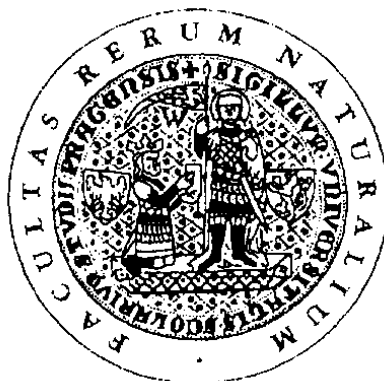


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RNDr Alena Bartoňová

Role expozice při vytváření strategií pro snížení zdravotních rizik ve vztahu ke kvalitě ovzduší

The role of exposure assessment in development of risk reduction strategies for air quality

Disertační práce

Vedoucí závěrečné práce/Školitel: Prof. RNDr Martin Braniš, CSc

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Poděkování

Tato práce je shrnutí některých výsledků mé odborné činnosti za poslední roky. Poděkování tak patří mnohým mým kolegům, se kterými jsem měla možnost spolupracovat a jejichž názory byly pro mne důležité:

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Abstrakt

Vztah mezi zhoršenou kvalitou vnějšího ovzduší a lidským zdravím je jedním z nejvíce studovaných problémů v oblasti životního prostředí. Jak však charakterizovat kvalitu ovzduší? Pojem expozice jako spojujícího článku mezi stavem ovzduší a lidským zdravím se výrazněji objevil koncem 70. let 20. století, jako concept, který umožní přesněji popsat zátěž, které jsme vystaveni. Až do té doby byla tato zátěž převážně charakterizována měřeními na pevných monitorovacích stanicích. Snaha charakterizovat expozici jednotlivce nebo subpopulace přesněji, jinak než přímo měřenou koncentrací, nás nicméně přivádí k otázce jak smysluplně využít těchto informací pro legislativu a management kvality ovzduší, kde je přímo měřená koncentrace jediným regulovaným indikátorem.

Tato práce se zabývá odhadem expozice z různých hledisek. Cílem je ozřejmit roli expozice v managementu ochrany ovzduší. Studujeme, je-li informace o expozici relevantní pro rozhodování o opatřeních na zlepšení kvality ovzduší, jakou informaci poskytne odhad expozic pro podskupiny obyvatel a jak vyřešit konkrétní situaci, kdy přímá informace o expozicích není k dispozici. Dále studujeme, jak experti hodnotí kvalitu informací o expozici v poměru k informacím v ostatních krocích odhadování rizik.

Opatření na snížení znečištění ovzduší je možné uplatnit ve všech krocích takzvaného “úplného řetězce“ s (legislativní opatření, zdroje znečištění, koncentrace znečišťujících látek v ovzduší, expozice, zdravotní stav a společenský dopad zhoršeného zdravotního stavu). Odhad expozice pro evropskou populaci a její podskupiny jasně naznačuje, že ochranná a mitigační opatření je třeba navrhovat diferencovaně tak, aby došlo k ochraně např. dětí - skupiny, která je zároveň považována za zvláště citlivou, a je nejvíce exponována.

Dále jsme zjišťovali, jak hodnotí experti kvalitu informací o expozici v poměru k ostatním krokům při odhadu rizik. Ve studiích na téma environmentálních zdravotních rizik jsme se ptali expertů “Jaká je míra důvěry, kterou máte ve schopnost předpovědět... (jednotlivé prvky “úplného řetězce“).” Expozice je často identifikována jako limitující oblast. Je pro to pravděpodobně mnoho důvodů, jedním z nich je i to, že odhady expozice vyžadují spolupráci týmu odborníků z různých oborů. Ilustrujeme to na příkladu odhadu expozic v případě, kde chybí základní informace o kvalitě ovzduší. Expozici jsme odhadli s pomocí emisí a úspěšně jsme tento odhad použili k odhadu rizika spojeného s mírou zatížení bydliště pacienta.

Interdisciplinární podstata expozice jako disciplíny je výzvou pro vědeckou práci metodicky i komunikačně. Práce v závěru ukazuje, jaké jsou běžné problémy, a jak je možné v těchto situacích postupovat. Na příkladu velkého multidisciplinárního projektu jsme ukázali, že univerzální metoda pravděpodobně neexistuje: nejlepší, co můžeme udělat je se poučit od druhých disciplín a kolegů, v jednotlivých případech se spolehnout na vyjednávání, a soustavně se učit z praxe.

Abstract

The relationship between deteriorated outdoor air quality and human health is one of the most studied environmental health issues. The concept of exposure, the link between environmental status and human health, has emerged in the late 1970's, recognizing that fixed monitoring stations do not represent concentrations at the places where persons spend time. Many advances have been made since. Characterizing the individual's exposure reduces uncertainty in links with health, but it implies a question about how exposure (as opposed to directly using concentrations) can be used in the regulatory process.

This thesis addresses exposure assessment from several perspectives, with the aim to address its role in air quality management. We are interested in how to use exposure information for policy- and decision making, we investigate if a European-level subgroup-based exposure estimate can provide useful information for designing differentiated measures to protect specific groups, we design an exposure estimate for risk assessment in a specific situation with limited health and air pollution data, and we describe the challenges of the inherent inter-disciplinarity and suggest how to deal with them.

We introduce the “full chain” approach to environmental health that links policy – pollution source – concentration – exposure – effect – impact, and show that mitigation measures can be taken in all of its steps. The estimated European-level exposure differences between population subgroups imply the need for mitigation measures to address the subgroups specifically.

Exposure matters, but is it widely acknowledged? We investigate how “exposure assessment” is perceived compared to other elements of the “full chain” framework. Based on six case studies, where experts are asked “what is your level of confidence in the scientists' ability to predict... (individual elements of the framework)”, we find that exposure is often perceived as the issue where least knowledge is available. We illustrate how exposure was assessed using emission inventorying aided by remote sensing and used for risk assessment relating respiratory disease and local emission strength at the patient's home.

The interdisciplinary nature of exposure assessment poses challenges to scientists in their choice of methods, and in communication within and outside the research community. In this thesis, we describe a concrete example. Experiences from a large interdisciplinary project tell us that there probably is no universal method and that the best we can do is to learn from each other, rely on contextual negotiation and learn from experience.

Abbreviations

DPSEEA	Drivers-Pressures-State-Exposure-Effect-Action framework
DPSIR	Drivers-Pressures-State-Impact-Response framework
DST	Decision support tool
EEA	European Environment Agency
ESF	Exposure scaling factor
EU	European Union
FP6 R&D	6 th Framework Program for Research and Technological Development
HENVINET	Health and Environment Network (coordination action in Framework Program 6 for Research and Development of the European Communities)
HETUS	Harmonized European Time Use Survey
IPCS	International Program for Chemical Safety
MTUS	Multinational Time Use Study
NO _x	Nitrogen oxides
PM, PM ₁₀	Particulate matter, Particulate matter in size fraction of less than 10 µm aerometric diameter
SO ₂	Sulphur dioxide
US EPA	United States of America Environment Protection Agency
US NRC	United States of America National Research Council
WHO	World Health Organization

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1. Introduction

The now recognized relationship between deteriorated outdoor air quality and human health is one of the most studied environmental health issues. Link between the status of the environment and the human health is exposure¹. The concept of exposure has emerged in the late 1970's and early 1980's (Ott (1982), Duan (1982)) recognizing that fixed monitoring stations do not represent concentrations at the places where persons spend time. Ott (1985) summarizes the five key elements of human risk assessment related to environmental pollution (sources of pollution, transport of pollutants from source to humans, exposure of humans to pollution, doses received by those exposed, and adverse effects related to the doses), and defines total human exposure within the linked chain of the full risk model. Later, exposure to a chemical is defined as the contact of that chemical with the outer boundary (US EPA (1992)), and expressed as a function of both concentration (at a location where the person is present) and interval of time (Lioy (1990)). Further, the US EPA (1992) guidance document introduces the concepts of intake, uptake and dose, which offers a framework to consider the processes that take place after the contact of the contaminant with the outer boundary, and lays basis to exposure assessment through biomonitoring (Lewtas et al (1993), Møller and Loft (2010), Paustenbach and Galbraith (2006); Smolders et al (2010)).

Exposure science has enjoyed a number of developments. An authoritative review of the first 40 years of exposure assessment by Lioy (2010) concludes with two questions with high relevance to this thesis: ***What does one do with such (exposure, comment AB) information?, and What role does exposure science play in regulations and prevention beyond analyses of observational data and their interpretation?***

On the first question, Lioy (2010) argues that exposure information is seldom used for prevention of health effects, and that the effects on exposure of measures to limit pollutants are seldom checked. For ambient air quality, the methodology of guideline setting is based on averaging exposures over a population, which may lead to missing important populations or hot spot situations. This is seldom investigated or taken into account in relation to regulatory process, and can lead to undesired effects with wide societal consequences. Unanswered research questions are connected both to the methods

¹ Exposure is defined as contact over time and space between a person and one or more biological, chemical or physical agents. In this thesis, exposure denotes the external contact of the polluting agent with the body through e.g. inhalation, dermal exposure, or other similar exposure route. Source: US NRC 1991a.

for assessment of exposure that would allow to account for the spatial and population variability in exposure, and to the need for this science to be recognized as input for policy-making.

The second question also implies future directions for research. According to Liroy (2010), the whole chain “source to dose” needs to be considered. Liroy then concludes among other: “The need to link exposure science to risk management and intervention is well known, but additional resources are required to ensure that the field plays a more pivotal role in preventing or mitigating exposures. This will also lead to better simulation protocols and models to characterize contact under many types and varieties of conditions before they occur as well as increase the use of exposure science regulatory strategies that prevent contact across populations stratified by age, sex, susceptibility, and culture, thus stimulating innovation. Focused and more enriched observational studies can be designed to evaluate models and improve the understanding of the levels of contact and the intensity of exposure in populations,...” (p. 1088).

Liroy’s questions and his assessment of research gaps led us to ask the following research question: ***What is the role of exposure assessment in decision making on risk reduction strategies related to environmental contaminants in general and air quality in particular?***

The evidence used by legislators to identify levels of air pollution that are considered harmful is derived from epidemiological studies. The exposure metric varies widely between studies, as shown by e.g. Zou, Wilson and Zeng (2009). It includes air pollution level indicator such as, proximity to a source e.g., traffic (Van Roosbroeck et al (2008)), information from monitoring networks that is used as representative for a specified area (Medina et al (2009)), air quality estimates using statistical information such as land use regression (e.g., Hoek et al (2008)) or using physical models such as atmospheric dispersion models (e.g. Clench-Aas et al (2000)), personal monitoring (Wallace and Ott (1982), Jantunen et al (1998), Edwards et al (2005)), biomarkers (Ott, Steinemann and Wallace (2007), Demetriou et al (2012)) , or using a combination of some of the methods (e.g., the Escape project (2010), Hoek et al (2009), Svecova et al (2012)).

Fann et al (2011) in their commentary on the use of epidemiological studies for risk assessment point out that one of the challenges for risk assessors is to ensure that the treatment of modelled or observed air quality changes or exposure estimates is compatible with the treatment of air quality in the epidemiological study, i.e., the need to link the metric from the epidemiological studies to the metric used by the legislator. This can relate to the composition and relative levels of pollution mixtures over space and time, methods used to estimate exposure, or the characterization of pollutant exposures.

Taking into account “exposure” as opposed to air pollution levels is clearly more health relevant, but implies that other exposure factors than concentration levels need to be considered, including population behaviour and lifestyle. This implies that locally specific health effect data are needed for the local regulator to set local limits, or to take local action. Such debate in Europe has led to instigation of the APHEA (Samoli et al (2005)) and APHEIS (Medina et al (2009)) studies.

Studies have to respect not only established epidemiological methodologies, but also availability of local information or the ability to generate it, sometimes dependent on local custom that may influence how data are collected or stored. We demonstrate that within an urban area, spatially sufficiently resolved emission estimate can be used in the absence of air quality data as a proxy for exposure, and as a basis to derive a relationship between air quality and health outcome.

Having developed additional methodologies to estimate exposure, we answer the final research question related to those asked by Lioy (2010): ***How can we as scientists support the use of exposure assessment results in decision making?*** An interdisciplinary experience allows us some insight into the processes of transfer of knowledge to the decision making process, and illustrates the attitudes of researchers and perception of their roles as knowledge suppliers.

The matter of exposure to air pollution has been my long-term research interest, and in this Dissertation I present a conceptual approach and illustrate elements of the system that allows to answer the two concerns of Lioy (2010). This is drawing on my work over the last several years, when I have designed or co-designed and executed a number of research projects where exposure was a central research topic, in combination of other elements of integrated assessment. The studies were funded nationally and from the European Union 6th Framework Program for Research and Scientific Development.

I co-designed two integrated projects funded by the EU FP6, INTARESE (Integrated Assessment of Health Risks of Environmental Stressors in Europe), where I designed and led the sub-project on integrated monitoring, and HEIMTSA (Health and Environment Integrated Methodology and Toolbox for Scenario Assessment), where I designed and led the sub-project on exposure assessment.

I designed and co-ordinated FP6 Specific targeted research project ENVIRISK (Assessing the risks of environmental stressors: contribution to development of an integrating methodology).

I co-designed and was the Norwegian Principal investigator in a series of investigations in collaboration with Indian Institute of Technology, Kanpur, India, on air quality and health, funded by the Royal Norwegian Embassy in New Delhi. The main purpose was to support quality controlled air quality

monitoring and assessment and to provide a first estimate of health risks from air pollution for a three-million city, Kanpur, Uttar Pradesh, India.

I also designed and co-ordinated a FP6 co-ordination action HENVINET (Health and Environment Network), a 30-partner multidisciplinary project with a number of case studies on knowledge availability for concrete environmental health issues. HENVINET has applied the Integrated Environmental Health Impact Assessment or “Full Chain” framework of the INTARESE and HEIMTSA, and developed and applied tools for expert assessment of environmental health issues. It also offered a systematic review of available decision support tools related to the “full chain”, supporting thus in a concrete way the uptake of scientific results for policy/air quality management.

In the WeBIOPATR (Particulate matter: research and management in the West Balkan region) we studied origin of particles collected in urban background in Belgrade, Serbia, and brought the results into a wider societal arena, to be a part of the national air quality management efforts. We organized international conferences and workshops with topics following the full-chain, with the aim to provide a national forum for information exchange between environmental science and national policy. I co-designed this project, was its Norwegian Principal Investigator, and have participated in the research work.

Chapter 2 of this thesis defines the concrete tasks addressed in the thesis. Based on work done in ENVIRISK, INTARESE and HEIMTSA, we further develop the concepts of full chain approach and exposure assessment within environmental health risk assessment (Chapter 3 of this thesis). We became very much aware of the difficulties related to inter-disciplinary collaboration and the science-policy interface, in the area of environmental health. With this background, we have in HENVINET developed methods for knowledge assessment and interdisciplinary collaboration in relation to 6 environmental health issues including different types of exposures, illustrated in this thesis on three of them (Chapter 4, Attachments 1-3). In the investigations in India, we have applied the concepts of integrated environmental health impact assessment, and we had to develop an exposure estimate to suit the local situation (Chapter 5, Attachment 4). Finally, to aid using scientific results directly for decision-making, in HENVINET we have developed a method how to describe decision support tools for environmental applications (Chapter 6.1, Attachment 5). The experiences with interdisciplinary work and practical examples we addressed in science-policy interface are summarized (Chapter 6.2, Attachments 6 and 7). Chapter 7 concludes this thesis.

2. Aims

This thesis aims to develop methods that would complement current knowledge on exposure assessment for air pollution and enhance the current ability to use exposure assessment in decision making and air quality management. Specific aims are:

1. Define a framework for addressing environmental health issues and an approach to exposure assessment. Investigate if a differential approach to pollution mitigation measures based on exposure estimate for population subgroups can be supported.
2. Investigate the perception of “exposure assessment” in relation to decision making and what tools are available to support environmental health decision making.
3. Develop an exposure metric for a case study aiming at a first screening of risks from air pollution.
4. Provide practical guidance to the research community on how to better use exposure assessment in decision making, and in general, on science-policy interface and interdisciplinary communication in the environment and health area.

3. Exposure assessment in risk related frameworks

Risk related frameworks were recently reviewed by Liu et al (2012), suggesting to strengthen the needs of exposure assessment in environmental health related monitoring. This reflects the findings of Liou (2010) and addresses his concerns about how to use the exposure assessment in decision making. These concerns provide part of the motivation of the recent HEIMTSA study (Lebret, Hurley and Briggs (2008)), where we suggest to use a “full chain approach” (Fig. 1), with strengthened elements that allow taking into account the “people” aspects in the assessment: the context of the assessment, its social and economic aspects, individual and group behaviour, and perceptions of risk.

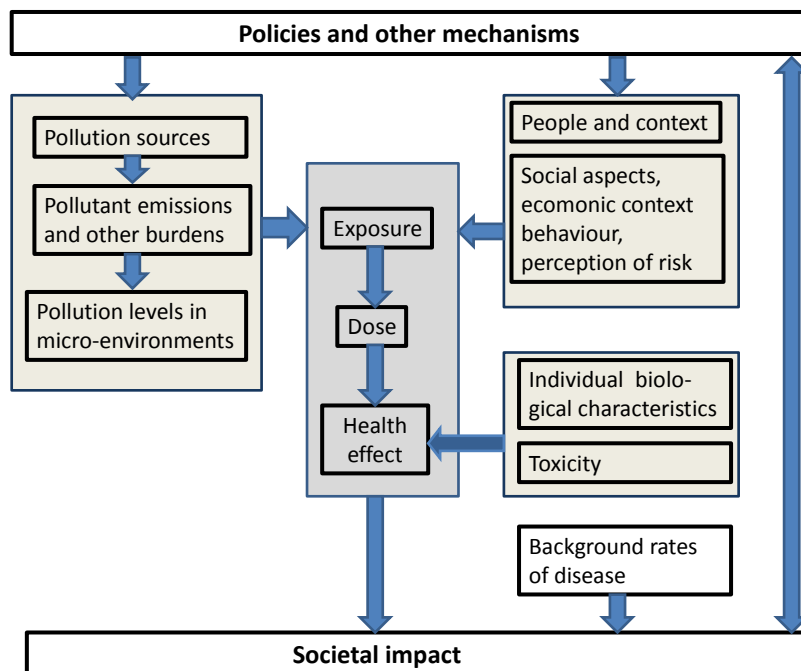


Figure 1. A “full chain approach” to integrated assessment related to air pollution.

This extension of the usual integrated assessment framework allows the development of exposure assessment: this important step links the environmental status (air quality) with its effects, allowing for differences between groups or individuals. In turn, this leads to a development of mitigation strategies that combine measures targeting the source of pollution directly, and also allow to control the levels to which individuals are exposed by limiting the contact of individuals or special groups with air pollution, e.g. by providing air pollution warnings, or suggesting alternative behaviours (Fig. 2).

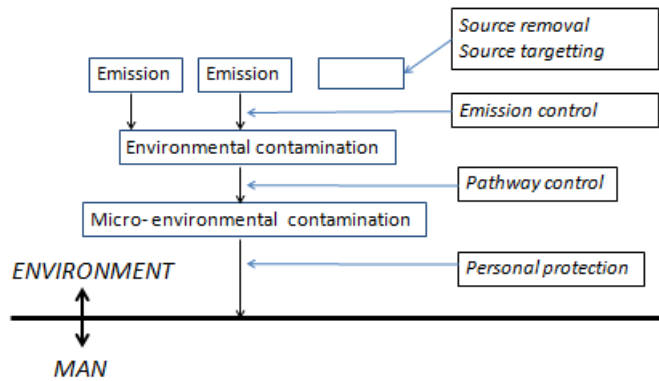


Figure 2. A schematic diagram indicating possible entry points for mitigation measures that reduce health-relevant exposures to air pollution.

We have developed an example (Kuhn et al (2009), Yang et al (2011)) that quantifies the effect of concentration gradients of gaseous compounds between background and hot spots, and the effect of different time spent by different population groups in certain micro-environments (IPCS (2004), p.103), outdoors, in traffic, at home, at work, on the overall exposure. This is done on European level, but can be easily applied also for urban assessments. An exposure scaling factor ESF is a weighted average of concentrations in given micro-environments, with weights corresponding to the time spent in each microenvironment, specific for each population group considered. ESF is based on a combination of data on time spent in the selected micro-environments by different demographic groups (gender, age groups, and employment status). The population data are derived from European-level datasets from the Harmonized European Time Use Survey HETUS (<https://www.h2.scb.se/tus/tus/default.htm>) and the Multinational Time Use Study MTUS (<http://www.timeuse.org/mtus/>). The ESF is furthermore developed using a probabilistic approach, and is represented by a probability distribution. An illustration of calculated exposure differences between groups is given in Figure 3. Seniors (65 years of age and older) have clearly the lowest exposure values, while children are exposed most: the median exposure of children is about twice as high as for the seniors.

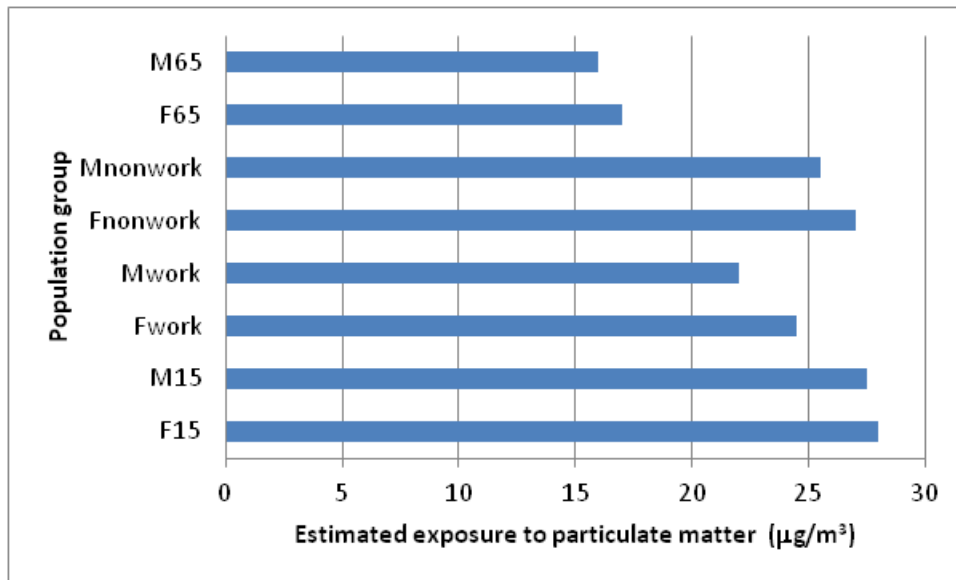


Figure 3. An example of exposure estimates using the exposure scaling factor. Theoretical example based on European particulate matter levels prediction from EMEP 10x10 km²grid model for the year 2020, and MTUS and HETUS data for population parameters. Population groups considered: F15/M15 female and male up to 15 years of age; Fwork/Mwork adult females/males aged 16-65 years, gainfully employed outside their home; Fnonwork/Mnonwork females/males aged 16-65 years, not gainfully employed outside their home. F65/M65 female/male senior population.

