ESTIMATION OF RISK COEFFICIENTS FOR HEALTH IMPACT ASSESSMENT OF AMBIENT AIR POLLUTION IN EUROPE

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On behalf of WHO Task Group for estimation of risk coefficients for health impact assessments

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.WHO, through its European Centre for Environment and Health, Bonn Office, is in the final stages of a review of the health effects of ambient air pollution for the Clean Air For Europe (CAFE) programme of the European Commission (DG Environment). This review has focussed on the role of pollutants as health hazards and is now considering how the available evidence should be used to develop risk coefficients for health impact assessment (http://www.euro.who.int/document/e79097.pdf). In this paper we describe how epidemiological evidence from time series studies (both ecological and panel), has been systematically collected and synthesized to provide meta-analytic estimates suitable for use in health impact assessment models.

There is now a very large body of published time series studies . A database developed at St George's Medical School contains the results of these studies. These results will be used to derive risk coefficients that will be suitable for application in Europe. This will require consideration of a number of issues, including:

1. Exposure: pollutant of interest, averaging time, lag.
2. Outcome: mortality or morbidity, age group, diagnosis.
3. Availability of baseline data for outcomes.
4. Relevant geographical area.
5. Multiple studies of one city.
6. Seasonal vs all year analysis.
7. Single or multi-pollutant models.
8. Sensitivity to statistical model used.
9. Meta-analytic issues: minimum number of estimates, heterogeneity.
10. Publication bias.
11. Sensitivity analyses.

The Task Group has considered these issues and agreed a protocol. The design of the analysis and its results will be presented at the NERAM conference.

AIR POLLUTION AND CARDIOVASCULAR ADMISSIONS SHORT-TERM RELATIONSHIP IN 16 SPANISH CITIES: RESULTS WITHIN THE EMECAS PROJECT

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Introduction: EMECAS is a collaborative project that seeks to evaluate the short-term effect of air pollution on hospital admissions for cardiovascular and respiratory diseases and for mortality in 16 Spanish cities, i.e.: Barcelona, Bilbao, Cartagena, Castellón, Granada, Gijón, Huelva, Las Palmas, Madrid, Oviedo, Pamplona, Sevilla, Tenerife, Valencia, Vigo and Zaragoza, accounting for 10 million inhabitants. In this paper the results for cardiovascular admissions are presented.

Methods: The period of the study goes from 1995 to 1999. The number of daily emergent admissions for all cardiovascular diseases(CVS) (ICD-9: 390-459) and heart diseases(HD) (ICD-9: 410-414, 427, 428); were obtained from hospital records. We collected data for air pollutants from Air Pollution Networks in each city and constructed variables for 24 hours daily levels of black smoke, total suspended particles (TSP), particles smaller than 10 μ (PM_{10}), SO_2, and NO_2; 8 hours maximum moving average of CO and ozone; and, lastly, 1 hour maximum of SO_2, NO_2 and ozone. Magnitude of association in each city was estimated using generalized additive models (GAM) of Poisson controlling for confusion and overdispersion. For each cause, lagged effects, up to three days, of each pollutant were examined. Data were analyzed using S-Plus GAM function with more stringent convergence criteria. Combined estimates were obtained under a 'fixed effects' model, and, if heterogeneity, under 'random effects' ones. For ozone the analyses were restricted to the warm period (May to October).

Results: Local estimates were, mostly, positive and more consistent in lags 0 (concurrent day) and 1, except for ozone with a more delayed relationship. Following that, we selected the average of the concurrent and one day lag for all the pollutants, except for ozone (average of the 2 and 3 day lags) to show the estimates of the relationship. As a summary, combined estimates showed an association with cardiovascular admissions. An increase of 10 $\mu g/m^3$ in the PM10 levels was associated with a 0.9% (95% CI: 0.3-1.5%) increase in the number of hospital admissions for CVS, and 1.6% (95% CI: 0.8-2.3%) for HD. The same increase in concentrations of NO_2 was significantly associated with a 0.3% increase in CVS, and 0.8% in HD admissions. For ozone the corresponding estimates were 0.6 and 0.7, respectively. An increase in 1 mg/m^3 levels of CO was associated with an increase of 1.7% in CVS, and 3.3% in HD admissions. The estimates for TSP, black smoke and SO_2 were lower and in some cases non-significant.

