may be more useful when comparing or transferring impacts across national borders.
**Annex 2**

**Tables and graphs**

Table 1. Mid-year population and number of deaths in England and Wales, 1995 by sex and 5-year age groups

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Mid-year populations</th>
<th>Deaths</th>
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</thead>
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<td>Males</td>
<td>Females</td>
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<tr>
<td>0 – 4</td>
<td>1 736 000</td>
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<td>55 – 59</td>
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<td><strong>26 388 950</strong></td>
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Fig. A1. Hazard rates by sex and one-year age groups, England and Wales, 1995
Fig. A2. Cumulative survival for males and females based on different sets of hazard rates
Table 2. Estimated from baseline hazards for England and Wales 1995

<table>
<thead>
<tr>
<th>Age at start of follow-up</th>
<th>Expected life remaining (years)</th>
<th>Expected survival to age 65 (%)</th>
<th>Expected survival to age 75 (%)</th>
<th>Expected life remaining (years)</th>
<th>Expected survival to age 65 (%)</th>
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Table 3. Schematic layout showing organisation of population and data and simulated life-table calculations for prediction of mortality effects
Table 4. Schematic layout showing pattern of predicted output from mortality simulations

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<th>Age</th>
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<th>- - -</th>
<th>1999</th>
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\[ d = \text{number of deaths} \quad y = \text{total person years} \]

Table 5. Predicted gain in life-years for 1% reduction in hazard rates in population alive in 2000 in England and Wales by delay to full effect

<table>
<thead>
<tr>
<th>Response</th>
<th>Delay to full effect (years)</th>
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<tr>
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<tr>
<td>Total life-years gained (millions)</td>
<td>4.7</td>
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<tr>
<td>Life-years gained (thousands) per 100 000 population</td>
<td>8.9</td>
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</tbody>
</table>
Annex 3

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