The example of exposure scaling factor illustrates that exposure assessment draws on different kinds of information sources and techniques, ranging from sociological data on population behaviour to modelled data on future air quality derived from advanced European-level dispersion modelling. Linking these data is often not trivial, but the exercise provides a good insight into the complexities of population exposure: it clearly illustrates the need to differentiate between different population groups when designing mitigation strategies for air pollution.

The ESF is a methodology that can be applied on European level: it was developed to be coupled to the modelling system ECO-SENSE (<http://ecosenseweb.ier.uni-stuttgart.de/>), see also EnviroWindows, (<http://scenarios.ew.eea.europa.eu/fo1079729/online-model-inventory/ecosense>). ESF be used together with any regional or global level atmospheric dispersion model that would provide averaged air quality estimates for a grid square or a geographical unit; whenever population data are available, the factor can be calculated, to evaluate what would be e.g. variability of exposures in that unit. This implies that ESF may be used in an air quality management framework.

4. The perceived role of exposure assessment in environmental health decision making

Exposure assessment with its forty years tradition still does not seem to have fully become the part of decision-making process. For chemicals, decisions are often made as part of the regulatory risk assessment process where exposure assessment is an established part of the framework (IPCS (2004), p. 14). This seems less so in the case of air pollution where outdoor air concentrations are often used as a proxy for exposure on population level. But can anything be said in general about the relative import of exposure assessment for the legislative process? We have investigated gaps of knowledge for several types of environmental health issues This includes health impacts of the brominated flame retardants decabrominated diphenylether (decaBDE) and hexabromocyclododecane (HBCD) (Ravnum et al (2012)), phthalates highlighting di(2-ethylhexyl)phthalate (DEHP) (Zimmer et al (2012)), the pesticide chlorpyrifos (CPF) (Saunders et al (2012)), nanoparticles (Attachment 1), the impacts of climate change on asthma and other respiratory disorders (Attachment 2), and the influence of environment health stressors on cancer induction (Attachment 3).

The approach to identifying gaps of knowledge was unified in these studies. First, we defined a common framework. In the environmental disciplines, operational frameworks such as the Pressure-State-Impact or the Drivers-Pressures-State-Impact-Response (DPSIR) framework (EEA (1999)) have been used since the 1980s. DPSIR provides an intuitive operationalisation for a large variety of issues. Approaches of integrated environmental assessment (Briggs (2008)) expand this concept. A clearly relevant framework is the extension by WHO, the Drivers-Pressures-State-Exposure-Effect-Action - DPSEEA (Schirding (2002)). It puts emphasis on exposure and effect; essential factors when dealing with health (Hambling, Weinstein and Slaney (2011)).

We have adapted the DPSEEA framework for each of the case studies, informed by developments in integrated environmental health impact assessment (Briggs (2008)), and used it also as a communication tool in all the topical case studies. As we note in Attachment 3, the diagrams constructed along the DPSEEA to help the experts in the evaluations, provide an excellent visual communication tool, also suitable for discussions with non-experts.

In each case study, we have developed a web-based questionnaire with a set of questions along the DPSEEA diagram, formulated as “What is your level of confidence in the scientist’s ability to...”.

Numbers of questions in case studies varied between 27 and 63, with answers on a scale 1 (very low, less than 10%) to 5 (very high, higher than 90%). To interpret the results, we need to define what constitutes consensus, or the lack of it. A methodology was adopted from Tassle and Wierman (2007) who propose a mathematical measure, developed to yield a logical determination of dispersion around a category value. A Likert 5-category scale was constructed (Very High confidence (VH), High Confidence (H), Medium confidence (M), Low confidence (L), and Very Low confidence (VL)), assigning these categories ordinal values (scores): VH=5, H=4, M=3, L=2, VL=1. This allows the calculation of a “Consensus value” for each question. A complete lack of consensus generates a value of 0, and a complete consensus of opinion yields a value of 1. The consensus value is then interpreted together with the mean score for each question (for formulas, see Tassle and Wierman (1989)). To identify areas that merit interest, we ranked the consensus values and then further explored the questions that ranked lowest, or highest.

We can compare the consensus values and scores across the different case studies (Figure 2, Attachment 5). Lowest average ranking (ie, least average confidence that science has the knowledge) is for Brominated Flame Retardants, but on most questions, there is a relatively high level of agreement. In Climate Change, there is on average high confidence in available knowledge (high score), but a comparatively large spread in consensus. On Cancer, there is a large spread of confidences (scores), and the largest spread of consensus values. No data have been found in the literature that would allow us to compare these findings, and to interpret them in relation to other studies, but the results do reflect our intuitive understanding: the Brominated Flame Retardants were evaluated in a framework very similar to risk assessment, familiar to the participating experts. For Cancer, such an evaluation and the use of the DPSEEA framework have never been reported before: the result may thus reflect both the large differences in knowledge in the different elements of the framework, and the uncertainty from the relative novelty of the approach. Based on the results, we feel that this quantitative procedure provides a good basis for expert discussions leading in the next step to identification of possible actions.

In each of the six case studies, a sub-set of questions was dealing with exposure assessment. When the experts were asked to prioritize what knowledge needs to be improved (Ravnum et al (2012), Zimmer et al (2012), Saunders et al (2012), Attachment 2&3), the exposure was invariably among the first three issues mentioned.

5. Emission-based exposure metric and human health

Fann et al (2011) in their commentary on the use of epidemiological studies for risk assessment point out that one of the challenges for risk assessors is to ensure that the treatment of modelled or observed air quality changes or exposure estimates is compatible with the treatment of air quality in the epidemiological study, i.e., the need to link the metric from the epidemiological studies to the metric used by the legislator. To demonstrate the need to control an emission source, we have developed an emission-based exposure metric, and have shown that it can be directly related to hospital admissions for respiratory disease (Attachment 4).

The study was done in Kanpur, the capital of Uttar Pradesh, one of the least economically developed states in India. In a preliminary investigation in 2003-2005 (Bartonova and Sharma (2005)) we have established the feasibility of different ways to estimate exposure, and to assess health effects. This first investigation was a pilot health investigation on short term respiratory health using questionnaires and spirometry measurements. This work has shown a number of methodological challenges, as well as opportunities, and a second investigation was developed. One of the main challenges was how to develop a relevant exposure estimate in the absence of air quality monitoring data. Attachment 5 examines the effect of outdoor air pollution on admissions to the respiratory ward of a Kanpur hospital based on data from the calendar year 2006. Exposure to air pollution is represented by annual emissions of SO₂, PM₁₀ and NO_x from eleven source categories, established as a GIS-based emission inventory in 2 km × 2 km grid. Respiratory disease is represented by number of patients who visited the specialist pulmonary hospital with symptoms of respiratory disease. The results show that: (1) the main sources of air pollution are industries (SO₂ and NO_x), domestic fuel burning (SO₂, PM, NO_x) and vehicles (NO_x and PM₁₀); (2) the emissions of PM₁₀ per grid are strongly correlated to the emissions of SO₂ and NO_x; and (3) there is a strong correlation between visits to a hospital due to respiratory disease and emission strength in the area of residence. The results clearly indicate that appropriate health and environmental monitoring, actions to reduce emissions to air, and further studies that would allow assessing the development in health status are necessary.

Clearly, more information is available in the data from Kanpur than we have used in the analysis, but we feel that our result is robust, and should be sufficient to trigger both work by the authorities, and research. Our analysis can be supplemented by adding daily variability in pollution

concentrations available from the monitoring network, allowing an analysis of short term effects. Further, the findings from this study suggest that long term, systematic, prospective epidemiological studies on exposure to air pollution and its respiratory health effects are needed.

The paper documents that the polluted air was a clear threat to human health in Kanpur in 2006. A mitigation will require a combination of technical measures on all sources (this study was conducted before the full conversion of the public transport to compressed natural gas) and urban planning. Also it is necessary to establish adequate monitoring systems both for air quality and for human health, to be able to assess the current status and trends, and to evaluate the effectiveness of measures taken.

6. Support to decision making

6.1 Practical tools for decision support

A practical support to decision making can be through facilitating access to tools for use in concrete processes of assessment of environmental hazards. One way to make scientific results available for practical use is through decision support tools (DSTs). We have developed a meta-database of DSTs relevant to four “priority” health issues: asthma and allergies, cancer, neurodevelopment disorders, and endocrine disruptors. The primary product is an open access web-based MetaDataBase filled with 67 DSTs, accessible through the HENVINET networking portal www.henvinet.eu and <http://henvinet.nilu.no> .

The HENVINET DST MetaDataBase is an open product that enables the public to get basic information about the DSTs, and to search the DSTs using pre-designed attributes or free text. Registered users are also able to review and comment on existing DSTs, to evaluate each DST, and to add new DSTs, or change the entry for their own DSTs.

More than 25% of the DSTs address only one pollution source and 25% of the DSTs address only one environmental stressor. 60% of the DSTs’ results are used only by national authority and/or municipality/urban level administration and almost half of the DSTs are can only be used by environmental professionals and researchers. Only two DSTs deal primarily with exposure assessment. This indicates that there is a need to develop DSTs covering an increasing number of pollution sources, environmental stressors and health end points, and not least, to better cover exposure assessment, one of the identified knowledge gaps.

6.2 Scientists in the science-policy link

Scientific support to decision making in the field of environment and health can take many forms. Two examples will be given in this section, of a bi-lateral project with an outreach including an interdisciplinary conference, and a EU FP6 coordination action.

In a research project funded by the Research Council of Norway within a collaboration between Norway and Western Balkan Countries, one of the aims was to create a collaborative platform on air quality on the background of own particulate matter research. Within the project, and as a follow-up, three bi-annual conferences were organized with a scientific program following the “full

chain” approach (Attachment 6). This has allowed putting the findings from individual disciplines into a holistic perspective, giving the scientists the necessary background for making their work relevant for decision making, and giving the decision-makers and those who implement legislation scientific information relevant to their decision-making.

The EU FP6 for R&D co-ordination action HENVINET approached the science-policy interface through development of an interdisciplinary expert network, where the HENVINET consortium took a role as a facilitator or mediator. The motivation was a desire to form a “permanent network” of all stakeholders in environmental health. We summarize the methodology in Attachment 7.

Initially the focus of the project was on identifying knowledge gaps in the state of the art in scientific knowledge. Literature reviews covered all elements that compose the causal chain of the different environmental health issues from emissions to exposures, to effects and to health impacts. Through expert elicitation, knowledge gaps were highlighted by assessing expert confidence using calibrated confidence scales. We have developed an extended method for expert elicitation, and explored its usefulness to the policy process.

During this work, we acquired a complementary focus to that of identification of knowledge. By extending the scope of the endeavour from only a scientific perspective, to also include the more problem solving oriented policy perspective, the question of which kind of policy action experts consider justifiable was addressed. Experts identified using specified procedures were invited to answer a questionnaire, and then using a second questionnaire asked to analyze and assess priorities for decision making. The results of both questionnaires were finally discussed in a workshop that provided a basis for policy briefs. This process, and the development of focus of the study team, is described in Keune et al (2012).

The expert elicitation, the application of the calibrated confidence levels and the problem solving approach were all experienced as being quite challenging for the experts involved, as these approaches did not easily relate to mainstream environment and health scientific practices. Even so, most experts were quite positive about it. In particular, the opportunity to widen one’s own horizon and to interactively exchange knowledge and debate with a diversity of experts seemed to be well appreciated in this approach. Different parts of the approach also helped in focussing on specific relevant aspects of scientific knowledge (e.g. the exposure assessment described in previous chapters), and as such can be considered of reflective value.

The approach developed by HENVINET was part of a practice of learning by doing and of interdisciplinary cooperation and negotiation. Ambitions were challenged by unforeseen complexities and difference of opinion. As no standard or benchmark method was at hand to copy or follow, it was a challenging endeavour, and an acceptable consensus seemed out of reach all the time. Nevertheless, the scientific experts involved were quite positive about the process and its results. It seems that many felt that it fitted some important needs when addressing policy making on such important issues. Challenging questions remain on the quality of such approach and its product. Practice tells us that there probably is no best method and that the best we can do is dependent on contextual negotiation and learning from experiences that we think are relevant.

7. Conclusions

This thesis explores different aspects of exposure research that are essential for improved use of exposure assessment in the decision-making process. The first methodological requirement of any such process is a development of common framework and its acceptance of all stakeholders. All elements of this thesis use the “full chain approach”, an expanded version of the DPSEEA framework of the WHO. Specific aims of the thesis were fulfilled in the following manner.

1. We have applied the “full chain” and demonstrated how taking into account personal characteristics combined with spatially resolved pollution estimates affect exposure estimate. We provide a general exposure model, and suggest a population based methodology to modify large scale concentration estimate into a more relevant population exposure estimate. We show that this knowledge is necessary in development of mitigation strategies if the goal is the highest gain in improved health: in our example, children, the most vulnerable group, are most exposed.
2. We have designed and implemented a set of case studies to investigate how exposure assessment is perceived in relation to other elements of the “full chain”: do we have enough knowledge? By comparing knowledge assessment along the “full chain” for selected chemicals and air quality parameters, we conclude that often, exposure is among the most problematic issues. This calls for further development of methods for exposure assessment that can be used for decision-making.
3. We have developed an emission-based exposure metrics, and showed that this can be used for assessment of risk related to respiratory health.
4. We have studied how scientists perceive the decision-making process, and developed and implemented approaches that allow scientists to improve their participation in the science-policy interface.

Exposure assessment (and scientific knowledge) is often underused in decision making for various reasons, one of them connected to the role of scientists in the process. The results summarized in this thesis may bring more attention to exposure assessment as a discipline, and will support the use of exposure information and scientific information in general in order for air quality management to become more relevant.

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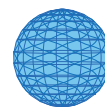
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9. Attachments

1. Smita S, Gupta SK, **Bartonova** A, Dusinska M, Gutleb AC, Rahman Q: Nanoparticles in the environment: assessment using the causal diagram approach. *Environmental Health* 2012, 11(Suppl 1):S13 (28 June 2012)
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6. **Bartonova** A, Jovasevic-Stojanovic M: Integrated assessment and management of ambient particulate matter – international perspective and current research in Serbia. *Chemical Industry and Chemical Engineering Quarterly* 18(4/II), 605-615, (December 2012)
7. **Bartonova** A: How can scientists bring research to use: the HENVINET experience. *Environmental Health* 2012, 11(Suppl 1):S2 (28 June 2012).

Attachment 1

Smita S, Gupta SK, **Bartonova** A, Dusinska M, Gutleb AC, Rahman Q: Nanoparticles in the environment: assessment using the causal diagram approach. *Environmental Health* 2012, 11(Suppl 1):S13 (28 June 2012)



REVIEW

Open Access

Nanoparticles in the environment: assessment using the causal diagram approach

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Brussels, Belgium. 14 April 2010 - 15 April 2010

Abstract

Nanoparticles (NPs) cause concern for health and safety as their impact on the environment and humans is not known. Relatively few studies have investigated the toxicological and environmental effects of exposure to naturally occurring NPs (NNPs) and man-made or engineered NPs (ENPs) that are known to have a wide variety of effects once taken up into an organism.

A review of recent knowledge (between 2000-2010) on NP sources, and their behaviour, exposure and effects on the environment and humans was performed. An integrated approach was used to comprise available scientific information within an interdisciplinary logical framework, to identify knowledge gaps and to describe environment and health linkages for NNPs and ENPs.

The causal diagram has been developed as a method to handle the complexity of issues on NP safety, from their exposure to the effects on the environment and health. It gives an overview of available scientific information starting with common sources of NPs and their interactions with various environmental processes that may pose threats to both human health and the environment. Effects of NNPs on dust cloud formation and decrease in sunlight intensity were found to be important environmental changes with direct and indirect implication in various human health problems. NNPs and ENPs exposure and their accumulation in biological matrices such as microbiota, plants and humans may result in various adverse effects. The impact of some NPs on human health by ROS generation was found to be one of the major causes to develop various diseases.

A proposed cause-effects diagram for NPs is designed considering both NNPs and ENPs. It represents a valuable information package and user-friendly tool for various stakeholders including students, researchers and policy makers, to better understand and communicate on issues related to NPs.

Background

Within HENVINET, an FP6 funded project, causal diagrams were developed as a tool to evaluate areas of agreement and disagreement between scientists and to identify gaps of knowledge [1,2]. The method of expert elicitation was applied by the HENVINET consortium to assess the health and policy implications of phthalates, where all details in the methodology behind the results presented here of the decaBDE and HBCD elicitation can be found [2]. In addition, an extensive review of the

methodology with an overall discussion and analysis of the outcome for all the priority areas of the HENVINET consortium has been made [3]. Furthermore evaluations on advantages and disadvantages of the expert elicitation methodology have been made by others [4,5]. This approach has been chosen as one potential method to handle complex issues that are typically faced by the environment and health community and decision-makers. The current manuscript describes a proposed cause-effect diagram for nanoparticles (NPs) applicable to both naturally occurring NPs (NNPs) and man-made or engineered NPs (ENPs), and provides a short justification for the inclusion of the proposed elements into the presented cause-effect diagram. However, it has to be

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noted that the presented cause-effect diagram has not been the topic of an expert- elicitation yet.

At the moment, it is unclear whether the benefits of nanotechnologies outweigh the risks associated with environmental release and exposure to NPs and there are concerns that NPs can also lead to a new class of environmental hazards [6]. Until now, relatively few studies have investigated the toxicological and environmental effects of exposure to NPs and ENPs. However, there is enormous effort at national and at international levels including the OECD and the European Union to investigate the impact of NPs on the environment and health. No clear guidelines exist on how to evaluate and quantify these effects, the provision of systematic information following NPs from releases to effects was requested [7] and furthermore it was argued to apply an integrated approach [8]. NPs differ in size, shape, chemical composition and in many physico-chemical properties. It is therefore crucially important to know which properties may cause adverse health effects [9].

Natural and engineered NPs present in the environment are influenced by a large number of physico-chemical processes and show different behaviour in organisms, soil, and water. The accumulation of engineered NPs (ENPs) has been shown in various organisms and environmental compartments, such as blue and green algae, fish and other aquatic organisms as well as soil and sediments [10-16]. Due to the low number of systematic studies and lack of knowledge on physicochemical properties and behaviour of NPs, these reports show an inconsistent picture of the effect of NPs on various environmental processes and their impact on human health. In the present work, we attempt to describe the elements of a cause-effect diagram as already developed within HENVINET for other environmental hazards and disease complexes [1,2]. The diagram for NPs is designed on the basis of current understanding of NPs mediated toxicity reports and review articles already available (Figure 1). These diagrams have been shown to be helpful to evaluate the level of confidence in the current ability of scientists to predict the magnitude of a disease burden that are expected to occur as a result of the release of NPs in the environment [1].

Elements of the NP cause-effect diagram

Sources of nanoparticles

Sources of NPs can be classified as natural or intentional and unintentional anthropogenic activities. NPs exist in the environment since the beginning of Earth's history and are common and widely distributed throughout the earths' atmosphere, oceans, surface and ground water, soil and even in living organisms. Major natural processes that release NPs in the atmosphere are forest fires, volcanic activities, weathering, formation from clay minerals, soil erosion by wind and water, or dust storms from desert.

Atmospheric dust alone is estimated to contain as much as several million of tons of natural NPs within a year [17]. Naturally occurring ambient NPs are quite heterogeneous in size and can be transported over thousands of kilometres and remain suspended in the air for several days.

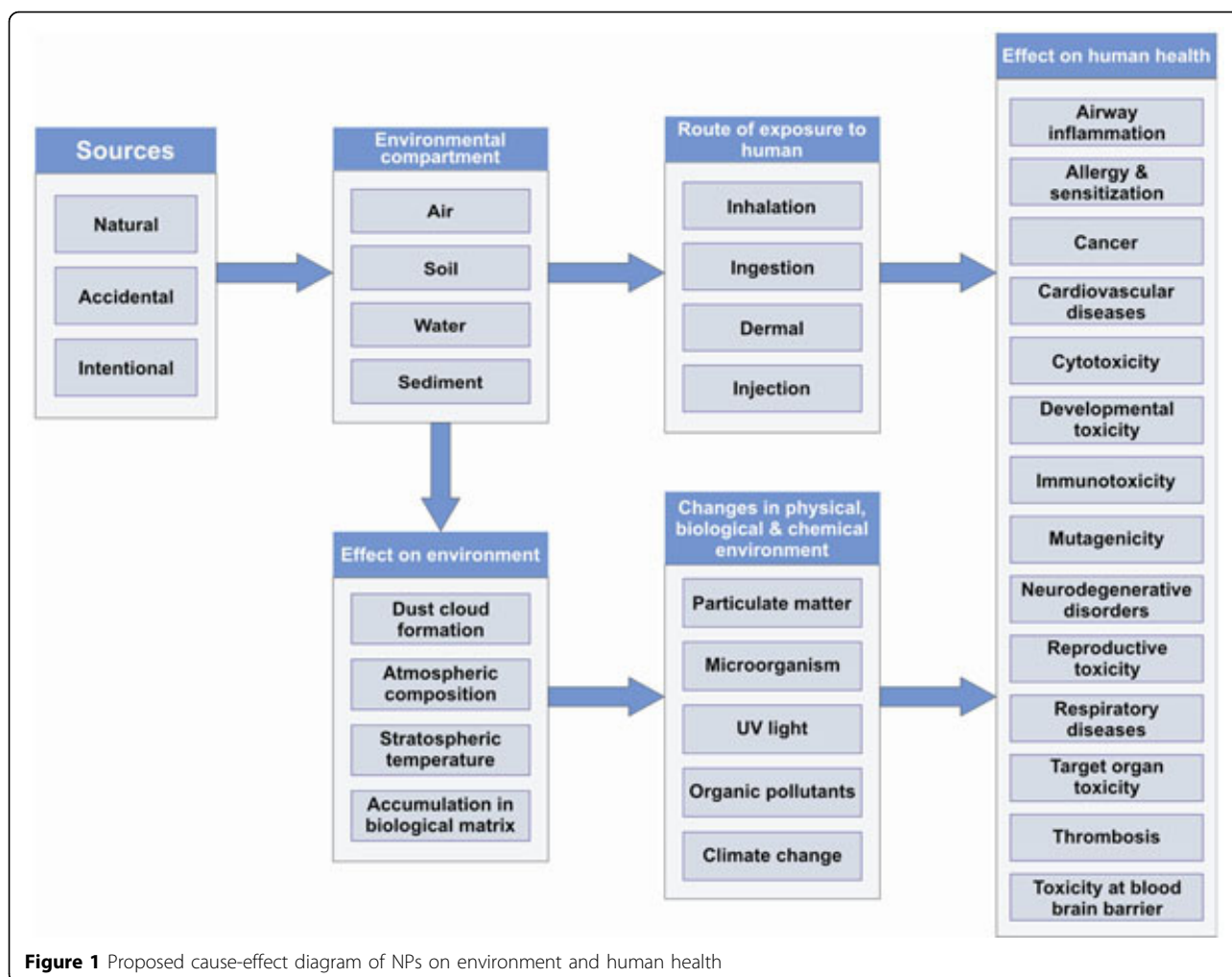
Man-made ENPs are unknowingly or purposely released in the environment during various industrial and mechanical processes (Figure 2). These NPs are very heterogeneous in nature and currently it is difficult to measure the impact on human health. The annual release of ENPs into the environment cannot be accurately estimated [6] while production volumes are strongly increasing [18]. The unfiltered exhaust gases from diesel engines contain large quantities of potentially harmful NPs from the incomplete combustion of fuel. In the fireplace at home, fullerenes like buckyballs or buckytubes are formed when wood is burned. In industrial processes, coal, oil, and gas boilers release tons of NPs unintentionally [19].