Conclusions: This is the first multicenter study assessing the impact of air pollution on cardiovascular hospital admissions in Spain. A short-term association between increases in daily levels of air pollutants and the number of daily admissions for cardiovascular diseases in the Spanish cities has been described. There is a specificity in the effect with greater estimates for hearth diseases than for all cardiovascular ones. These study provide an estimation of the impact of air pollution useful for environmental actions in preventing health of the Spanish population

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DIVERGING AIRWAY INFLAMMATORY RESPONSES TO DIESEL EXHAUST EXPOSURE IN HEALTHY AND ASTHMATIC SUBJECTS WITH AND WITHOUT INHALED CORTICOSTEROID TREATMENT.

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Diesel exhaust (DE) is a major source of particulate matter (PM) pollution. Epidemiological data suggest asthmatics to be a sensitive group with respect to air pollution.

This study was performed to compare the airway inflammatory responses of subjects with asthma with (n=16) and without inhaled corticosteroids (ICS) (n=16) to that of healthy (n=24), when exposed to DE (100 $\mu g/m^3$) and air for 2 hours. Bronchoscopy with endobronchial biopsy sampling, bronchial wash (BW) and bronchoalveolar lavage (BAL) was performed at 18 hours post-exposure.

At baseline, asthmatics without ICS had significantly higher numbers of BW-eosinophils ($p=0.006$), BW-mast cells ($p<0.001$), submucosal eosinophils ($p=0.012$) and epithelial mast cells ($p<0.001$) compared with healthy. Further, asthmatic subjects on ICS had significantly higher numbers of mast cells in BW ($p=0.008$) and neutrophils in submucosa ($p=0.02$) as well as reduced expression of the endothelial adhesion molecule VCAM-1 ($p=0.03$) vs. the healthy group.

In healthy, DE induced a neutrophilic airway inflammation in BW ($p=0.01$) and in the submucosa ($p=0.02$), together with an increase in submucosal mast cells ($p=0.02$). In asthmatics without ICS, no DE induced inflammatory responses were found, whereas a trend towards an increase in submucosal eosinophils ($p=0.066$) was detected in asthmatics on ICS after DE exposure.

The absolute change (DE-air) in BW-neutrophils was significantly greater in healthy compared to asthmatics without ICS ($p=0.04$).

In summary, DE exposure at a high ambient level induced a significant airway inflammatory response in healthy subjects. In contrast, no DE induced inflammatory effects were detected in asthmatics without ICS and the BW-neutrophilic response was significantly different between these two groups. In asthmatics with ICS, only a trend towards an increase in submucosal eosinophils was detected after DE exposure. These data suggest a diverging airway inflammatory response to diesel exhaust exposure between healthy and asthmatic subjects with and without inhaled corticosteroid treatment.

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MEASURING THE HEALTH IMPACTS OF ACTIONS TO IMPROVE AIR QUALITY: THE HEI RESEARCH PROGRAM

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A large scientific literature currently provides evidence for adverse effects of ambient air pollution on a range of health outcomes from eye irritation to premature mortality (see, for example, Bascom et al 1996, Holgate, Samet, Koren, and Maynard 1999, ATS 2000). Based on this collective evidence, guidelines and standards designed to improve air quality are promulgated by governments and public health agencies, from the local to the national level, with the expectation that past reductions of levels of air pollution must have benefited public health and prevented some amount of human disease and death, and that future efforts will be protective as well. Nonetheless, efforts to improve air quality entail large financial costs, and perhaps substantial consequences for the activities of a society, and, therefore, policy makers and other stakeholders have sought evidence that interventions to improve air quality, do in fact produce health benefits. Such evidence contributes importantly both to assessments of the public health efficacy of air quality regulation, and to economic valuations, which seek to compare the relative costs and benefits of regulations designed to improve ambient air quality, and which are intended to provide what some have called regulatory "accountability."