As a growing and widely applied science, nanotechnology has a global socioeconomic value, with applications ranging from electronics to biomedical uses [20]. With the advancement of industrial processes and nanotechnologies, a large number of ENPs are been manufactured and it is inevitable that during the use of the related products, ENPs are released in the air, water and soil both intentionally and unintentionally.

Because of their small size (less than 100 nm) and the very high surface to volume ratio, NPs usually display an enormously elevated reactivity potential. NPs can be assigned to a transitional range between single atoms or molecules and bulk material. The physicochemical features of NPs differ substantially from those of their respective bulk materials. Most of the ENPs are made up of carbon, silicon, metal or metal oxides and are believed to adversely affect the environment and human health directly or indirectly together with naturally occurring NPs [3]. Certain carbon nanotubes can cause the onset of mesothelioma, a type of cancer previously thought to be only associated with asbestos exposure, once inhaled [4,5,21]. However, this is not caused by the fact that nanotubes have two dimensions smaller than 100 nm but because they in fact interact with cells similarly to asbestos [4].

Natural occurrence of NPs in environmental matrices and their effects

NNPs can serve as a model for ENPs in the environment and naturally occurring mineral NPs. Their behaviour can point out important mechanisms in which NPs can move through environments and affect various environmental systems [22]. Once NPs are released in the environment from either natural or man-made sources, very little is known about their environmental fate. Especially NNNPs in the atmosphere have been studied in atmospheric sciences



[23]. After release in the environment, NPs will accumulate in various environmental matrices such as air [23], water, soil and sediments including wastewater sludge [24-28].

Effects of NPs on the environment

Various environmental processes that depend on the presence of physical entities are likely to be altered by the accumulation of NPs in the environment. Some of these processes are dust cloud formation, environmental hydroxyl radical concentration, ozone depletion, or stratospheric temperature change.

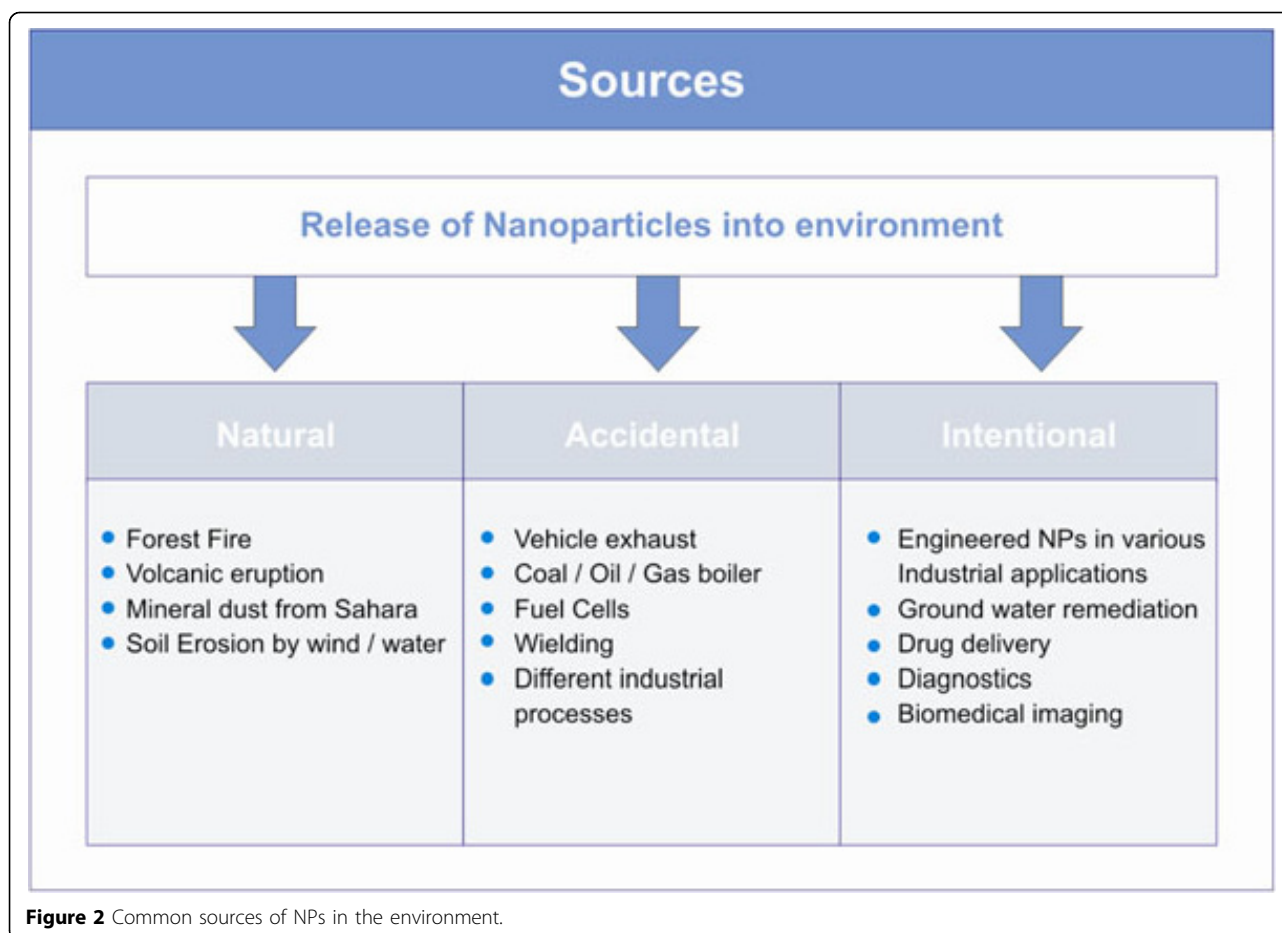
Effect of NNPs on dust cloud formation and decrease in sun light intensity

NNPs are thought to play an important role in dust-clouds formation after being released into the environment as they coagulate and form dust cloud [29]. 70% of the brown clouds over South Asia are made up of soot from the burning of biomass; largely wood and animal dung used for cooking and mainly contains

particulate matters and carbon NPs from unprocessed fuel [30]. The regional haze, known as atmospheric brown clouds, contributes to glacial melting, reduces sunlight, and helps create extreme weather conditions that impact agricultural production. The pollution clouds also reduced the monsoon season in India [31,32]. The weather extremes may also contribute to the reduced production of key crops such as rice, wheat and soybean [29].

Asian brown clouds impact on Himalayan glaciers

Asian brown clouds carry large amounts of soot and black carbon which are deposited on the glaciers. This could lead to higher absorption of the sun's heat and potentially contributing to the increased melting of glaciers [30]. The Himalayan glaciers provide the source of many of Asia's great rivers, with millions of people depending on them for food and water and because Asian brown clouds increase atmospheric temperature these glaciers have been decreasing over the past decades.



Asian brown clouds impact on agriculture

Dimming induced by atmospheric brown clouds is considered the major cause of the changing pattern of rainfall in Asia, with decreasing rainfall in some parts while other parts experience intense floods. Asian brown clouds are interfering with centuries old monsoon patterns with disastrous consequences for food production [29]. The large concentration of ozone in atmospheric brown clouds could decrease crop yields by as much as 20% [29,31].

Asian brown cloud impact on human health

A large part of the aerosol particles that make up atmospheric brown clouds are the result of the incomplete combustion of fossil fuels and bio-fuels. This increased exposure to particulate matter also increases the risk of exposure to pathogenic bacteria/ fungi [33,34]. The health impact of these particles is an increase in cardiovascular diseases, pulmonary illnesses, fungal/ bacterial diseases and chronic respiratory problems (Figure 3). The report estimates that in India and China alone, Asian brown clouds result in over 330,000 excess deaths per year mainly due to cardio-pulmonary diseases [29].

Effect of NNPs on environmental hydroxyl radicals concentration and ozone depletion in the atmosphere

The hydroxyl radical, which is one of the most reactive free radicals in the environment and plays an important role in the photochemical degradation of natural organic matter and organic pollutants in the environment. NNPs being very reactive immediately bind with hydroxyl radicals and ultimately result in the overall reduction of hydroxyl radicals [35,36]. As hydroxyl radicals are strong oxidants and thereby degrading many pollutants, its reduction is responsible for the increase in green house gases, which are ultimately responsible for ozone layer depletion (Figure 4) and cause severe environmental damage [37]. Furthermore it increases the exposure to UV radiation [38], which leads to the increase in incidences of various types of skin cancer in humans.

Effect of NNPs on the decrease of environmental stratospheric temperature

NPs in the troposphere interact with molecular hydrogen accidentally released from hydrogen fuel cells and other sources [39,40]. Molecular hydrogen along with NPs moves up to the stratosphere, resulting in the abundance of water vapour in the stratosphere. This will

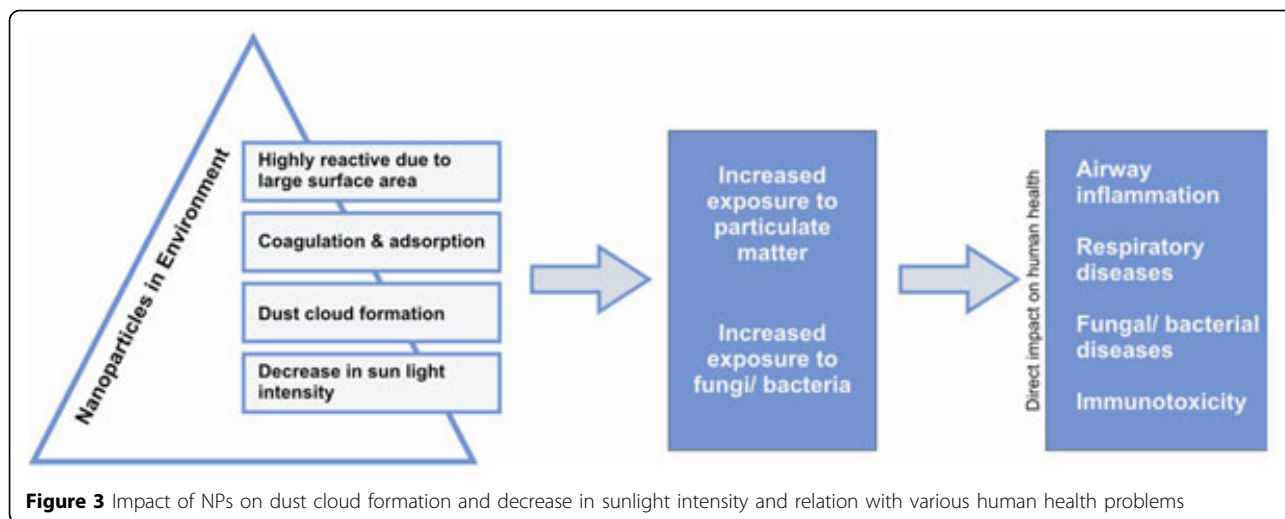


Figure 3 Impact of NPs on dust cloud formation and decrease in sunlight intensity and relation with various human health problems

cause stratospheric cooling, enhancement of the heterogeneous chemistry that destroys ozone, an increase in noctilucent clouds, and changes in tropospheric chemistry and atmosphere-biosphere interactions (Figure 5). Noctilucent clouds are composed of tiny crystals of water ice 40 to 100 nm in diameter and exist at a height of about 76 to 85 kilometres, higher than any other clouds in Earth's atmosphere. Similar to the more familiar lower altitude clouds, the noctilucent clouds are formed from water collecting on the surface of nano sized dust particles. The sources of both the dust and the water vapour in the upper atmosphere are not known with certainty. The dust is believed to come from micro meteors, although volcanoes and dust from the troposphere are also possibilities. The moisture could be lifted through gaps in the tropopause, as well as forming from the reaction of methane with hydroxyl radicals in the stratosphere. There is evidence that the

relatively recent appearance of noctilucent clouds, and their gradual increase, may be linked to climate change [39].

Accumulation of ENPs in selected biological matrices

It is inevitable that ENPs will be released into the soil and waters during their use and increase the load of ENPs in different environmental matrixes reflected by an increasing concern over the potential impact of ENPs in the environment on aquatic and terrestrial organisms [6,11,15,41]. Once released in the environment ENPs may enter plants and other microorganism by active or passive uptake [Figure 6]. NPs absorbed by microorganisms and plants, may enter into the food chain and cause serious alterations in humans and animals [42-44]. NPs due to highly reactive nature and large surface areas have potential to carry toxic materials, such as lipophilic pollutants and heavy metals [45].

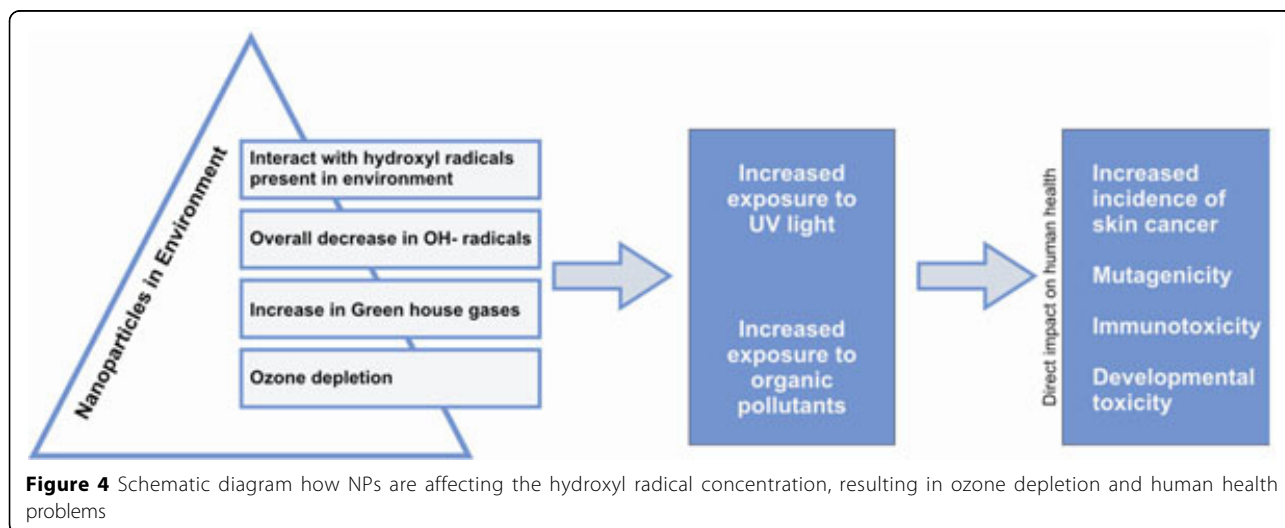
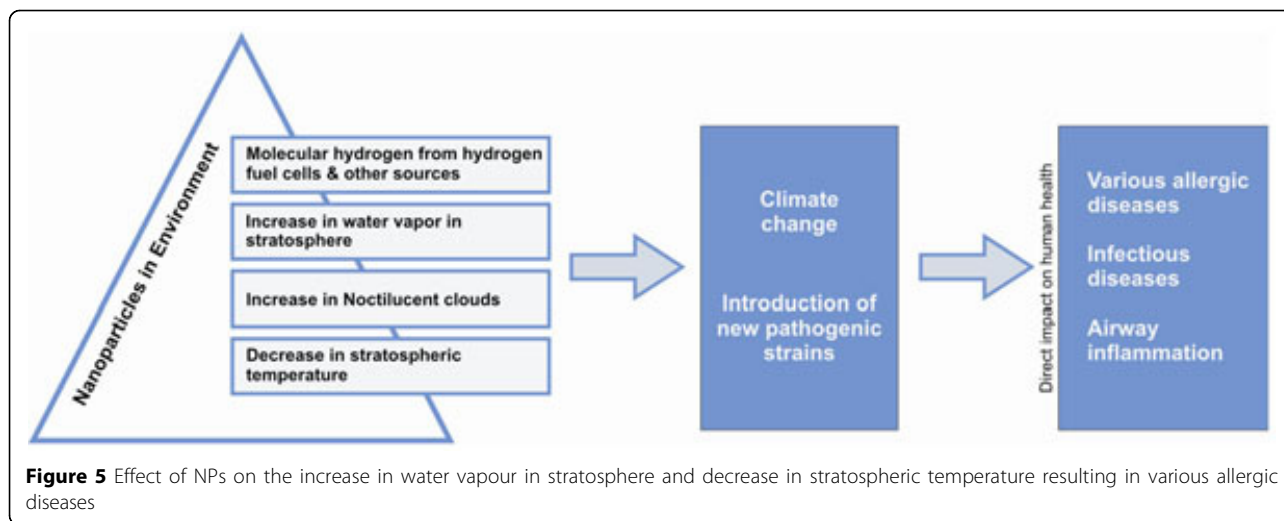
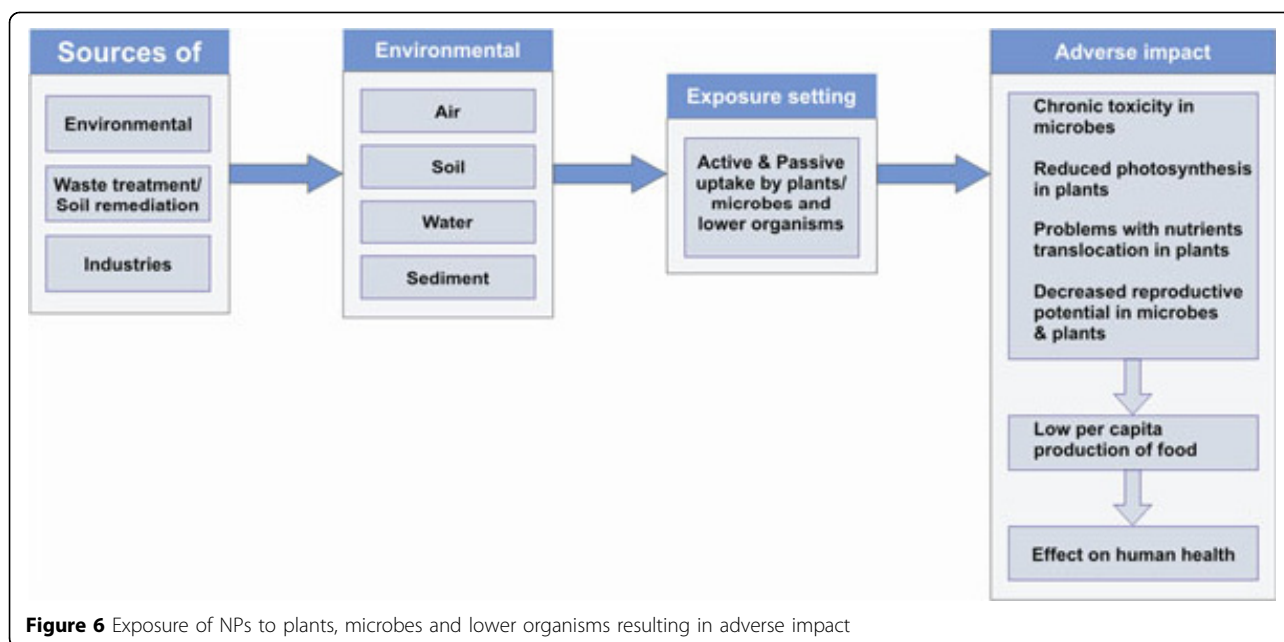


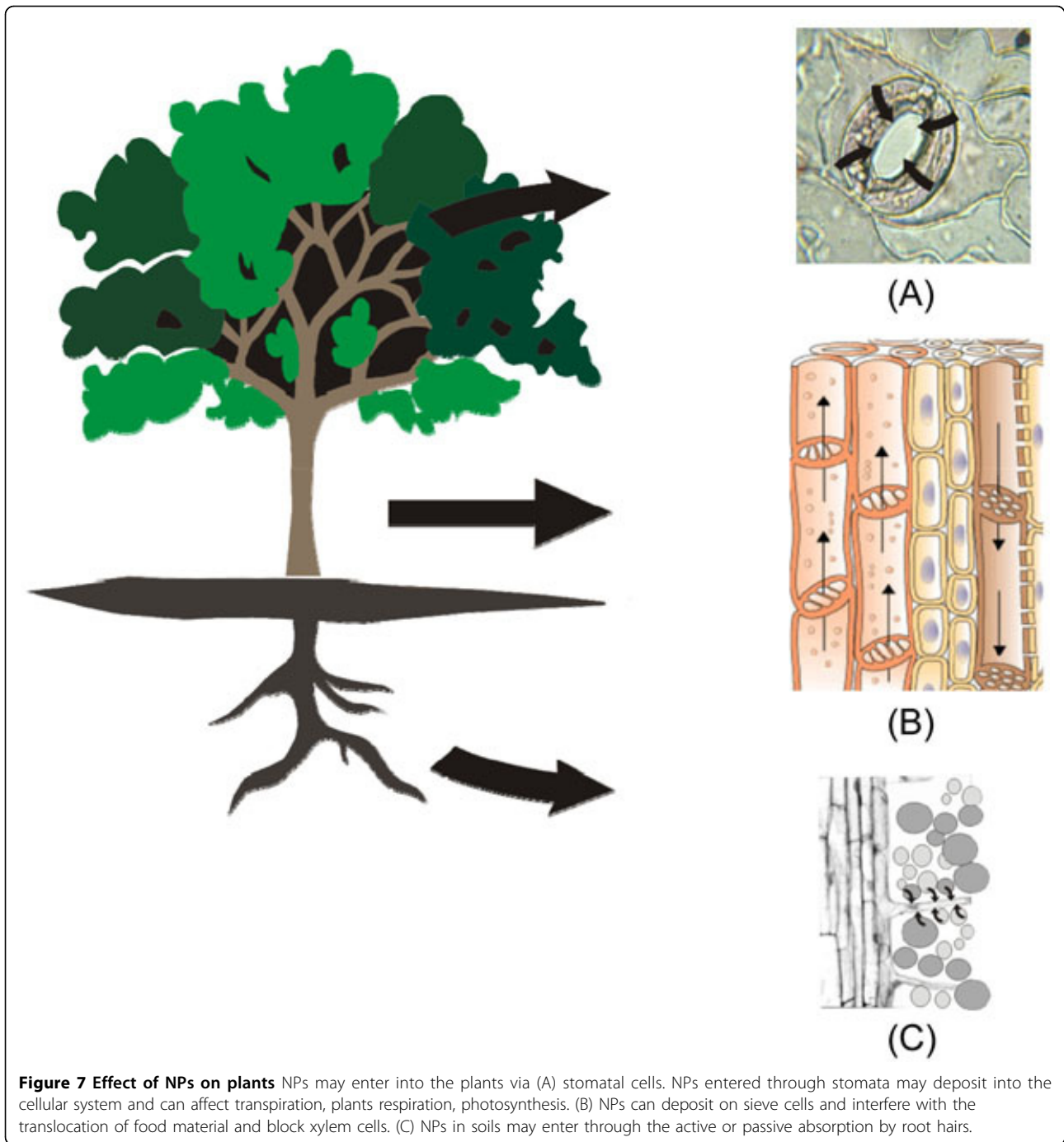
Figure 4 Schematic diagram how NPs are affecting the hydroxyl radical concentration, resulting in ozone depletion and human health problems



Some type of NPs may enter the plants via the root cell walls [Figure 7] [46-48]. Cell walls are semi-permeable and have pores with a size ranging from 5 to 20 nm that allow the passage of small particles. Thereby NPs and their aggregates with sizes smaller than the pore diameter may pass through the cell wall and reach the plasma membrane. There is some evidence that NPs may enter cells via embedded transport carrier proteins and ion channels and that they may interfere with normal metabolic processes, possibly by the production of reactive oxygen species (ROS) [11]. Airborne NPs accumulate over leaf surface and may enter into the cell through leaf stomata. Thus, plants with a high leaf area and stomatal indices may expect to have the higher

interception potential for airborne NPs. Accumulation of NPs on stomatal tissues might alter the gas exchange; resulting in the foliar heating and adverse effects on plant physiology [49]. Carbon nanotubes and aluminium NPs have been identified to inhibit root growth in various economically important plant species by interacting with root surface [50,51]. Carbon black that aggregate on the sperm cells of a marine seaweed (*Fucus serratus*) were found to reduce the fertilization success rate [52]. Recent reports show the impact of NPs on various food crops. Carbon NPs diminished rice yields and made wheat more vulnerable to other pollutants [45,53], while again it has to be noted that this effect may be due to the asbestos-like behaviour of carbon nanotubes. Thus





NPs are one of the major concerns for a future risk of low per capita food production. The accumulation of NPs on photosynthetic surfaces may cause shading effects, i.e. reduced sun light availability and hence reduced photosynthetic rate.

While the description of the ecotoxicity of NPs is not a central aim of this manuscript NP exposure related effects have been shown for a range of test organisms and NPs. TiO₂ NPs were shown to adsorb on algal cell

surface, resulting in the increase of cellular weight by more than 2 fold and affecting the algae's ability to float and resulting in reduced sunlight availability for photosynthesis [11]. The toxicity of TiO₂ NPs on green algae *Desmodesmus subspicatus* has been shown to be size dependent. Smaller NPs (~ 25 nm) showed a clear concentration-effect relationship (EC₅₀ of about 40 mg/L), whereas the large particles (~ 100 nm) were found to be less toxic [10]. Silver NPs exerted considerable toxicity

in a nematode (*Caenorhabditis elegans*), especially decreasing the reproduction potential and increased enzyme induction and protein formation [54] but have been shown to also affect a range of other organisms too [55]. NPs may impair the function or reproductive cycles of earthworms, which play a key role in nutrient cycling [56] hence possessing a hazard to induce ecological imbalances.

Human exposure to nanoparticles

Exposure of humans to NPs mainly occur through natural routes (oral, pulmonary or skin uptake). Exposure assessment is difficult but necessary [8,57-59]. Furthermore many intentional processes such as medical applications may directly inject ENPs into the human body. Under practical conditions the most important routes of uptake for ENPs are inhalation or oral uptake [7], but this has not been specifically studied. More information

is available for accidentally released NPs from combustion engines especially diesel exhaust [60,61]. In case of aerosolized silver-containing NPs that are widely used in consumer products due to their antimicrobial properties, environmental and human health risk were reviewed in detail [62]. NPs come in the direct contact with skin as they are widely used in various cosmetics and personal care products, and hence the assessment of toxicity due to dermal route of exposure is very critical [6][63][64]. While NPs are already present in food products such as ketchup, intake of NPs through food is another area where exposure assessment is crucial but very little information available on population exposures through ingestion [65]. To facilitate the toxicity assessment of NPs exposure to human, the establishment of exposure registries were recommended to enable the conduct of large-scale prospective multi-center epidemiologic studies [66].

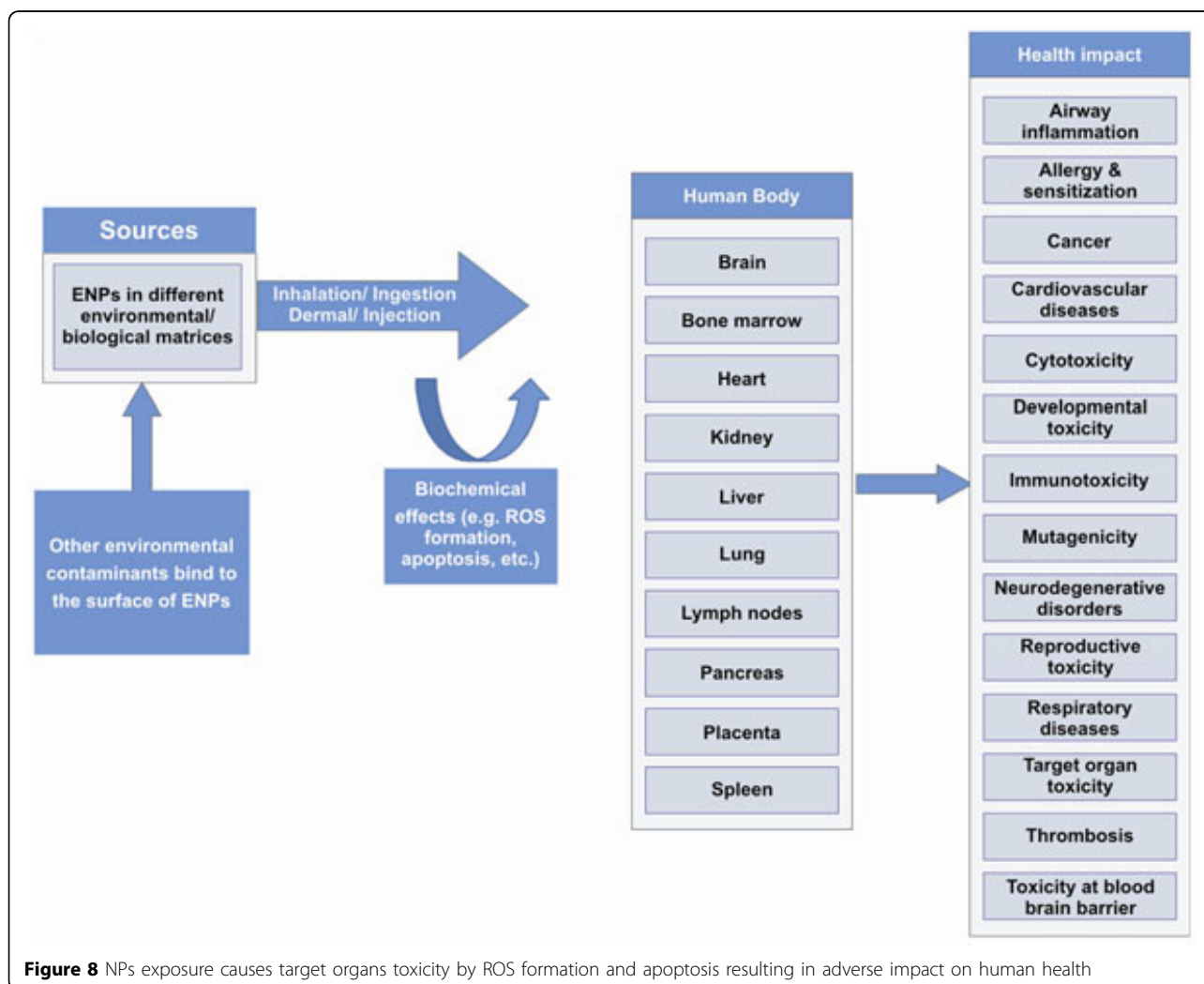


Figure 8 NPs exposure causes target organs toxicity by ROS formation and apoptosis resulting in adverse impact on human health

Human health impact of nanoparticles

Change in the physical, biological and chemical component of the environment directly influences human health. Among them aggregation, agglomeration, dispersability, size, solubility, surface area, surface charge and surface chemistry/ composition have been identified to be most important parameters [9]. A number of potential health effects have been identified probably being related to the exposure of humans to ENPs (Figure 8).

Inhaled NPs are likely to evade phagocytosis, penetrate lung tissue, reaching interstitial spaces and enter blood circulation [67-69]. In the cardiovascular system platelet aggregation, and enhanced vascular thrombosis were observed [70]. Via the blood stream NPs can finally reach sensitive target sites such as lymph nodes, spleen, heart, kidney, liver, pancreas, bone marrow and brain [19,67,68,71-73]. Cell membrane penetration and particle accumulation in diverse cellular organelles (e.g. mitochondria) can finally lead to injurious responses within the crucial target organs and inflammation, immunotoxicity, cytotoxicity, genotoxicity and malignancy have been attributed to the nanoparticle-associated oxidative stress [18,21,74-77]. The oxidative stress resulting from the exposure to quartz and carbon black NPs can pose pronounced effects like interstitial fibrosis and airway inflammation [78-80].

Conclusion

Nanotechnology, as a strongly growing and widely applied science, has a high potential of global socioeconomic value. On one hand, the new features of designed NPs provide unprecedented technical capabilities thereby enabling them to perform absolutely novel tasks in technology and science. Unfortunately, just the same new qualities can concurrently also include undesired intrinsic features, which sometimes lead to harmful interactions with exposed organisms.

In coherence with the described alarming aspects it seems to be a high time to establish linkages between direct and indirect health impact of NP exposure and evaluate the consensus among researchers and policy makers regarding the knowledge base. The causal diagram approach has proven to be a suitable conceptualization, simplification and visualization technique that allows communication linking the scientific disciplines involved, as documented by a wide range of examples [1,2,81,82]. In the near future it is envisaged to use this diagram as the basis for an internet-based tool for knowledge assessment. These causal diagrams provide an important platform to identify knowledge gaps and potential agreements or disagreements on the effect of NPs on various environmental processes and their impact on human health and can contribute to sustainable governance regarding the future use of NPs.

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Authors' contributions

SS, SKG and QR conceived and designed the review, collected the data and drafted the manuscript. ACG, AB and MD commented and revised the draft manuscript and contributed with some sections. AB is HENVINET project coordinator and contributor to the framework development. All authors read and revised the final version of the manuscript.

Competing interests

None declared

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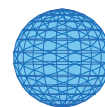
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Attachment 2

Forsberg B, Bråbäck L, Keune H, Kobernus M, Kraye von Krauss M, Yang A, **Bartonova** A: An expert assessment on climate change and health - with a European focus on lungs and allergies. *Environmental Health* 2012, 11(Suppl 1):S4 (28 June 2012)



METHODOLOGY

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An expert assessment on climate change and health – with a European focus on lungs and allergies

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Abstract

Background: For almost 20 years, the Intergovernmental Panel on Climate Change has been assessing the potential health risks associated with climate change; with increasingly convincing evidence that climate change presents existing impacts on human health. In industrialized countries climate change may further affect public health and in particular respiratory health, through existing health stressors, including, anticipated increased number of deaths and acute morbidity due to heat waves; increased frequency of cardiopulmonary events due to higher concentrations of air pollutants; and altered spatial and temporal distribution of allergens and some infectious disease vectors. Additionally exposure to moulds and contaminants from water damaged buildings may increase.

Methods: We undertook an expert elicitation amongst European researchers engaged in environmental medicine or respiratory health. All experts were actively publishing researchers on lung disease and air pollution, climate and health or a closely related research. We conducted an online questionnaire on proposed causal diagrams and determined levels of confidence that climate change will have an impact on a series of stressors. In a workshop following the online questionnaire, half of the experts further discussed the results and reasons for differences in assessments of the state of knowledge on exposures and health effects.

Results: Out of 16 experts, 100% expressed high to very high confidence that climate change would increase the frequency of heat waves. At least half expressed high or very high confidence that climate change would increase levels of pollen (50%), particulate matter (PM_{2.5}) (55%), and ozone (70%). While clarity is needed around the impacts of increased exposures to health impacts of some stressors, including ozone and particulate matter levels, it was noted that definitive knowledge is not a prerequisite for policy action. Information to the public, preventive measures, monitoring and warning systems were among the most commonly mentioned preventative actions.

Conclusions: This group of experts identifies clear health risks associated with climate change, and express opinions about these risks even while they do not necessarily regard themselves as covering all areas of expertise. Since some changes in exposure have already been observed, the consensus is that there is already a scientific basis for preventative action, and that the associated adaptation and mitigation policies should also be evidence based.

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Background

For almost 20 years, the Intergovernmental Panel on Climate Change (IPCC) has been assessing the potential health impacts of climate change, with increasingly convincing evidence that climate change presents existing risks to human health and that without timely and effective interventions, these risks will increase with additional climate change [1].

According to the summary statements from the Intergovernmental Panel on Climate Change 4th Assessment Report [1]: over the past 50 years, it is very likely (defined as >90% likelihood) that hot days and hot nights became more frequent, and it is likely (>66% likelihood) that heat waves will become more frequent over most land areas. It is very likely that heavy precipitation events will become more frequent; and likely that tropical cyclones will become more intense, with larger peak wind speeds and heavier rainfall; that in areas already affected by drought will increase; as will the incidence of coastal flooding from extremely high sea levels.

However, the changes in climate will differ by region. The increase in temperature will be greater at higher latitudes. The estimated increases in extreme precipitation are much larger for northern Europe than in southern Europe [2]. Modeled estimates of climate change induced increases in near-surface ozone concentrations and accumulated ozone, exposure over a threshold of 40 ppb (ppb hrs), are much larger in southern Europe [3].

Warnings from experts on health threats have become increasingly dire. McMichael et al in 2006 stressed that climate change will affect human health in many ways [4]. In this paper the authors discussed the problems of detecting global warming effects on health outcomes at an early stage, but showed that estimations in some cases are possible. They also concluded that research on climate change and health risk so far has mostly focused on thermal stress, extreme weather events, and infectious diseases and are lacking in other areas.

Given the observed and predicted detrimental health impacts of climate change, broadening the current focus within the public climate discourse is an important challenge for the health sector [4,5]. Although most of the adverse effects of climate change will threaten human health, the assessments that have gained most attention from governments have focused mainly on economic effects, suggesting that the economy was the most important issue for society. Experts in environmental health and public health agencies need to engage further in the process of understanding and communicating the implications of climate change on public health and wellbeing. Recently there have been an increasing number of initiatives by health scientists and physicians designed to increase the public interest of the threat.

A recent position statement on climate change and health impacts from the European Respiratory Society (ERS) was developed after a workshop co-organized by the HENVINET Project and the American Thoracic Society [6]. The position statement highlights climate related health impacts, including deaths and acute morbidity due to heat waves; increased frequency of acute cardio-respiratory events due to higher concentrations of ground level ozone; changes in the frequency of respiratory diseases due to transboundary particle pollution; and altered spatial and temporal distribution of allergens (pollens, mold and mites) and some infectious disease vectors. According to the report these impacts will not only affect those with existing respiratory disease but will likely increase the incidence and prevalence of respiratory conditions.

The effect of heat waves on mortality is well documented [7]. The increase in respiratory mortality (relative risk) is larger than total or cardiovascular mortality [8]. Although the association between heat and the number of hospital admissions is less studied, and less evident, admissions are, however, also more apparent for respiratory disease than for cardiovascular [9]. Air pollution is the environmental factor with the greatest impact on respiratory health in Europe. Particle pollution, vehicle exhaust and ground level ozone are the most important types of hazardous pollutants. Pollution models for climate change scenarios predict an increase in ozone concentrations over large areas, while the effect on particle concentrations is less clear [10]. Higher temperatures, clear skies and stagnant conditions will favor ozone production. The short-term effects of ozone on daily mortality [11] and respiratory disease [12] are extensively studied, while there is only limited documentation of long-term effects on mortality [13].

The climate in general and weather extremes may have an effect on allergic diseases and asthma via the impact on allergen exposures. Higher temperatures and concentrations of CO₂ are associated with an increase in pollen production [14], and with climate change the timing of the pollen season may change [15]. Heavy rain and flooding may cause water damage on buildings and lead to increased mould exposure. Although mould allergy is rare there is a clear relationship between damp houses and respiratory diseases such as asthma [16]. Additionally while asthma in children and young adults has been less common in areas with colder winters and lower humidity than along the wetter coastal areas [17,18], more severe rainfall and storms could increase this risk. House dust mites are rare in cold winter climates in the north and at high elevation where the heated indoor air becomes dry in winter. A cold winter could be enough to reduce exposure to mite allergens [17], however, with milder winters mite allergies may become worse and more common.

Since mortality is higher in the cold season, without also considering influenza epidemics, and cold spells associated with greater mortality, a milder winter could result in less cold-related mortality especially in countries not well adapted to cold [19].

Despite the likelihood that most of the adverse effects of climate change will threaten human health, health effects have not featured greatly in the climate discourse. Therefore we wanted to study how health experts look upon the health risks, and upon knowledge gaps. We also wanted to identify potential differences of opinion amongst scientists. Since there is a large body of literature on air pollution levels, allergens and respiratory morbidity and mortality and potential health effects of climate change, we sought the opinions of experts in these fields for our study.

Methods

We used an expert elicitation method for assessment of knowledge on climate change and health risks [20]. On the basis of the literature on climate change and health risks in Europe, a causal diagram (proposed pathways to health effects) outlining eight different pathways to asthma/allergies and other respiratory endpoints was developed. The causal diagram was presented in an online questionnaire, accompanied by general motivations without a presentation of supporting references [21]. The causal pathways dealt with extreme heat, extreme cold, ozone, particulate pollution, allergenic pollens, mould spores, damp buildings and dust mites. A first test of the online questionnaire was organized in 2008 among a group of participants registered for the European Respiratory Society workshop [6]. The questions were formulated based on the rating of confidence levels inspired by the IPCC quantitatively calibrated levels of confidence [22]. Each relationship in the causal model had a corresponding question, for example: "What is your level of confidence in the claim that increased levels of secondary fine particles also will result in an increased population exposure?" The respondent's confidence in current scientific methods for predicting the magnitude of the effect could be assessed as very high (at least a 9 out of 10 chance of being correct), high (at least an 8 out of 10), medium (at least a 5 out of 10), low (at least a 2 out of 10) or very low (less than a 1 out of 10). In the analysis we coded the score "very high" = 5, "high" = 4 and so on down to "very low" = 1. We analysed the consensus for answers in the online questionnaire using a consensus index following the method proposed by Tastle and Wierman [23]. This index attains consensus values between 0 (perfect disagreement) and 1 (perfect agreement). The test among workshop participants resulted only in minor revisions in the formulating of questions/

claims, in particular to make it clear that potential changes in exposure or health due to other reasons than climate change were not included in the claims, and that the individual sets of questions were to be treated independently irrespective of the state of knowledge of other elements of the diagram.

The online questionnaire also asked to rank from 1 (highest importance) to 8 (least importance) the relative importance of the health impact to be expected via each pathway in comparison with the others. The questionnaire moreover asked: "Does the diagram take into account all the important parameters..." where the answer "no" was followed by a request for comments. Another question on the causal model was: "Are the different causal relationships adequately structured? If no please explain!"

For the 2009 study we invited 48 experts in the field of respiratory and environmental medicine, public health and/or epidemiology. All invited experts had recent publications listed in PubMed on asthma and air pollution or climate change, and had been studying European populations. They could all be considered health experts with expertise relevant for an assessment of potential health impacts related to climate change in their country or Europe in general.

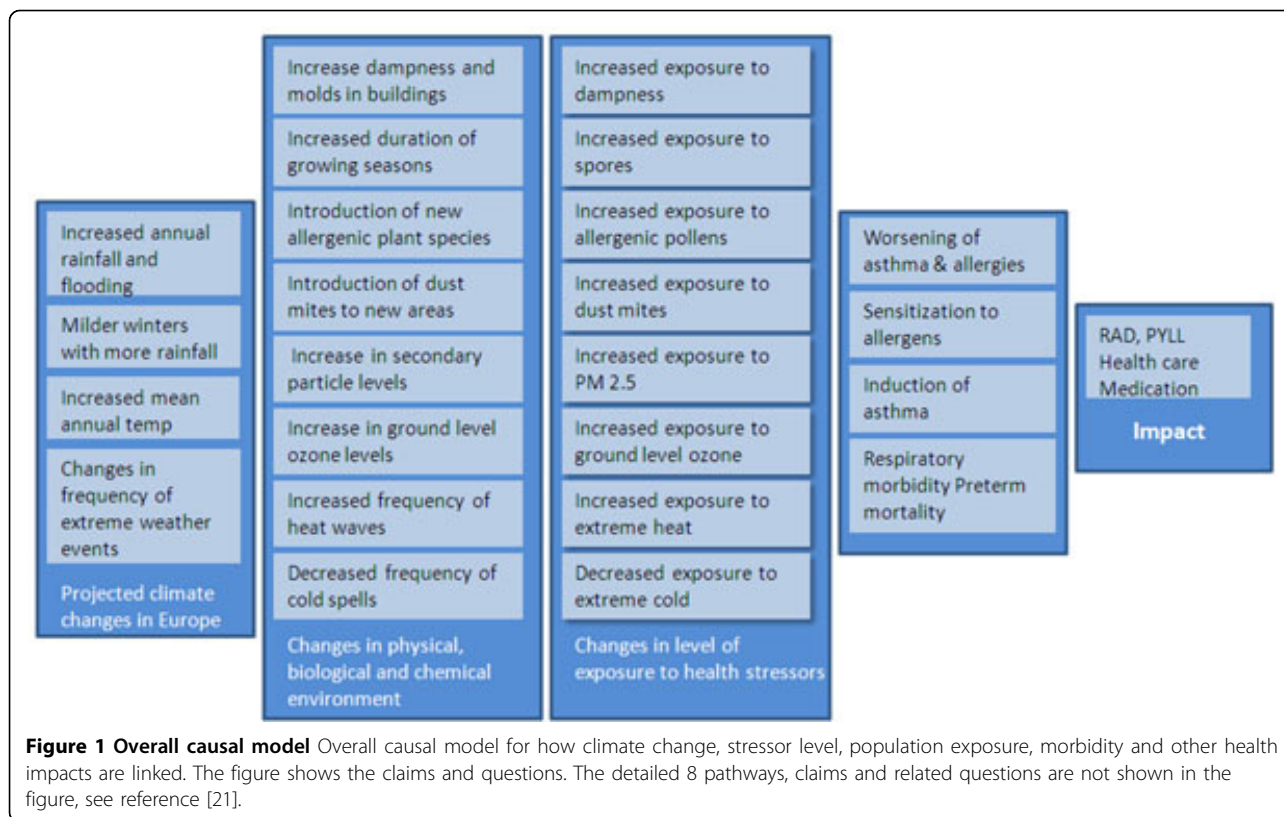
Sixteen out of 48 experts accepted the invitation to participate in the online evaluation of the revised causal diagram with proposed relationships and the associated questionnaire (Figure 1). The participating experts are listed in appendix 1. Nine of the 16 experts also responded to a second questionnaire on the kind of policy action they considered justifiable based on the identified state of scientific knowledge, thereby determining the applicability of the current evidence to health policy [20]. In a follow-up workshop held two months later in September 2009, eight of these nine experts discussed the outcomes of the first and the second questionnaire. The workshop was organized parallel to the annual conference arranged by the European Respiratory Society, with a focus on respiratory health.