In response, national governments and public health agencies have attempted to quantify past health impacts of air quality improvement and to estimate future impacts. These efforts have used risk estimates from epidemiologic studies to calculate the adverse impact on public health using various measures under hypothetical (counterfactual) air quality scenarios (EPA 812 reports, Künzli et al. 2000). However, these efforts have not been supported by studies of the health impacts of actual interventions. Direct evidence concerning effectiveness, if obtained, would greatly strengthen the evidentiary basis for regulatory and public health policy and for scientific inference about the health effects of air pollution and reduce the uncertainty associated with these influential estimates.

The Health Effects Institute (HEI) was strongly urged by both its public- and private-sector sponsors to undertake research on the health impacts of interventions to improve air quality (an interest evinced by others as well, including the US Congress, NGO's and WHO), and this work is an important component of HEI's 2000-2005 Strategic Plan.

This presentation will describe the rationale, scope, and content of HEI's research program in this area which currently has two components:

- A multi-authored monograph, entitled *Assessing the Health Impacts of Air Quality Regulations: A Monograph on Concepts and Methods* to be published in June 2003, which explores theoretical and practical issues in the design, conduct and interpretation of research to measure the health impacts of actions to improve air quality. It is intended to provide 1) a coherent basis for planning future studies, funded by HEI and other agencies; and 2) produce an overall strategy for HEI's work in this area. The monograph is addressed to a broad group of stakeholders, including government regulators, public health officials, industry, environmental groups, and academic researchers.
- An ongoing program of funded research to measure the health impacts of actual interventions to improve air quality. The presentation will describe two studies that are currently underway in Europe, one in Dublin and one in Erfurt, and efforts to begin to develop web-based approaches to the surveillance of health endpoints that could be used to track the results of air quality interventions.

ISSUES IN ESTIMATING THE PUBLIC HEALTH IMPACTS OF AMBIENT AIR POLLUTION – WHAT ARE THR MORBIDITY IMPACTS THAT MATTER AND WHAT ARE THE MAIN SOURCES OF UNCERTAINTY?

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In early analyses of the public health impacts of ambient air pollution, the overall estimates of impacts were 'driven' in particular by the mortality effects of acute exposure. In recent years, it has become accepted that the effects on life expectancy of long-term exposure to ambient particles constitute the single greatest impact.

In considering morbidity impacts, it is 'natural' to pay particular attention to acute hospital admissions, particularly respiratory admissions, because (i) these endpoints have been studied intensively, in many well-conducted studies in different locations, and so estimates of relative risk are relatively well-established; and because (ii) an unplanned admission to hospital is a serious event, especially for the individual admitted, but often for many other people also.

It does not follow, however, that acute hospital admissions constitute the morbidity impact of greatest public health importance. Indeed, if 'importance' is measured by total cost, assessed using methodologies such as willingness-to-pay, then several studies show that the costs associated with acute hospital admissions may be small compared with the costs of other morbidity impacts – a point we will illustrate with results from studies in the UK and elsewhere in Europe.

Although such comparisons are clouded by uncertainties, especially in the reliability with which other morbidity impacts can be estimated, these results identify several other endpoints as deserving attention. We will focus on three in particular – the development or exacerbation of chronic lung disease, especially bronchitis; days of restricted activity; and occurrence of respiratory symptoms in the general population – because (i) underlying the impact estimates for each of these endpoints there are different kinds of uncertainties which can be illustrated by these three examples, while (ii) nevertheless, if estimates are even approximately reliable, all three carry greater costs than acute hospital admissions.