Results

Knowledge evaluation

Ability to predict the magnitude of changes

As shown in Figure 2, the participating scientists rated with high confidence the ability of current scientific methods to predict the magnitude of the change in the frequency and duration of heat waves (mean score 4.5), and increase in population exposure to extreme heat (mean score 4.25). The mean score was also high for the ability to predict the magnitude of the increase in the frequency of acute asthma and respiratory morbidity as a result of increased exposure to ozone (mean score 4.2), and for the previous link in the pathway, the increase in



exposure to ozone (mean score 4.07). Mean scores of 4 or higher were found for the two causal pathways related to heat and ozone, indicating high confidence. Levels of particles, as PM_{2.5}, (mean score 2.56) and the distribution and levels of house dust mites rated a mean score of 3.0 indicating moderate confidence. The latter two pathways were overall considered to be poorly understood due to lack of evidence from relevant studies.

Consensus in judgements

The consensus was highest for the ability of current scientific methods to predict the magnitude of the increase in the frequency of acute asthma and respiratory morbidity as a result of increased exposure to mould and spores in buildings (Figure 2), where 13 out of 16 experts answered that we have high ability to predict the magnitude of this effect (consensus index 0.85). Second highest consensus was seen for confidence of scientific methods of predicting the magnitude of the increase in population exposure to ground-level ozone, where 10 experts answered high ability, three answered very high and two medium high (consensus index 0.85). For questions dealing with house dust mites and PM_{2.5} the consensus among experts was generally the lowest in this study.

Relative importance of stressors

When the respondents in the questionnaire had to rank (from one (highest) to eight (lowest)) the relative importance of the health impacts of the various pathways,

extreme heat stood out as most important, with 3.25 as the mean rank, and the first rank by 7 out of 16 experts. Thereafter followed ozone (3.94), PM_{2.5} (4.19) and ranked most important by three experts, damp buildings (4.63), pollen (4.69), mould and spores (4.88), extreme cold (5.38) and dust mites (5.69). Extreme heat, extreme cold, PM_{2.5}, mould and spores and, damp buildings had all been ranked both as the most and least important climate related pathway to health impacts.

Among the experts that later participated at the follow-up workshop the highest ranking was given to extreme heat (2.89), ozone (4.33), damp buildings (4.33) and PM_{2.5} (4.56).

Comments on the causal diagram

Eight out of sixteen respondents considered that all the important parameters were taken into account, while the other half had additional comments. Their recommendations included: broadening the focus from asthma and allergy; considering the effects of drought, thunderstorms, psychosocial stress, other air pollutants (coarse particles and emissions from heating), infectious agents and adaptation (air conditioning); as well as variations in susceptibility, and the potential positive effects on respiratory infections and allergies. Two respondents additionally recommended building a more complex model with a network of arrows or feed-back loops.

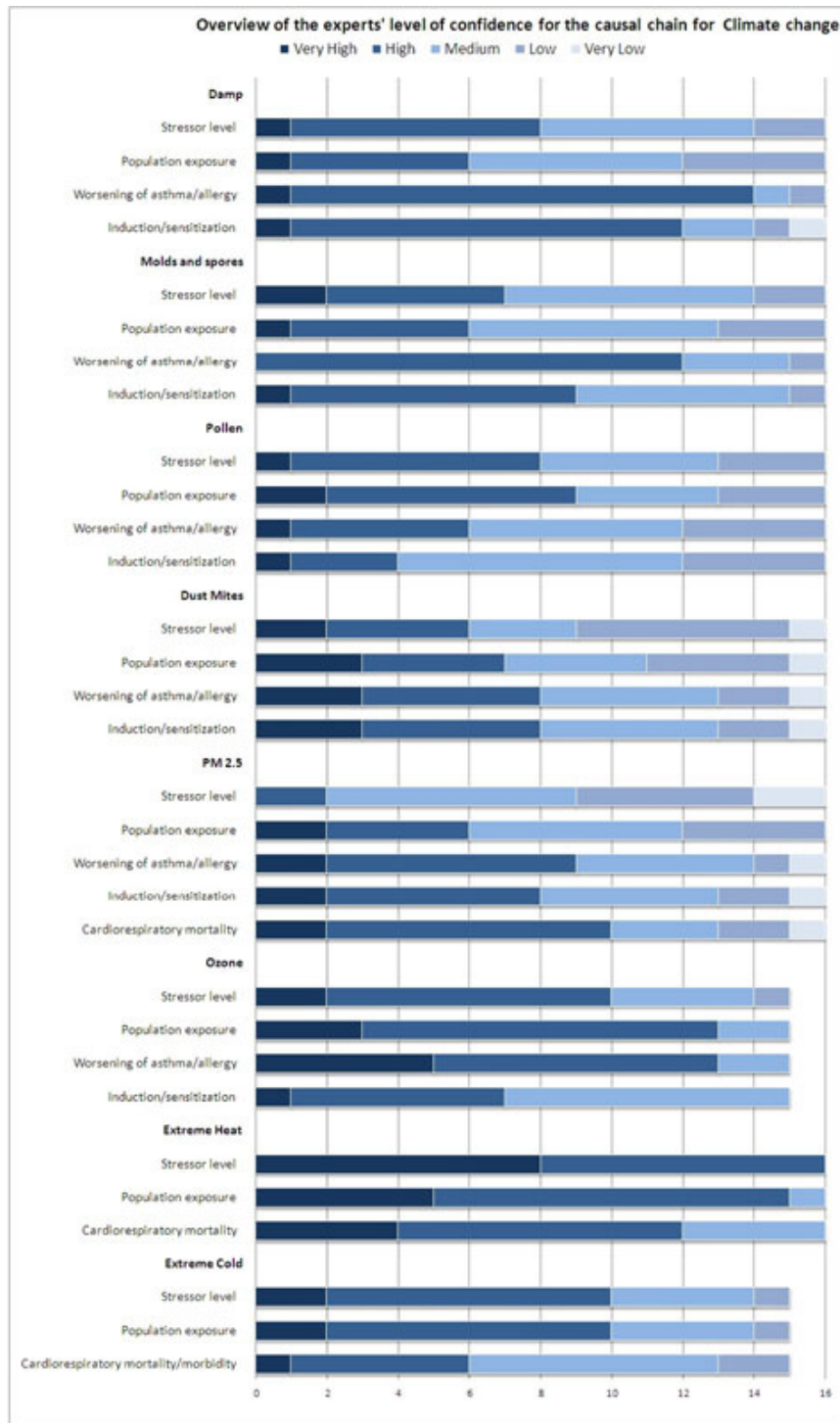


Figure 2 Evaluation of the proposed relationships in the causal diagram on asthma and allergies Evaluation of the proposed relationships in the causal diagram used this study by 16 experts.

Policy interpretation questionnaire

Most important causal elements

The experts participating in answering the second questionnaire very clearly considered that “exposure” to be

the most important element to the influence health within the causal diagram. For several specific exposure elements the following specific statements were made. With respect to ozone, there is sufficient evidence for

the causal diagram on health outcomes. Furthermore relatively small changes will induce changes in health outcomes. Moreover, the ozone impact will increase with rising temperatures. There is however a need for research to clarify seasonal variations in ozone, the influence of sunshine and chemicals, and long term effects of ozone. With respect to dampness, there is enough evidence for health effects, as small changes in exposure will have effects on asthma. In Europe the risk of flooding is generally considered to be lower than the risk of drought, thus limiting exposure to a fraction of population, which may lower the priority of flood related health policy action. Regarding extreme heat, health impacts particularly in the elderly population are expected increase, and there is sufficient evidence for respiratory and other health effects. With respect to PM 2.5 the consensus was that there is sufficient evidence that small changes will induce changes in many health outcomes for the general population. While there is sufficient evidence that pollen exposures are expected to increase with climate change, and that this will impact on the large population of people with pollen allergy, the health impact is considered to be a limited issue due to its seasonal nature.

Policy action

A wide range of policy actions is covered by the response of the experts, ranging from fundamental and applied scientific research to concrete policy actions, both monitoring and awareness raising, and restrictive or prohibiting activities. We discuss a few concrete examples. Regarding ozone, extreme heat and pollens specifically, a combination of monitoring and warning systems and medical advice is proposed. Regarding ozone, specifically the problem of conflicting data is mentioned as a problem to be solved. Better insulation against heat is specifically mentioned regarding extreme heat events. With

respect to dampness a wide range of actions is mentioned: indoor ventilation, water leak repairs, insulation, better heating, implementing best practices, better standardized detection, prohibiting risk activities indoor and outdoor, awareness raising and testing buildings for extreme weather conditions. PM_{2.5} is considered best handled by the following types of actions: congestion pricing, clean cars, less power plant emissions and prohibiting risk activities indoor and outdoor.

Confidence in science and policy; weight of knowledge

Most participating experts have high confidence that conducting more scientific research will yield decisive knowledge within the next five years (Figure 3).

Reasons given for a rating of high confidence was that although a five year period is short it is enough time for research to produce results. Furthermore the available mechanistic knowledge (or confidence in causal pathways) is considered a basis for preventive actions, and the available evidence is considered sufficient for policy action, even if there is still a need for “action knowledge” to be further researched. One expert expressed low confidence with the concern that policy is rarely evidence based.

The experts rated their confidence in the possibility that policy actions to effectively manage this health risk will become technically (not politically) feasible within the next five years, confidence was rated lower than their confidence that conducting more scientific research will yield decisive knowledge within the next five years (Figure 4).

Most experts have medium confidence in this respect as while some relevant policy actions are feasible, there is disagreement about their effectiveness. Reasons for high confidence are the availability of both scientific knowledge and of good examples; however concern that the main element that is still missing being political will.

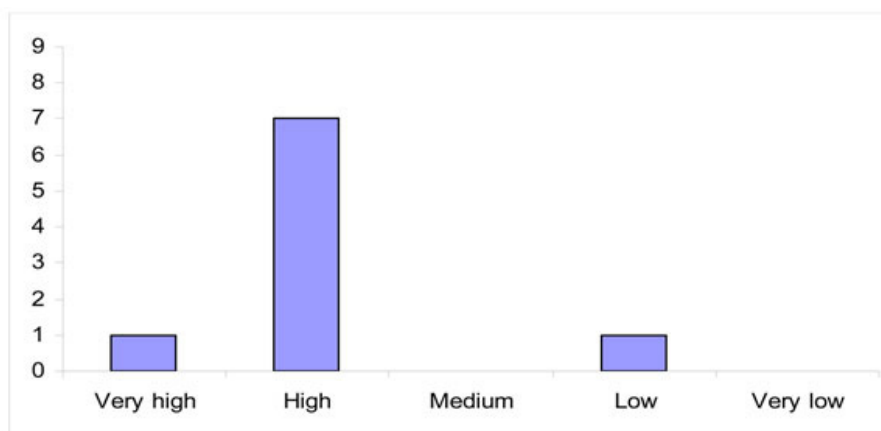


Figure 3 Level of confidence whether conducting more scientific research will yield decisive knowledge within the next five years (distribution of answers)

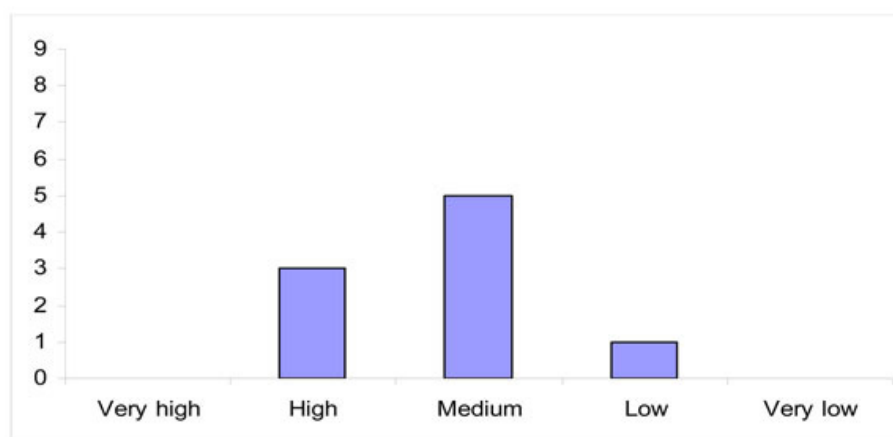


Figure 4 Level of confidence whether policy actions to effectively manage this health risk will become technically (not politically) feasible within the next five years (distribution of answers)

Low confidence is attributed due to the fact that current actions do not seem to result in convincing positive effects.

There is consensus among the health experts that there is sufficient evidence to justify policy measures to decrease the existing health risks associated with the stressors based on the current scientific knowledge. Main discussion points are mentioned below:

- Scientific evidence on both health effects and effective solutions is available
- Enough is known for prevention, however criteria for setting priorities policy action may favour reactive measures even though prevention is more effective Exposure to known health stressors will rise, so action is needed; research based evidence required to determine the actions that will be most effective
- Definitive knowledge is not always a prerequisite for policy action

Follow-up workshop

Amongst the workshop participants there was a concern that the composition of the group of experts, especially the workshop panel, may bias the responses and conclusions. Especially since each person does not consider him/herself to be an expert in all research areas examined by the evaluation. However HENVINET representatives at the workshop observed that “at home” (in their country, institute or department) all participants are expected to have an expert opinion on all parts of the causal diagram. Some of the panel members concurred that they answer these kinds of questions from a general understanding they have based on current scientific knowledge.

There was consensus among the experts that at least no important pathway was missing in the causal diagrams presented. They also agreed that the relevance of

different stressors and health risks could be different within different regions in Europe.

The workshop participants had been asked to prioritize the most important pathways. Since the causal diagram was intended for asthma/allergies and respiratory health, many of the experts said this influenced their rating (i.e. some had given heat a lower ranking than they may have without this focus on the respiratory system). Other experts, however, stressed that increased exposure to heat is the effect that is most likely to occur, and that extreme heat is an important cause of mortality in the elderly, particularly in people with COPD and some other diseases.

When discussing high priority mitigation and prevention of health impacts, the workshop participants identified that mitigation and adaptation strategies are sometimes in conflict. For example air conditioning may prevent heat related mortality, but may increase CO₂ and particle emissions from power plants. On the other hand sometimes adaptation strategies can double as a mitigation strategy. For example measures to increase active transport reduce traffic emissions also result in reduced health effects due to reduced emissions and ozone formation. The experts emphasised that policy making should take such interrelations into account.

Discussion

The study perspective was European, which may mean that some global effects of climate change were not considered. The participating experts were mainly from the field of environmental and respiratory research, hence the focus was on asthma/allergies and respiratory endpoints. This was in one respect a limitation, but according to the literature the effects of heat waves, ozone and particles, pollen, flooded buildings etcetera, are strongest

on respiratory morbidity and mortality, at least in relative terms. This means that experts in this field can be expected to contribute to the discussions on effects of climate change.

There could possibly have been a selection bias from the online evaluation to the follow-up workshop. During the workshop discussion it seemed that, in general, prioritizing causal elements in the case of climate change induced health risks was not easy. One of the reasons for this was that several of these elements are interrelated, and moreover characterized by huge complexity. Another reason was that experts felt somewhat biased by their own expertise, and were sometimes tempted to attribute higher priority to issues within their own expertise or research interest. However, after the follow-up workshop the answers from the first questionnaire were studied by both the workshop panel and the rest of the respondents, showing no striking differences in the answers between these two groups.

Restricting the focus on how respiratory diseases are expected to be affected by climate change may have led some experts to place less emphasis on the effects of heat waves than they may have otherwise done. Among the experts that later participated at the follow-up workshop however, the highest ranking was given to extreme heat (2.89), this is in agreement with research and the IPCC who predict with high certainty, an increase in heat waves.

During the workshop discussions it became clear that all participating experts found the current scientific evidence on health effects from climate change sufficient to take policy actions, even though there still are a lot of unknowns. Despite a high confidence rating that decisive new knowledge will be produced within the next five years, there was much less confidence that decisive policy actions will become possible within the same time frame.

Conclusions

A group of experts in environmental and respiratory medicine identify clear health risks associated with climate change. Direct health effects of more severe heat waves are an obvious threat. Increasing ozone levels are also seen as a likely health problem. While the researchers do not regard themselves as experts in all related topic areas, they concur that they provide opinion in their role as an expert in public health or as a researcher. A common perception is that there is already a basis for action and prevention, but less confidence that the associated adaptation and mitigation policies will have an evidence base within the same timeframe.

Additional material

Additional file 1: Experts assessing the causal diagram List of experts that have been assessing the causal diagram on asthma and allergies

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Authors' contributions

All authors planned this work. MKvK, MJK, AB, AY, BF and LB designed the causal model questionnaire. BF, LB and AY evaluated the questionnaire results. BF, LB and HK arranged the follow up workshop. BF wrote the manuscript. HK and LB made the first revision. All authors approved the final version.

Competing interests

No competing interests are reported.

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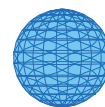
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Attachment 3

Merlo DF, Filiberti R, Kobernus MJ, **Bartonova** A, Gamulin M, Ferencic Z, Dusinska M, Fucic A: Cancer risk and the complexity of the interactions between environmental and host factors: HENVINET interactive diagrams as simple tools for exploring and understanding the scientific evidence. *Environmental Health* 2012, 11(Suppl 1):S9 (28 June 2012)



METHODOLOGY

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Cancer risk and the complexity of the interactions between environmental and host factors: HENVINET interactive diagrams as simple tools for exploring and understanding the scientific evidence

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Abstract

Background: Development of graphical/visual presentations of cancer etiology caused by environmental stressors is a process that requires combining the complex biological interactions between xenobiotics in living and occupational environment with genes (gene-environment interaction) and genomic and non-genomic based disease specific mechanisms in living organisms. Traditionally, presentation of causal relationships includes the statistical association between exposure to one xenobiotic and the disease corrected for the effect of potential confounders.

Methods: Within the FP6 project HENVINET, we aimed at considering together all known agents and mechanisms involved in development of selected cancer types. Selection of cancer types for causal diagrams was based on the corpus of available data and reported relative risk (RR). In constructing causal diagrams the complexity of the interactions between xenobiotics was considered a priority in the interpretation of cancer risk. Additionally, gene-environment interactions were incorporated such as polymorphisms in genes for repair and for phase I and II enzymes involved in metabolism of xenobiotics and their elimination. Information on possible age or gender susceptibility is also included. Diagrams are user friendly thanks to multistep access to information packages and the possibility of referring to related literature and a glossary of terms. Diagrams cover both chemical and physical agents (ionizing and non-ionizing radiation) and provide basic information on the strength of the association between type of exposure and cancer risk reported by human studies and supported by mechanistic studies. Causal diagrams developed within HENVINET project represent a valuable source of information for professionals working in the field of environmental health and epidemiology, and as educational material for students.

Introduction: Cancer risk results from a complex interaction of environmental exposures with inherited gene polymorphisms, genetic burden collected during development and non genomic capacity of response to environmental insults. In order to adopt effective preventive measures and the associated regulatory actions, a comprehensive investigation of cancer etiology is crucial. Variations and fluctuations of cancer incidence in human populations do not necessarily reflect environmental pollution policies or population distribution of polymorphisms

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of genes known to be associated with increased cancer risk. Tools which may be used in such a comprehensive research, including molecular biology applied to field studies, require a methodological shift from the reductionism that has been used until recently as a basic axiom in interpretation of data. The complexity of the interactions between cells, genes and the environment, i.e. the resonance of the living matter with the environment, can be synthesized by systems biology. Within the HENVINET project such philosophy was followed in order to develop interactive causal diagrams for the investigation of cancers with possible etiology in environmental exposure.

Results: Causal diagrams represent integrated knowledge and seed tool for their future development and development of similar diagrams for other environmentally related diseases such as asthma or sterility. In this paper development and application of causal diagrams for cancer are presented and discussed.

Background

Cancer incidence and mortality

The estimated global burden of cancer amounts to some 12,667,400 new cancer cases worldwide in 2008 [1]. Colorectal, lung, breast, prostate, stomach and liver cancer are the most frequently diagnosed cancers. Stomach, liver, oesophageal and cervical cancers incidence rates are higher in populations living in less developed regions (Figure 1) than in more developed regions [1]. These data show the significant role played by socioeconomic status in cancer risk.

Trends in cancer incidence between mid 1990s and early 2000 decreased in Northern and Western European countries with the exception of obesity related cancers. Although a decreased incidence and mortality was detected for tobacco-related cancers (i.e., cancers of the

lung, larynx, and oesophagus) for males in Northern, Western and Southern Europe, increased rates were observed among females nearly everywhere in Europe and for both sexes in central European regions. The estimated annual percentage change for lung cancer in men ranged between -0.4% and -4% while among women the observed increase ranged between 0.6% and 5% [2]. During the decade from 1997 to 2006, cancer incidence decreased in the United States by an average of 1 percent per year and overall cancer mortality declined also (Figure 2) [3]. The decline of death rates was bigger for men than women. Lung, prostate and colorectal cancers in men and breast and colorectal cancers in women, the most frequently occurring cancers, were responsible for the observed decline. Despite the observed reduction, increased incidence rates were found among men for

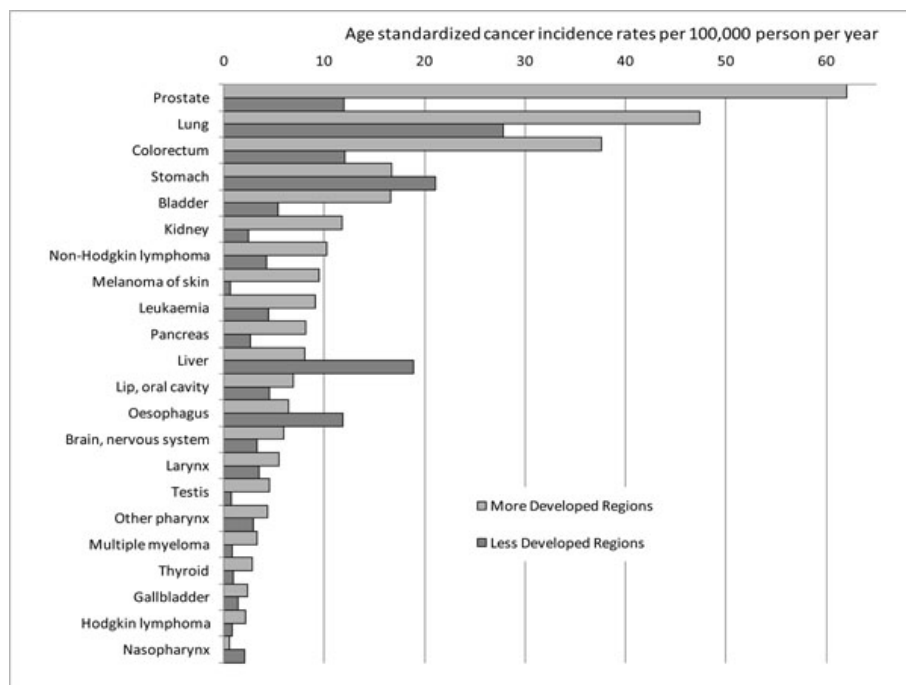
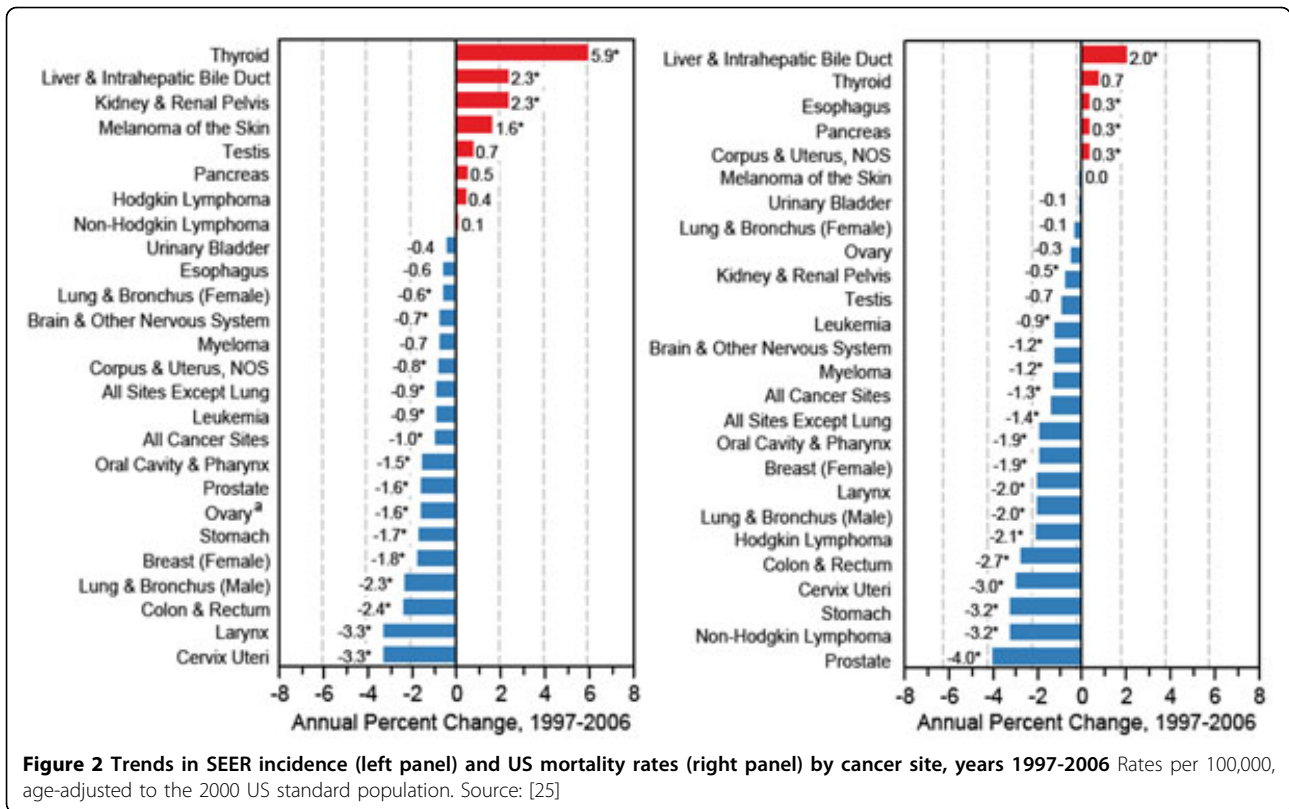
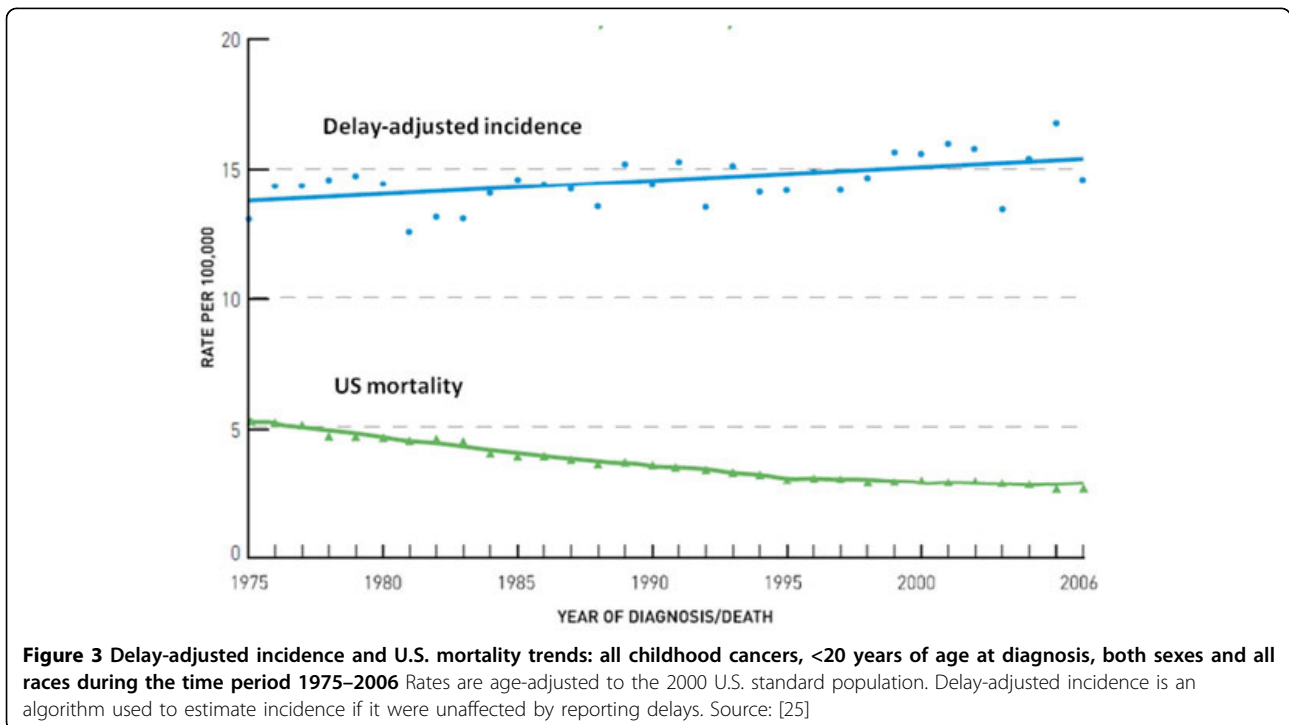


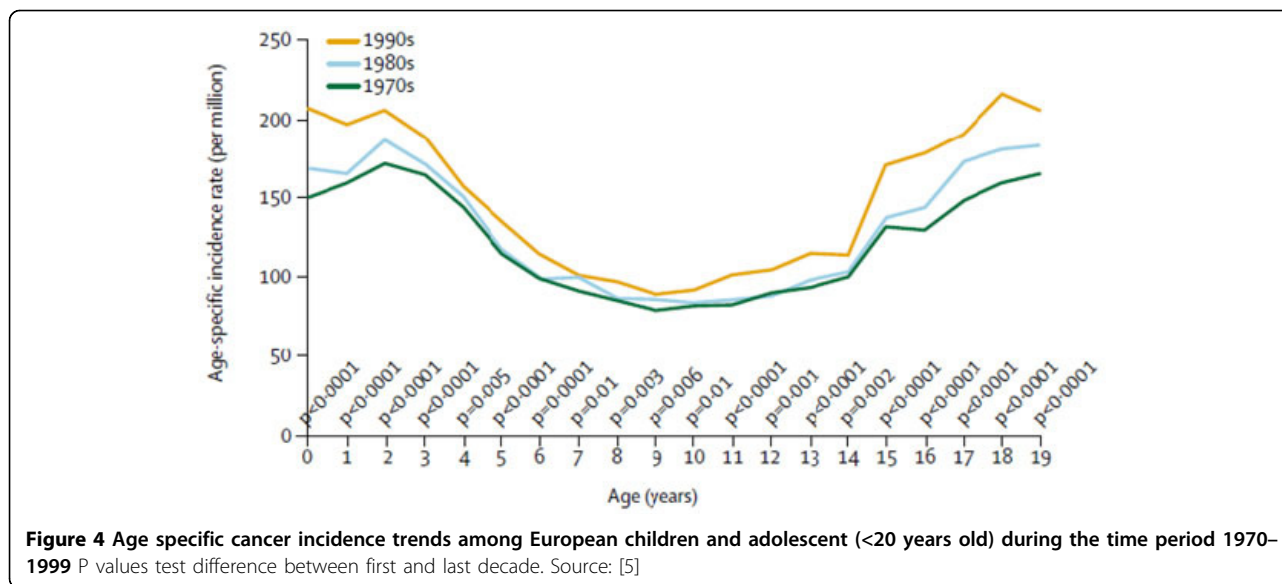
Figure 1 Cancer incidence rates in males (upper panel) and females (lower panel) in more and less developed regions worldwide
Source: [1]



cancers of the liver, kidney and oesophagus, and for melanoma and myeloma, and, among women, for cancers of the lung, thyroid, pancreas, brain and nervous system, bladder and kidney, and for melanoma. Rates of

leukaemia and non-Hodgkin's lymphoma increased in both sexes. Some 1,479,350 cases are expected to be diagnosed in 2009, excluding non invasive cancer (carcinoma in situ) of any site except urinary bladder, and basal and





squamous cell skin cancers (the latter are expected to be about 1 million cases). The probability of developing an invasive cancer for a male US citizen is 1.42 (1 in 70) from birth to the age of 39 and 43.89 (1 in 2) from birth to death. For a female US citizen is 2.07 (1 in 48) from birth to the age of 39 and 37.35 (1 in 3) from birth to death [4]. Cancer incidence increased during the same period among US children (Figure 3) [3] and amongst European children and adolescents during the period 1970–99 (Figure 4) [5]. For most cancer types incidence increased by 1.0% per year among European children (< 15 years old) and by 1.5% in adolescents (15–19 years).

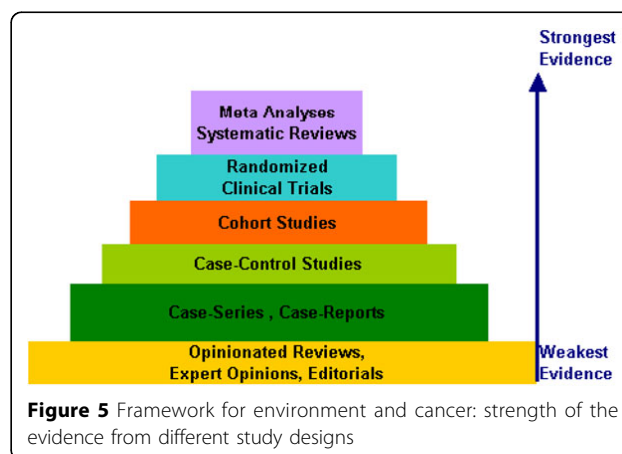
Environmental exposure complexity and need for action

Environmental exposures may modulate a variety of biologic processes such as gene expression and gene repair mechanisms, hormone production/function, and inflammation [6,7].

Moreover, the delayed adverse health effects of exposures occurring during critical windows of vulnerability (e.g., early life, including the prenatal period and puberty) remain largely unknown. One well known exception is in utero exposure to diethylstilbestrol (DES) which increases the risk of benign and malignant pathology in the third generation [8]. Other agents such as ambient air PAHs and PM2.5 have been shown to influence maturation of the immune system during gestation via shifts in cord blood lymphocytes distributions [9,10]. Whether these shifts will affect cancer risk (or other adverse health outcomes) later in life, need to be proven [11].

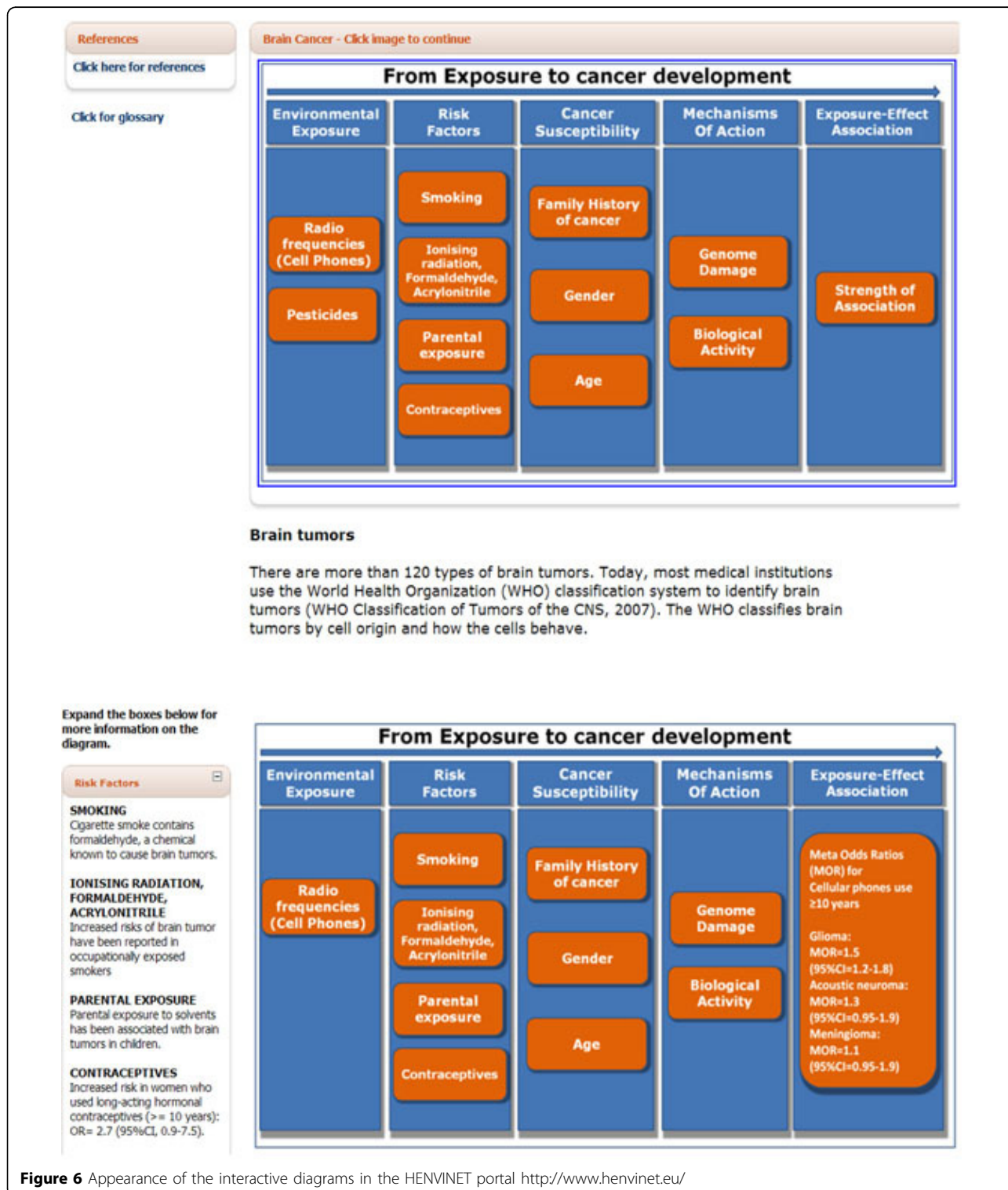
Providing undisputable evidence that environmental exposure to complex mixtures of pollutants results in increased cancer risk is challenging for human epidemiologic and experimental studies conducted in vitro and in

laboratory animals. Environmental epidemiology, despite its observational nature, is the scientific discipline attempting to make conclusions on disease etiology in human beings. Experimental studies, conducted under controlled conditions, provide “proof of action” of a given exposure in selected biological (e.g., cell culture) or animal models. The two types of scientific evidence are combined together by the scientific community to classify exposures as carcinogenic, probably/possibly or non carcinogenic to humans. Based on the evidence of carcinogenicity, governments and regulatory agencies should establish and implement effective regulation of environmental exposure. Current regulatory approach is of a reactive type (i.e., human harm must be proven before any action is taken). However, some 80,000 chemicals are in use today and 1,000-2,000 new chemicals are synthesized and enter the environment each year, a figure that is impressive especially if one considers that such chemicals may interact with each others, with



physical agents, viruses, and thousands of natural compounds [12]. Cancer incidence reflects lifetime exposure to man-made and naturally occurring carcinogens that are present in the living environment. Most of the evidence of the role played by environmental carcinogens has

accumulated during the last century [13]. Epidemiologic and animal studies significantly contributed to the discovery of the major causes of cancer and nowadays it is accepted that cancer risk is connected to the living environment through complex interactions between exposures



and host factors, the former playing a major role in cancer development. Host factors, such as single-gene inherited cancer syndrome and the polymorphic distribution of genes for cellular detoxification and DNA-repair processes are known to account for a small proportion of the cancer burden in human populations. A large proportion of cancers are believed to be the consequence of multiple exposures that occur over years or persist for a lifetime [14]. There is also evidence that cancer susceptibility resulting from environmental exposures may be inherited by a child when a carcinogen causes germ cell genetic damage in exposed parents [15,16].

Despite the fact that our knowledge of the biologic mechanisms underlying cancer development has been extensively improved, the mechanisms by which environmental contaminants contribute to cancer risk, and particularly how they interact, remain largely under investigated in humans [14].

Is it waiting for a “proof of harm” the right approach to protect human health by reducing exposure? The USA President’s Cancer Panel [14] assessed the state of environmental research on cancer, policy and programs receiving testimony from 45 invited experts from academia, government, industry, the environmental and cancer communities, and the public. The Panel made recommendations for policy, research, program, industry, and other actions aimed at minimizing the impact of environmental factors on cancer. A precautionary oriented approach instead of the reactionary approach currently used is recommended by the President’s Cancer Panel as the cornerstone of a new cancer prevention strategy based on primary prevention. Such a recommended approach should “shift the burden of proving safety to manufacturers prior to new chemical approval, in mandatory post-market studies for new and existing agents, and in renewal applications for chemical approval”. The European Commission has anticipated, to some extent, the US by adopting in 2007 a precautionary approach to chemical regulation. The Registration, Evaluation, Authorization, and Restriction of Chemical Substances (REACH)[17] is a major reform that requires industry to take a main role in managing risks from chemicals by providing safety information on its products. The final goal of REACH is to protect human health as well as the environment through better and earlier recognition of intrinsic properties of chemicals.

Methods

The HENVINET approach to environmental cancers

The Health and Environment Network (HENVINET) was funded by the Commission of the European Communities within the 6th Framework Programme on Research, Technological Development and Demonstration. The main objective of HENVINET was that of establishing a long-term co-operation between

researchers, policy makers and stakeholders in the area of environment and health research and assessment. To protect the health of populations and individuals, environmental and health policies need to integrate environmental and health knowledge: HENVINET is meant to support such informed policy making process. Based on the four priority health diseases of the European Environment and Health Action Plan 2004-2010 (EHAP)[18] (i.e., asthma and allergies, cancer, neurodevelopmental disorders and endocrine disrupting effects), HENVINET has reviewed, exploited and disseminated knowledge on environmental health issues [18]. EHAP is aimed at improving the health of European citizens, a goal requiring knowing exactly what impact environmental damage has on human health. EHAP was designed to provide the European Union (EU) with reliable information on that impact and to step up cooperation between stakeholders in the environment, health and research fields.

The identification of environmental causes of cancer is among the major thrusts of cancer and carcinogenesis research. The systematic review of the epidemiologic evidence available has been used as a tool for the evaluation of the exposure-effect association (causal association) in human studies. Scientific evidence comes from different epidemiologic study designs (Figure 6), of which some are considered to provide a stronger level of evidence than others. Based on their inherent characteristics, their

Table 1 List of cancers and environmental exposure considered within HENVINET

Cancer types	Environmental exposures
Breast Cancer	Alcohol
	DDT and DDE
	PCB
	PAHs
Lung cancer and Malignant Mesothelioma	Arsenic
	Asbestos
	PM2.5
Brain Tumors	Radon
	Radiofrequency
Colorectal Cancer	Pesticides
	Meat consumption
	Fruits and vegetables consumption
	Intake of calcium and Vitamin D
Leukemia	Intake of folic acid
	Low frequency electromagnetic fields
	Pesticides
Melanoma	Low level ionizing radiation
	UV light, artificial light
	Ionizing radiation
	Cosmetics (including sun screen)
	Photosensitizing drugs
	Exogenous hormones

hierarchy is graphically summarized in a pyramid (Figure 5). The pyramid depicts the strength of the evidence for commonly used designs. Such hierarchy should be taken into account in evaluating the published evidence. Therefore, HENVINET reviews on environmental exposure and cancer risk in human populations prioritized the available systematic reviews (i.e., meta-analysis). The elective epidemiologic measure of associations was the meta-relative risk or its estimates (meta-odds ratio, meta-rate ratios, etc.). In addition, the relevant biological aspects /mechanisms underlying cancer development reported by experimental studies were considered as proof of action supporting the epidemiological evidence. All this information was retrieved, scrutinized and summarized in the form of interactive cause-effect diagrams showing, in a simple fashion, the associations between complex environmental exposure and cancer development considered within the HENVINET project.