Implications will be considered, for example:

- in health impact assessment (HIA), whether or not to exclude potentially important impacts if the underlying epidemiological evidence is weak;
- how to represent uncertainty, which is an issue whether or not these impacts are included; and
- how HIA can guide future epidemiology towards studying issues which will be of greatest benefit to future policy, by reducing such uncertainties in the estimated impacts.

HEARTS PROJECT: BUILDING A TOOL FOR THE ASSESSMENT AND INTEGRATION OF HEALTH IMPACTS FROM URBAN TRANSPORT SYSTEMS

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Traffic remains a major issue in urban areas, where pollution levels often exceed the maximum level recommended by official guidelines. Urban traffic affects health in a variety of ways, from premature deaths to increased rates of hospitalised persons for respiratory diseases due to air pollution, from sleep disturbance due to noise to fatal and serious accidents due to traffic.

An integrated analysis of traffic-related air pollution, noise and accidents as a function of different policy options is a necessary input to a more informed decision-making process. Such analysis can also be valuable to produce overall estimates of the benefits associated with a given reduction in traffic-related health risks for general population and in particular for vulnerable groups.
HEARTS (Health Effects and Risks of Transport Systems) is a research project aiming at developing an integrated method to conduct health impact assessments of urban transport. HEARTS is part of the 5th Framework Programme of the EU (Quality of Life) and is run by an international consortium, including leading European research institutions and the WHO-ECEH. Since next September 2003, three European cities (Leicester, Lille and Florence) will experiment the methodology on the basis of realistic policy scenarios provided by local administrations.

There are numerous challenges that arise when attempting to develop an integrated assessment of traffic-related health effects, for example, this involves dealing with the difficult question of developing approaches for which the multiple effects are a precise output. Specifically, the challenges that are animating the research include the possible levels of integration relative to:

- Information about and modelling of time-activity and mobility of the population,
- Availability and use of dose/effect relationships,
- Aggregation of exposure/risk on time-space scales,
- Estimation of a disease burden encompassing different effects

The integration procedures require a deeper understanding of the geographic and social distribution of the different health risks of transport within urban areas and a clearer characterization of the population subgroups most at risk from multiple health effects. For this reason, the models and programmes will be linked, within a Geographical Information System and a data-warehouse.
Several methodological and empirical barriers need to be overcome to promote improved tools and clear guidelines as political supporting options. The area is cross-sectoral in nature and requires commitment and collaboration between departments responsible for transport, health, environment and planning. The improved ability to use and develop integrated models is intended to facilitate the dialogue between different sectors of urban agencies, policy makers and stakeholders, and explicit trade-offs in urban transport and land use planning decisions.

Key words: Health, Transport, Air pollution, noise, accidents

DEVELOPMENTS IN IMPACT ASSESSMENT FOR CHRONIC EFFECTS ON CAUSE-SPECIFIC MORTALITY

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The recent HEI-sponsored re-analysis of mortality data from US cohort studies has confirmed previous findings of associations between levels of particulate air pollution and mortality, particularly from cardiovascular causes. Estimates from these studies suggest that the medium- and long-term impacts on mortality may be considerable, and impact assessment requires a mechanism for making predictions of mortality patterns well into the future.

Attempts to predict future impacts on mortality have used a variety of methods. We have developed a method, based on standard life-table theory, that is based on a clear distinction and separation between the dimensions of age and calendar time. This allows the construction of a self-consistent framework for calculations, with great flexibility in input assumptions, and in constructing summary impact measures. The method has been implemented using a series of spreadsheets. Options available and used so far include cause-specific assessments, where impact are modelled on only some causes of death; flexibility in assumptions regarding the timing of effects relative to interventions, e.g. to examine the impact of lagged effects; flexibility in definition of target populations and summary statistics; stratification of populations, including but not limited to stratification by sex; and the ability to attach economic valuations or quality-of-life weightings (e.g. QALYs, DALYs) to the outputs in a matrix varying by stratum, by age and by calendar year of follow-up. For many output summaries, the predicted impacts are in direct proportion to the size of the effect, allowing simple scaling for routine use in health impact assessments.