Results

HENVINET interactive cause-effect diagrams

Cancer is not a single disease and cancer risk results from exposure to complex environmental settings (i.e., different exposures) jointly contributing to cancer development. In addition to the environmental risk factors, individual and genetic based susceptibility factors, known as host factors, are playing a role in the process of human carcinogenesis, acting as effect modifiers, which need to be included in the causal framework. The development of interactive diagrams is challenged by the need to provide a summary of the evidences of the exposure-effect associations while accounting for the complexity of the biological and statistical relationships detected along the path leading to cancer development and diagnosis. Environmental exposure (s), known risk factors (e.g., smoking and drinking habits, age, gender), including individual susceptibility (e.g., genetic polymorphisms, family history of cancer) known

What is your level of confidence in the current scientists' ability to predict the impact of environmental exposure to radiofrequency from using cell phones and the risk of brain tumours?*

Very High High Medium Low Very Low

What is your level of confidence in scientists' ability to predict the magnitude of the effect of in utero and/or early childhood exposure to radiofrequency and cancer risk?*

Very High High Medium Low Very Low

Given the available scientific evidence, would you be in favour or against preventive measures (precautionary principle)?*

In Favor Against

If you have any specific policy actions in mind, please specify them here:

When questions ask for your confidence level, please use these guidelines:

Very high - At least 9 in 10 chance of being correct.
High - At least 7 in 10 chance of being correct.
Medium - At least 5 in 10 chance of being correct.
Low - At least 3 in 10 chance of being correct.
Very Low - Less than 2 in 10 chance of being correct.

Figure 7 Questionnaire items used for the evaluation of knowledge (questions for radiofrequency and brain cancer)

to be of relevance in terms of differential risk were reported in the diagrams to provide an overview of the continuum from exposure to cancer development. Diagrams included also the evidence from experimental studies when providing a “proof of action” of the environmental exposures considered (i.e., mechanisms of action) and the estimated epidemiologic measure of effect (e.g., meta-relative risk estimates, relative risk, odds ratio). The cancer types and environmental exposures considered within HENVINET are reported in Table 1.

Glossary and references

A glossary and selected references are made available to users to ensure fluent browsing and transparency. The glossary is an important tool aimed at assuring a consistent terminology across the exposure-cancer diagrams (e.g., meaning of reported biological effects, biological activity). Diagrams were specifically developed to allow users to actively explore the depicted exposure-effect interactions within the continuum between cancer

initiation and detection. Their appearance is shown in Figure 6 as an example for exposure to radiofrequency and its association with brain tumours, one the hottest and most controversial topic in environmental health. The reader, after selecting a specific environmental exposure within a given cancer type, access a diagram showing the known risk factors, the evidence of susceptibility available, the reported mechanisms of action for a given environmental exposure/agent, and the quantitative measure of the exposure-effect association estimated by recent systematic review. The glossary and the reference list can be both accessed through a link placed on the left side of the interactive diagrams accessible on the HENVINET portal (Figure 6).

Evaluation of knowledge: the online questionnaires

For each interactive diagram a questionnaire including a limited set of items (questionnaire) was prepared to allow expert reviewers and users to express their level of confidence on the current scientific evidence and the

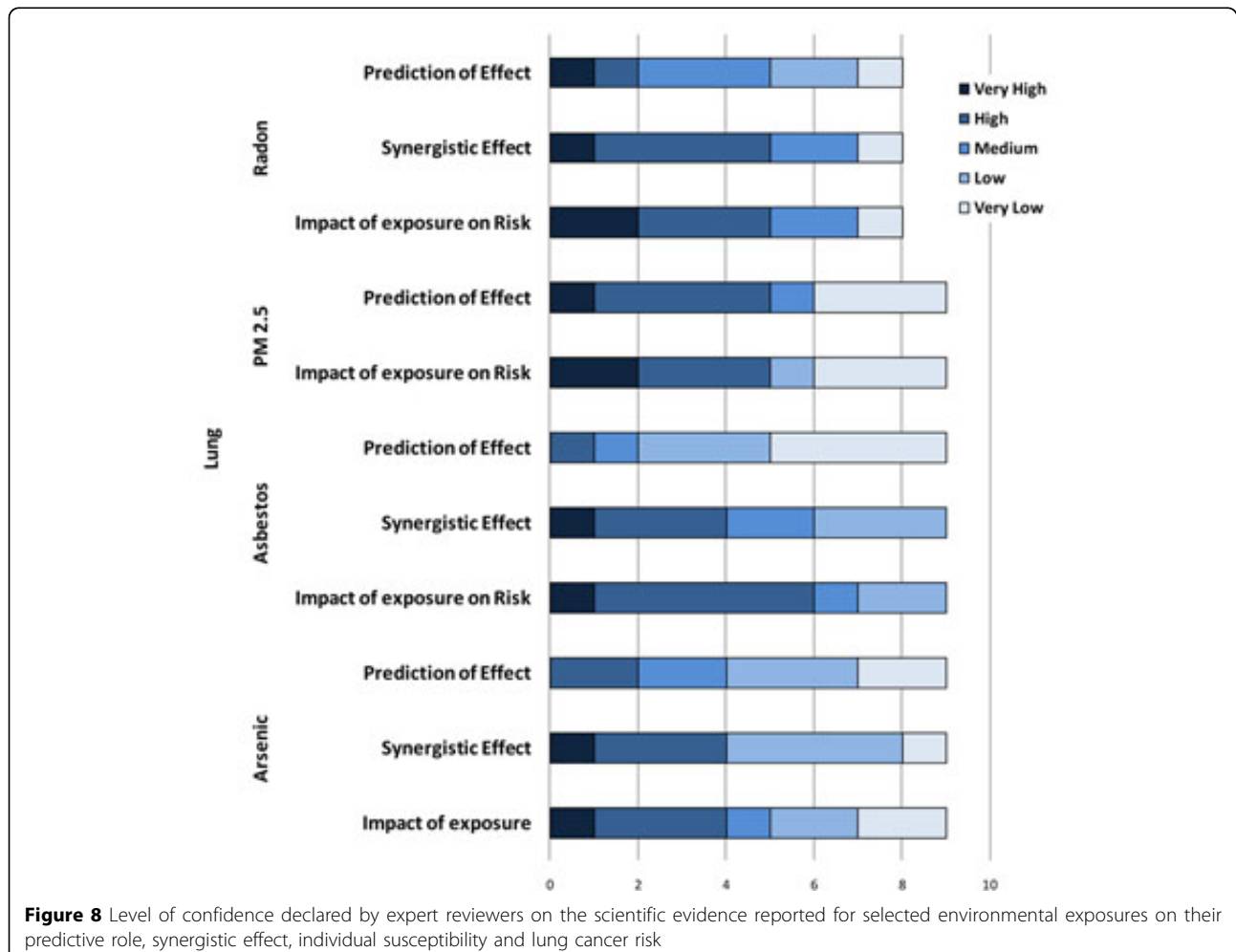


Figure 8 Level of confidence declared by expert reviewers on the scientific evidence reported for selected environmental exposures on their predictive role, synergistic effect, individual susceptibility and lung cancer risk

understanding of the various aspects of the exposure-cancer diagram examined. 13 expert reviewers included researchers from the following fields: environmental and occupational epidemiology, cancer epidemiology, risk assessment, exposure assessment, molecular/biomarkers epidemiology, medical statistics, and atmospheric pollution and health effects. Nine of them accepted to review the interactive diagrams and filled in the questionnaire.

The structure of the questionnaires has been standardized to provide similar questions across the paths of the exposure-adverse effects considered within the project (i.e., asthma and allergies, cancer, neurodevelopmental disorders, and endocrine disruptors). For each question included in the questionnaires the level of confidence was scored by expert reviewers as very high, high, medium, low and very low. An example of the questions included in

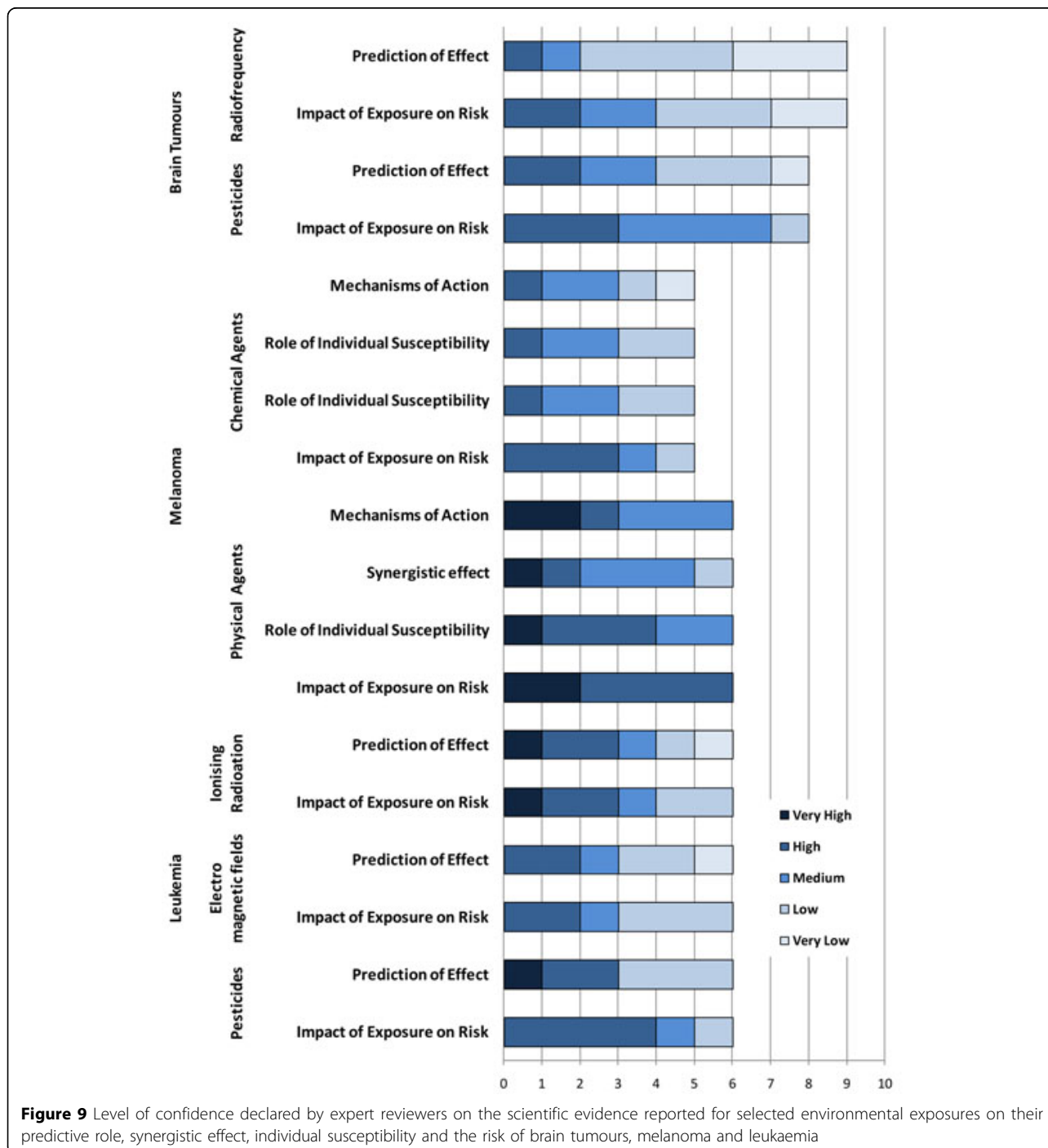


Figure 9 Level of confidence declared by expert reviewers on the scientific evidence reported for selected environmental exposures on their predictive role, synergistic effect, individual susceptibility and the risk of brain tumours, melanoma and leukaemia

the questionnaire for the association between exposure to radiofrequency and brain tumours is shown in Figure 7. The causal diagrams were made accessible to experts selected according to their experience in environmental health and/or oncology. This process is identified in the HENVINET portal as the evaluation of knowledge. Review of diagrams performed by experts was also an exercise for testing of the questionnaire which is meant to be used by readers with different background.

Causal diagram evaluation

HENVINET cancer causal diagrams were actually a new experience for experts as they offer a simultaneous

overview of all xenobiotics described in the etiology of selected site specific cancers.

Based on the assumption that expert reviewers should be able to come to exact agreement about how to apply the possible five levels of scoring to each questions, consensus indexes of interpreter reliability were computed as estimates of how experts shared a common interpretation of the construct. The consensus index ranges between 1 (full agreement) and 0 (no agreement). An unexpectedly low consensus index was detected for the questions related to the role of exposure to environmental level of arsenic (0.43), radon (0.54), and PM2.5 (0.27) on lung cancer risk and for polycyclic aromatic hydrocarbons (PAH) on breast

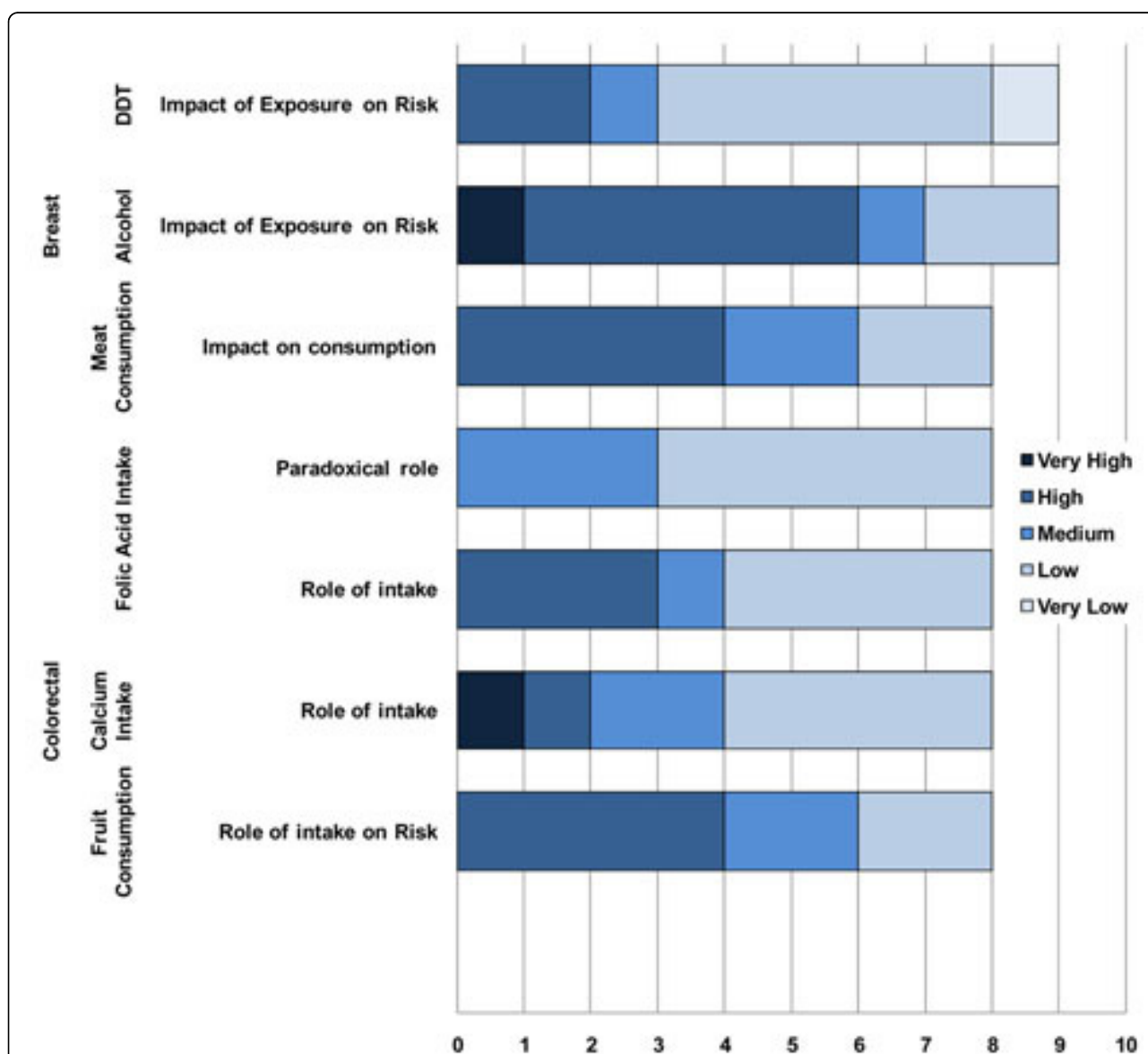


Figure 10 Level of confidence declared by expert reviewers on the scientific evidence reported for selected environmental exposures on their predictive role, synergistic effect, individual susceptibility and the risk of breast and colorectal cancers.

cancer (0.51) (Figure 8a-c). While for arsenic in drinking water and airborne PM_{2.5} the causal association with lung cancer is still subjects of controversy, there is clear evidence of a link between indoor radon and lung cancer risk. Indeed, residential radon is recognized as an important cause of lung cancer in the general population with an excess risk of 10% per 100 Bq m³ [19-24]. The generally low agreement between expert reviewers raises the need for better knowledge communication and inclusion of other media for knowledge dissemination. The highest consensus was reached for questions regarding melanoma, especially as far as the role played by physical agents (0.83), pesticides and leukaemia (0.73) and brain tumours (0.77). The experts have a high to very high level of confidence in the scientists' abilities to predict the impact of exposure and individual susceptibilities to physical agents (0.77) on melanoma cancer risk. The results of the evaluations are graphically presented in Figures 8-10.

The position of the expert reviewers on the scientific evidence based justification for precautionary policies aimed at containing environmental exposures to electromagnetic and radiofrequency fields and pesticides reported to be associated with brain tumours and leukaemia is shown in Figure 11. All reviewers agreed on the need for precautionary policies for pesticides and ionizing radiation while the consensus on the need for precautionary policies was lower for radiofrequencies and power lines electromagnetic fields.

Discrepancy between the state of the art (e.g. existing knowledge) and answers of experts shows that knowledge is not equally communicated to different professional areas, policy makers and the general public.

Discussion and conclusions

How to develop knowledge communication and self-learning interaction between science and policymaking system?

The complexity of the causal relations between exposure to environmental agents, their interactions, as well as the role played by host factors such as age at exposure (e.g., in utero exposure), gender, and polymorphisms of genes involved in the activation-detoxification of xenobiotics, cell cycle, in DNA repair and apoptosis, is not taken into account in current legislation. Environmental health regulatory policies should adopt a new approach which includes the knowledge of complexity. HENVINET interactive causal diagrams are an opportunity for collaboration between the scientific and regulatory communities and the society with its variety of populations, cultures, and environmental differences. The analysis of causal diagrams and the development of specific web sites which enable such an opportunity for an interactive dialogue may represent a starting point for accomplishing effective legislation aimed at protecting health and the environment. Policymakers have to learn the potential of present knowledge and timely deal with the scientific evidence generated by human and laboratory studies that investigate early health effects and or molecular markers that occur and can be measured along the pathways from exposure to disease manifestation. Within this modern and highly technological research framework a precautionary approach can be applied to environment and health issues (not just as an alternative to cost-benefit analysis), with the aim of improving future legislation. The recognition of environmental threats and the prediction of possible associated

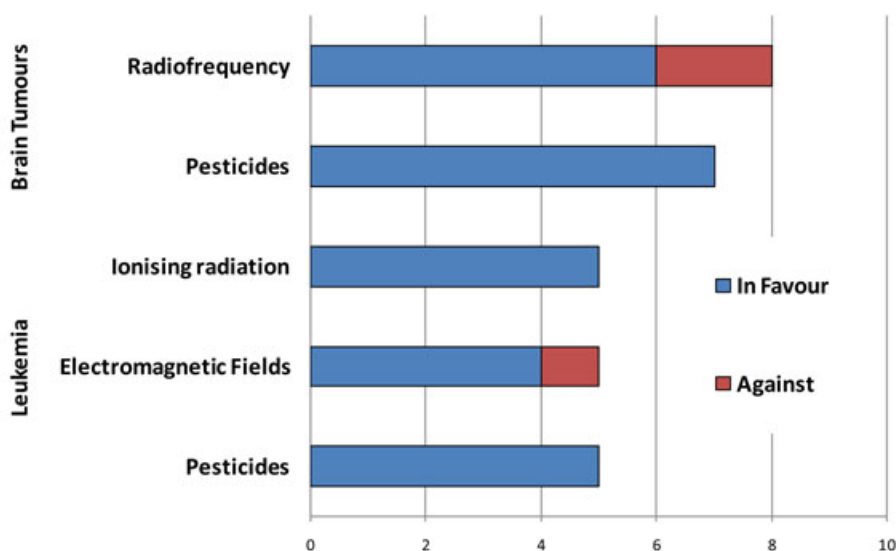


Figure 11 Expert reviewers' position based on the scientific evidence available concerning the need for precautionary policies for selected environmental exposures

cancer risks will allow putting scientific facts directly in a regulatory perspective, raise public confidence in science and administration.

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Authors' contributions

All authors contributed equally to the conduct of the research and the writing of the manuscript. DFM has leaded the work and drafted the manuscript. AF was co-responsible for all aspects of the study. RF, MG and ZF participated in the design, implementation and interpretation. MD participated in the design and interpretation. MK has been responsible for the web application and data management. AB coordinated the project and contributed to the concept and interpretation of the results. All authors have read and approved the manuscript.

Competing interests

None of the authors have conflict of interest to declare.

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Attachment 4

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Respiratory Disease in Relation to Outdoor Air Pollution in Kanpur, India

Hai-Ying Liu, PhD; Alena Bartonova, RNDr; Martin Schindler, PhD; Mukesh Sharma, PhD; Sailesh N. Behera, PhD; Kamlesh Katiyar, PhD; Onkar Dikshit, PhD

ABSTRACT. This paper examines the effect of outdoor air pollution on respiratory disease in Kanpur, India, based on data from 2006. Exposure to air pollution is represented by annual emissions of sulfur dioxide (SO₂), particulate matter (PM), and nitrogen oxides (NO_x) from 11 source categories, established as a geographic information system (GIS)-based emission inventory in 2 km × 2 km grid. Respiratory disease is represented by number of patients who visited specialist pulmonary hospital with symptoms of respiratory disease. The results showed that (1) the main sources of air pollution are industries, domestic fuel burning, and vehicles; (2) the emissions of PM per grid are strongly correlated to the emissions of SO₂ and NO_x; and (3) there is a strong correlation between visits to a hospital due to respiratory disease and emission strength in the area of residence. These results clearly indicate that appropriate health and environmental monitoring, actions to reduce emissions to air, and further studies that would allow assessing the development in health status are necessary.

[Supplementary materials are available for this article. Go to the publisher's online edition of *Archives of Environmental & Occupational Health* for material on emission of SO₂, PM, NO_x from various sources, and total number of inhabitants, total number of patients in grid squares covering the Kanpur city.]