Examples will be presented of impact predictions based on cause-specific mortality rates in Great Britain, prepared for the UK Department of Health and for UK government committees and working groups. Identification of the assumptions with greatest impact on predictions will highlight future research needs.

ESTIMATING THE HEALTH IMPACT OF GROUND LEVEL OZONE ATTRIBUTED TO VOC EMISSIONS: AN ALTERNATIVE SCIENCE-BASED APPROACH

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Estimating the economic value of the health impacts of air pollution is an important part of air quality initiatives. Recently, the marginal external costs of emissions of individual air pollutants in Europe were estimated (Beta Version E1.02A, Netcen, 2003). These values have found widespread use in air quality initiatives in Europe including the Economics and Cross Media Effects BREF, the EC Proposal for a Revised Sulfur in Fuels Directive, and the draft Decorative Coatings Directive. We undertook a critical review of the cost estimates for ozone attributed to emission of volatile organic compounds (VOCs). Since acute mortality from ozone comprised the vast majority of the marginal external cost of VOC emissions, we focused on the methodology used to value this health endpoint. Key issues identified were; 1) the weight of evidence supporting a causal relationship for health effects; 2) selection of the key study and corresponding exposure-response functions; 3) application of exposure-response functions to assess the impact of actual ambient exposures; 4) consideration of thresholds and modelling through background levels; 5) the number of life-years lost; and 6) the uncertainties involved in modelling ozone formation from VOC emissions in the presence of varying levels of NO_x concentrations. Our analysis indicates the methodology used in BeTa dramatically inflates the marginal external costs of VOC emissions. We suggest a number of alternate approaches to improve the accuracy of the cost impact estimates. The alternate approaches use a central exposure-response function which more accurately reflects impacts across Europe, assumes more risk is attributed to higher peak ozone exposures than lower constant level exposures consistent with recent "V" wave chamber data, considers only morbidity effects or morbidity effects and mortality with a threshold at background ozone levels, and assumes a lower number of life-years lost.

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MODELLING THE INTRA-URBAN VARIABILITY OF AMBIENT TRAFFIC POLLUTION IN TORONTO, CANADA

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Background: Policymakers and scientists have shown growing interest in the health effects of chronic exposure to air pollution. Traffic-related air pollution is of particular interest from a regulatory perspective because the demand for transportation will probably outpace improvements in vehicle technologies over the next decade. Yet scientific uncertainty in exposure assessment models continues to impede efforts by policymakers to implement effective traffic pollution control regimes. In this context, we sought to model determinants of intra-urban variation in ambient concentrations of nitrogen dioxide (NO_2) in Toronto, Canada, with a land use regression (LUR) model. Although researchers have conducted similar studies in Europe, this work represents the first attempt in a North American setting to characterize variation in traffic pollution through the LUR method.

Methods: NO_2 samples were collected over two weeks using duplicate two-sided Ogawa passive diffusion samplers at 95 locations across Toronto, Canada. Sampling locations were selected with a novel location-allocation model based on pollution levels measured at government monitoring sites and on residential population density. Independent variables employed in subsequent regression models as predictors of NO_2 were derived by the Arc 8 geographic information system (GIS). We tested 83 indicators of land use, traffic, population density, and physical geography.

Results: The range of variation (~ 17.5 ppb to 77 ppb) from the spatially extensive network of monitoring sites was higher than reported from government networks with fewer sites. The final regression model yielded a coefficient of determination (R^2) of 0.69. All coefficients have the expected sign. For the traffic variables 24-hour traffic counts and road measures display positive associations. For the land use variables, industrial land use and counts of dwellings within 2000 m of the monitoring location were positively associated with NO_2 mixing ratio levels or concentrations. Locations up to 1500 m downwind of major expressways had elevated NO_2 levels. A trend remained present in the data moving from higher values in the west to lower values in the east of the study area.

Discussion: Our results suggest that reasonable predictive surfaces can be derived for North American cities with the LUR method, although our results also show NO_2 concentrations are harder to predict in North America than in Europe. The lower overall prediction achieved in our models probably arises from the differences in land use between European and North American cities, particularly the homogeneity of land use and relatively high, but variable level of automobile use in North America.

Key words: Traffic pollution, exposure assessment, GIS, land use regression, health effects

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AN INTEGRATED ASSESSMENT OF AIR POLLUTION CONTROL STRATEGIES FOR EUROPE

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There is increasing recognition of the threat to human health posed by fine particulate matter. Robust associations were found between human exposure fine particulate matter and a variety of health-related endpoints, such as cardiovascular diseases and premature mortality. Fine particulate matter in ambient air originates from primary emissions of fine particles from various natural and anthropogenic sources as well as from the formation of secondary aerosols from precursor emissions of SO_2, NO_x, NH_3 and VOC. The typical residence time of the fine fraction of particulate matter (with aerodynamic diameter of less than 10) ranges between 10 and 100 hours, during which such aerosols are transported with the air mass over long distances. Recognizing the strong transboundary component, the issue of controlling concentrations of PM was taken up at the international level by the Commission of the European Union (the CAFE programme) and the Convention on Long-range Transboundary Air Pollution. Both bodies aim for international agreements on harmonized control strategies in 2005-2006. These agreements should be based, to the maximum possible extent, on substantive information about the effects of fine particulate matter to human health. To maximize the cost-effectiveness of the strategy, measures for reducing the various (primary and secondary) precursor emissions to PM should be balanced across all contributing economic sectors (including agriculture), and important side impacts on other environmental problems (e.g., acid deposition, ground-level ozone, etc.) should be taken into account.

To integrate all this information, the Regional Air Pollution Information and Simulation (RAINS) model developed at the International Institute for Applied Systems Analysis (IIASA) will be used in both policy forums as a tool for the integrated assessment of future emission control strategies. Based on results of the RAINS model, the presentation will outline the recent perspectives on the future development of the precursor emissions of fine particulate matter in Europe (the 'baseline' scenario) and review the present assessment of their health and environmental impacts. It will discuss the potential for and costs of further emission controls that go beyond current legislation and attempt to quantify their impacts on human health and ecosystems.

ASSESSING SOURCES OF $PM_{2.5}$ IN CITIES INFLUENCED BY REGIONAL TRANSPORT

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The human health effects of fine particulate matter ($PM_{2.5}$) have led to the establishment of new air quality standards or guidelines in many countries. This has led to the need for information on the main sources responsible for $PM_{2.5}$. In urban locations being impacted upon by regional-scale transport source-receptor relationships for $PM_{2.5}$ are complex and require the application of multiple receptor-based analysis methods in order to gain a better understanding. This approach is being followed to study the sources of $PM_{2.5}$ impacting southern Ontario, Canada, and its major city of Toronto. In this paper, we utilize the existing monitoring data in the region around Toronto and within Toronto itself to estimate that 30-45% of the $PM_{2.5}$ is from local sources, which implies that 55-70% are transported into the area. In addition, there are locations in the city that can be shown to experience a greater impact by local sources such as motor vehicle traffic. Detailed $PM_{2.5}$ chemical characterization data were collected in Toronto in order to apply two different multivariate receptor models to determine the main sources of the $PM_{2.5}$. Both approaches produced similar results indicating that motor-vehicle-related emissions, most likely of local origin, are directly responsible for about 20% of the $PM_{2.5}$. Gasoline engine vehicles were found to be a greater overall contributor (13%) compared to diesel vehicles (8%). Secondary $PM_{2.5}$ from coal-fired power plants continues to be a significant contributor (20-25%) and also played a role in enhancing production of secondary organic carbon mass (15%) on fine particles. Secondary fine particle nitrate was the single-most important source (35%) with a large fraction of this likely related to motor vehicle emissions. Independent use of different receptor models helps provide more confidence in the source apportionment as does comparison of results among complementary receptor-based data analysis approaches.

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