KEYWORDS: emission, outdoor air pollution, patients, respiratory disease

It is well known that air pollution causes respiratory and cardiovascular diseases.¹⁻³ Economic development, urbanization, energy consumption, transportation, and rapid population growth are major driving forces of air pollution in large cities, especially in megacities.⁴ Air pollution levels in developed countries have been decreasing dramatically in recent decades. However, in other countries, air pollution levels are still relatively high, although the levels have been gradually decreasing or have remained stable despite rapid economic development.^{4,5} In recent years, several hundred epidemiological studies, time-series studies in particular, have been conducted in developed countries, on short- and long-term effects of air pollution on human health covering different age groups, including children and young and old adults.⁶⁻⁸ Research has shown that long-term exposure to

air pollutants increases the risk of respiratory illnesses such as allergies, asthma, chronic obstructive pulmonary disease, and lung cancer.^{9,10} Children and elderly persons are particularly vulnerable to health effects of ozone (O₃), particulate matter (PM), and other airborne toxicants.^{11,12} Hospital admissions have been recognized as a more sensitive marker than mortality for assessment of the air pollution effects on human health.^{13,14} A literature review on outdoor air pollution and health in Asia identified over 400 studies of health effects of air pollution in 13 countries during the period 1980 to 2007.¹⁵ Over 80 time-series studies conducted in Asian cities also showed similar spectrum of adverse health effects from acute and chronic respiratory symptoms and changes in pulmonary function to increased mortality from cardiovascular or respiratory diseases or lung cancer, associated

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with exposure to PM, sulfur dioxide (SO₂), nitrogen dioxide (NO₂) and O₃, to those explored in Europe and North America.^{15–17}

Air pollution poses a global challenge, as adverse effects still exist even at relatively low air pollutant concentrations, and there may not be any safe or threshold pollution levels. The air pollution problem is more severe in Asian countries due to high pollution levels and high population densities.^{4,15–17} Important gaps still remain, as the studies do not necessarily cover enough variations in urban settlements, pollution levels, and economic conditions.¹⁵

Many of the Indian cities are highly polluted and available mortality and morbidity statistics indicate that respiratory infections and chronic conditions are widespread.^{18–24} However, there are very few Indian studies that link air pollution exposure to lung function deterioration, underlining the need for systematic studies.²¹

We carried out a pilot study to examine the correlation between outdoor air pollution (represented as annual emissions) and hospital visits due to respiratory disease in Kanpur (latitude 26°45' north and longitude 80°15' east; Figure 1), one of the most populous (4 million persons), industrialized, and polluted cities in India.^{18,22,25}

Pollution loads/emissions were estimated for SO₂, PM, and nitrogen oxides (NO_x), whereas respiratory diseases were estimated from total number of registered respiratory patients visits to the largest chest and tuberculosis hospital (Lala Lajpat Rai [LLR] Hospital) in Kanpur, Uttar Pradesh, India.^{22,26} This hospital receives patients from the whole district.

The broad objective of this study was to develop a methodology for air pollution health impact assessment, and to apply this approach in the city of Kanpur. The specific objective was to assess population-wide health effects of air pollution. This study lays a basis for further environmental health assessments, and provides rationale for improved air quality monitoring as well as mitigation measures.

METHODS

Data collection

Sampling Grids for Emission Assessment

The entire 28 km × 22 km area including the city was divided into 154 grids of equal size of 2 km × 2 km. Coordinates of the center point in each grid were recorded by the

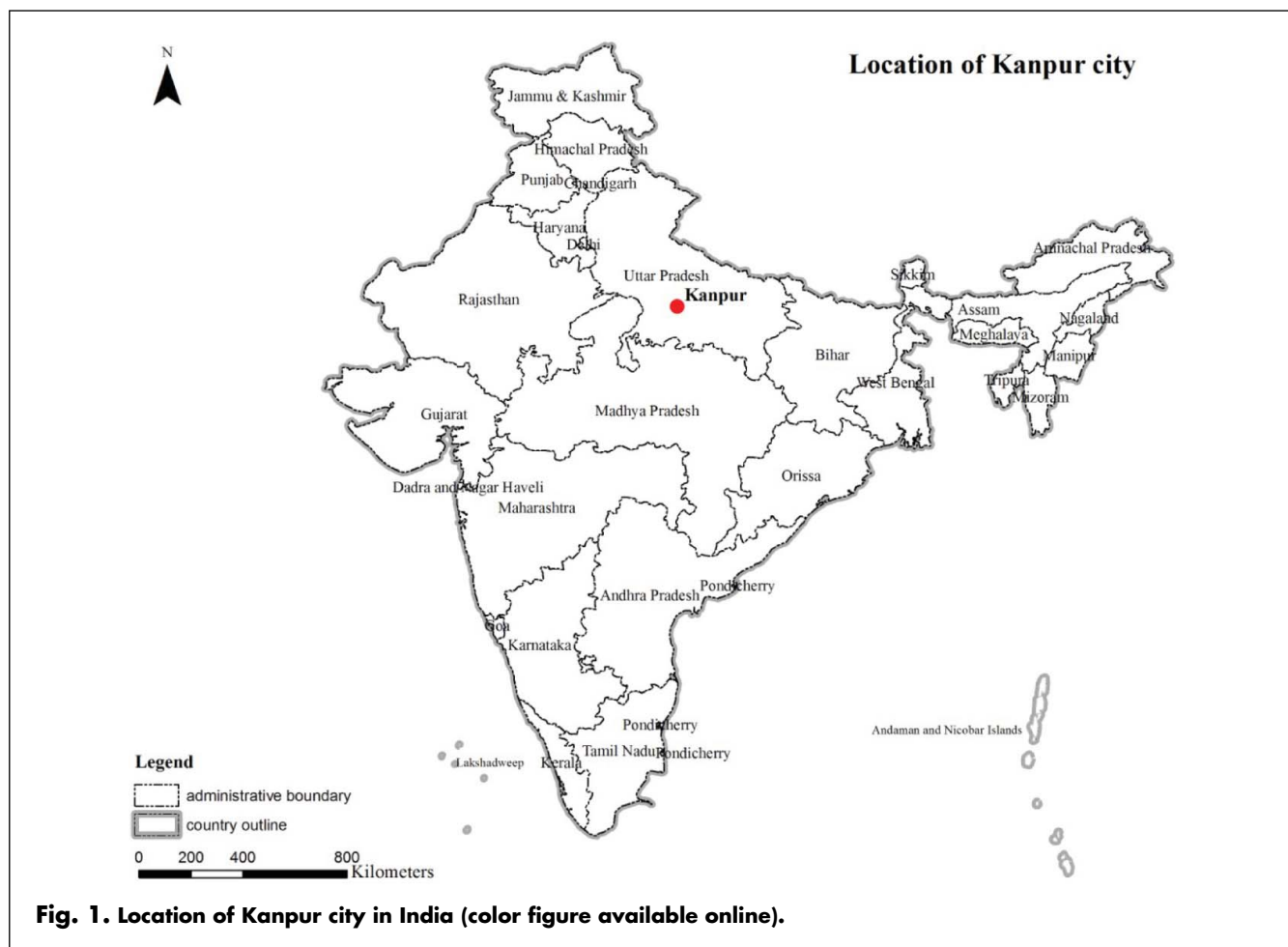


Fig. 1. Location of Kanpur city in India (color figure available online).

Table 1.—Overview of Grid Squares for Detailed Emission Survey

Center point number	Stations	Latitude	Longitude	Lands use types
1	Sidbi Centre	26°30'36"	80°13'48"	Institutional
2	Vikas Nagar	26°29'24"	80°17'24"	Residential
3	Dada Nagar	26°28'12"	80°20'24"	Commercial
4	Colonel Ganj	26°28'12"	80°20'24"	Commercial
5	Pared	26°27'00"	80°17'24"	Industrial
6	Ramadevi	26°26'24"	80°19'12"	Residential
7	Juhilal Colony	26°24'36"	80°23'24"	Residential

Global Positioning System (GPS) in Universal Transverse Mercator (UTM) system. The other recorded items include the grid number and land use type. Seven key grids inside the city (Table 1), having varied land use types, were studied in detail by conducting house to house surveys of each polluting activity in the grid (Figure 2).

Pollution Sources

Pollution sources taken into account in the emission inventory include vehicles, domestic fuel burning, garbage burning, restaurants, diesel generators sets, medical-waste incinerators, funeral pyre burning, industries with stack height lower than 25 m (area sources), industries with stack height

higher than 25 m (point sources), soil-road dust, construction and demolition recycling (Supplement Files 1–3). For point sources, the recorded items include the point sources number, grid number, industry name, production capacity (t/day), fuel consumption (t/day, fuel type), stack height (m), and latitude and longitude (Figure 2, Table 2).

Emissions as Surrogate Measure of Exposure

Each of the 154 grids was assigned a land use type based on the landscape map from the Central Pollution Control Board (CPCB), Delhi, India. Six land use types were identified (ie, agricultural, commercial, industrial, institutional, protected, and residential) in the entire city (Figure 3).

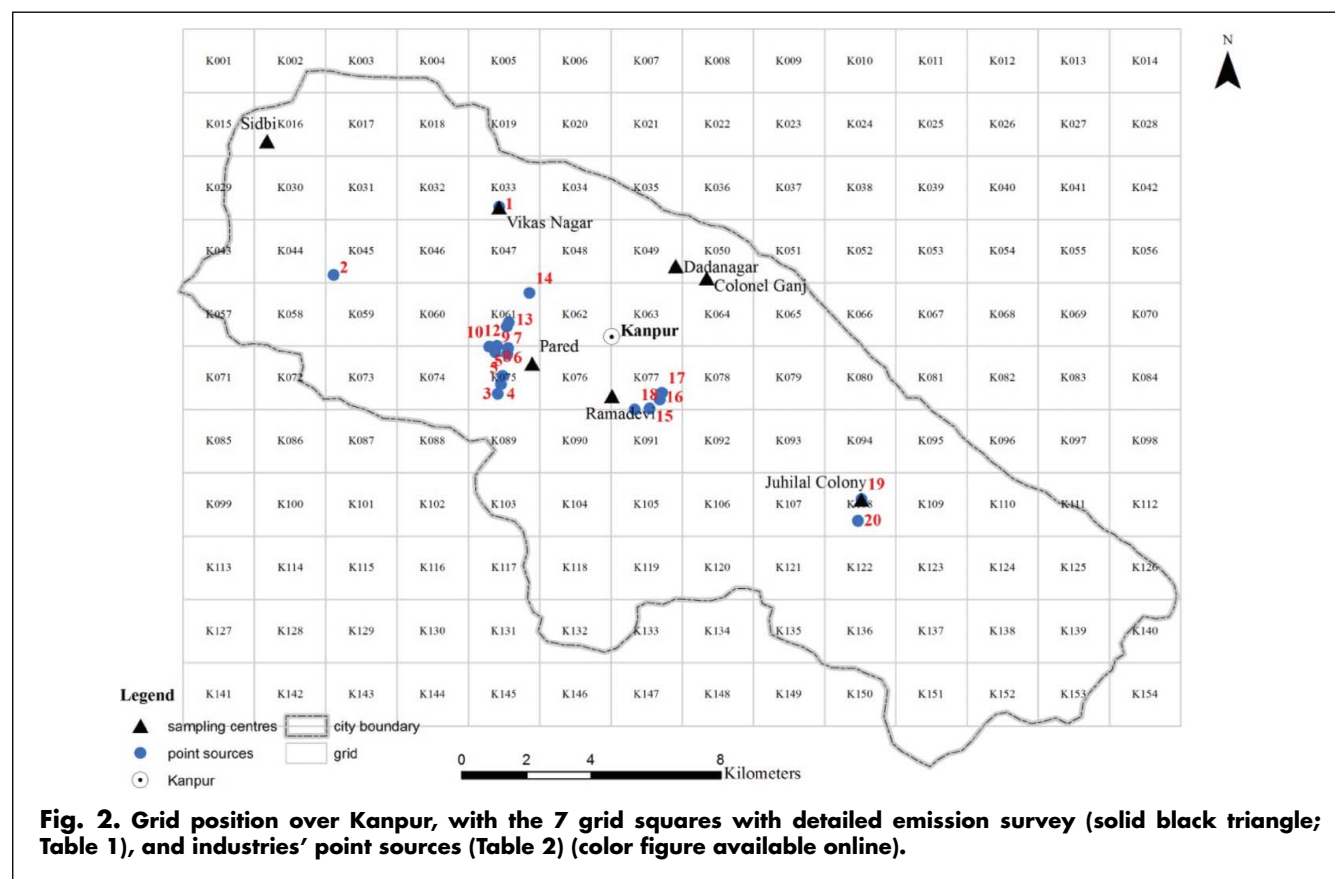
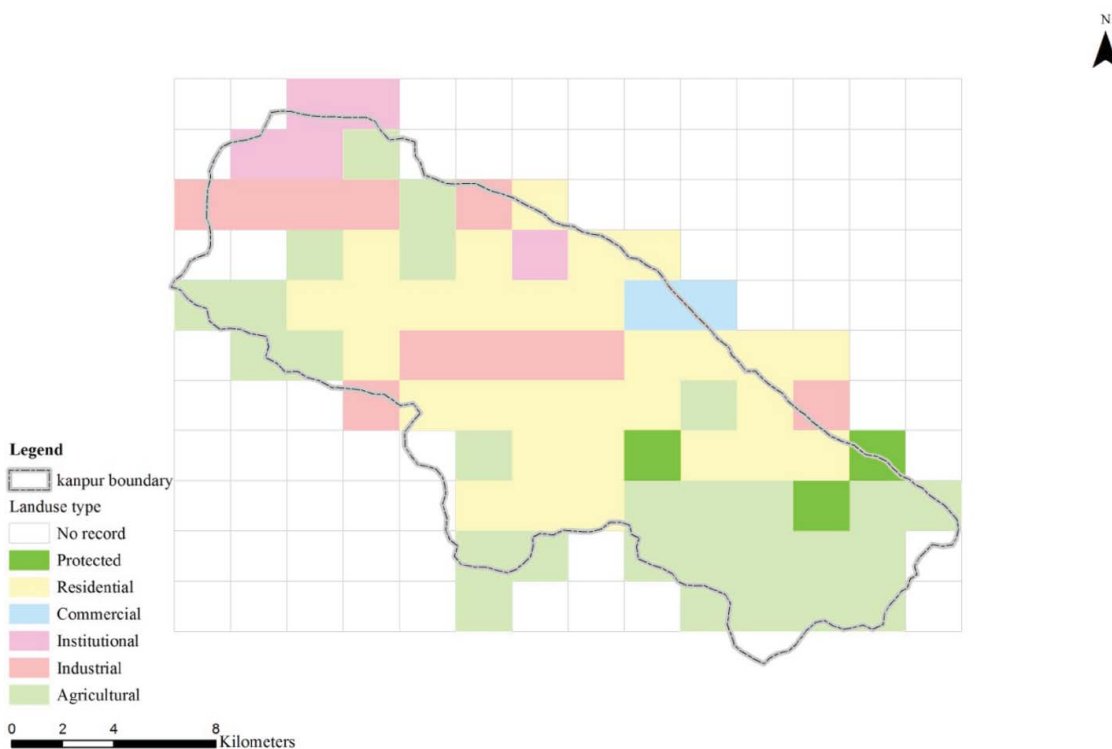


Table 2.—Overview of Industrial Point Sources

Point sources number	Grid number	Industries	Production capacity (t/day)	Fuel consumption (t/day, coal)	Stack height (m)	Latitude	Longitude
1	K033	Rice mill	48	0.64	30	26°29'40"	80°17'11"
2	K045	Thermal power plant	314	2,030	120	26°28'31"	80°14'26"
3	K075	Iron and steel industry	32	2.2	30	26°26'30"	80°17'10"
4	K075	Textile industry	7	700 L/day (diesel)	60	26°26'40"	80°17'13"
5	K075	Rice mill	150	2	35	26°26'48"	80°17'15"
6	K075	Iron and steel industry	20	20 L/day (diesel) and 18 t/day (coal)	25	26°27'11"	80°17'20"
7	K075	Iron and steel industry	50	4.5	30	26°27'12"	80°17'20"
8	K061–K075	Iron and steel industry	28	3	25	26°27'19"	80°17'10"
9	K061–K075	Oil industry	2	2	25	26°27'13"	80°17'8"
10	K061–K075	Textile industry	5	1	55	26°27'18"	80°17'2"
11	K075	Rice mill	25	0.375	30	26°27'16"	80°17'20"
12	K061	Textile industry	6	1	60	26°27'39"	80°17'19"
13	K061	Leather industry	5	960 L/day (diesel)	35	26°27'43"	80°17'21"
14	K061	Iron and steel industry	11	10 L/day (diesel) and 1 t/day (coal)	25	26°28'13"	80°17'42"
15	K077–K091	Oil industry	8	750 L/day (diesel)	30	26°26'15"	80°19'42"
16	K077	Rice mill	36	0.48	35	26°26'24"	80°19'52"
17	K077	Leather industry	5	5	35	26°26'31"	80°19'55"
18	K077–K091	Rubber industry	10	2	30	26°26'14"	80°19'27"
19	K108	Textile industry	12	1.2	80	26°24'43"	80°23'14"
20	K108	Rice mill	35	0.425	35	26°24'21"	80°23'11"

**Fig. 3. Grid squares and land use types (color figure available online).**

Based on the activity data of 7 grids with different land use, and 20 industries point pollution sources in detail (see Pollution Sources), the emissions in the other grids were obtained by mapping the 7 grids to the land use types of the other grids and by accounting for road length, number of vehicles on the road, and population in the grid. Emissions were estimated for PM, SO₂, and NO_x (for details of emission inventory, see Supplement Files 1, 2, 3).²⁶

In Kanpur, several monitoring stations are in place, operated by state and central authorities. Their placement is appropriate for air quality assessment, but not for estimating exposure. They offer daily time series, but do not capture the variability of the outdoor pollution field. For this reason, the study team decided to use the emission estimates as a surrogate measure of exposure. In this way, the time resolution is lost, but we gain exposure gradients within the city, which seems appropriate in relation to the nature of the other information in this study.

Health Data

Health data were collected from the LLR Hospital records. The data include grid number (representing residence of patients, Supplement File 4), age, sex, smoking status, occupation, respiratory symptoms, and resident location/street name. The data on 8,557 patients who visited the hospital at least once were collected for the period of January 10 to December 29, 2006. Quality assurance procedure required 2 physicians recording the data from journals to electronic form, and periodic double entries of portion of the data. The data entry resulted in 8,340 valid records. Of these, 3,948 had identified the domicile (home address). The large number of symptoms on the medical record was classified into 12 categories (Table 3).

Table 3.—Respiratory Disease Symptom Categories and Total Number of Patients Diagnosed in Each Category

Serial number	Symptoms	Total number of patients
1	Abdominal pain and epigastric pain	391
2	Breathlessness and dyspnea	4,318
3	Chest pain	3,446
4	Common cold	440
5	Bough	6,433
6	Fever	4,356
7	Hemoptysis and similar symptom	929
8	Loss of appetite	1,249
9	Weakness	475
10	Other aches and pains	626
11	Swellings	375
12	Other unspecified symptoms	544

Data analysis

The analysis aimed to relate the data on hospital visits to exposure index represented by the emissions. There are 3 emission parameters, and we first investigated their variability and dependencies (see Emission Clusters). Then, we investigated the relationship between the emissions and the hospital visits (see Correlation Between Air Pollution and Respiratory Disease), and we attempted to analyze the relationship between emissions and respiratory symptoms (see Analysis of Occurrence for a Respiratory Disease Symptom). Finally, we have investigated the temporal pattern of the hospital visits (see Analysis of Seasonal Differences). R version 2.7.1,^{27–29} packages “cluster” and “rgl”³⁰ and clustering functions “kmeans” and “pam,” were used for data analysis. ArcGIS 9.0 (ESRI, Redlands, CA, USA) was used for all data creation and map illustration.

A cluster analysis³¹ was conducted on the 3-dimensional emission data (SO₂, NO_x, PM) for each grid. The aim of this analysis is to group grids into certain number of clusters based on the level of air pollution load in the grids. We included emission data from all the pollution sources (see Pollution Sources), disregarding the point source from stacks higher than 25 m that are likely to influence larger area than the immediate grid. This step allowed us to conduct the analysis using statistical methods without incorporation of spatial dependence or autocorrelation, only using classical logistic regression model. We disregard also the observations in grids for which “land use” type is “protected.” For clustering, we used R functions “kmeans” and “pam” (a robust version of “kmeans”) from package “cluster.” Within groups, “sum of squares” and “average silhouette plots” were used to determine the optimal number of clusters.

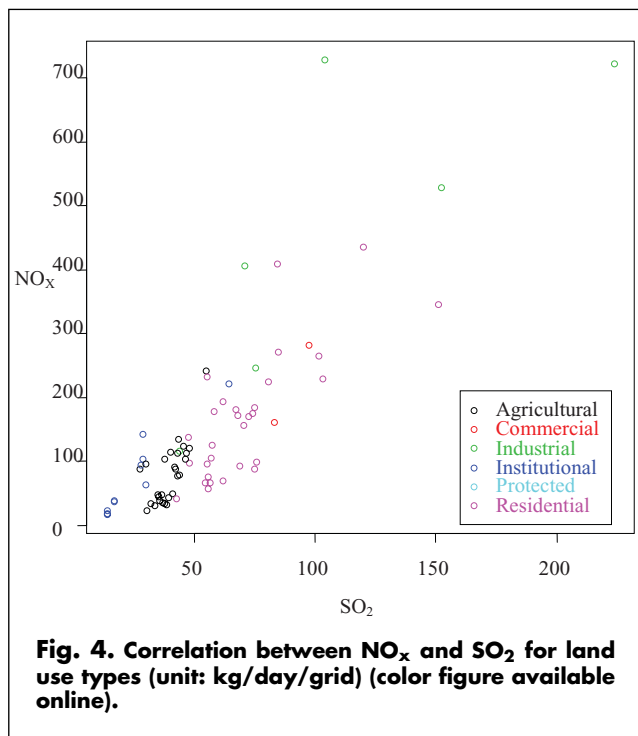
The relative number of hospital visits due to respiratory disease/symptoms was compared between the 4 clusters. In this analysis, the total number of inhabitants in each cluster was taken into account. The Pearson’s chi-square test³² for independence in the contingency table of number of respiratory patients and number of inhabitants who did not visit the hospital was conducted. Furthermore, we used a logistic regression^{33–35} to model an occurrence of a patient visit in LLR Hospital in relation to the cluster to which the home grid square belongs. The people who did not visit the hospital are the control group.

Further, the effect of time of the year on hospital visit occurrence was assessed. The Pearson’s chi-square test for independence in the contingency table of number of patients in each of 12 months classified by the cluster was performed (Table 7). The Wilcoxon 2-sample test³⁶ was conducted to assess differences between winter and summer seasons.

RESULTS AND COMMENT

Emission sources

The emission inventory estimates (total annual emissions of SO₂, NO_x, and PM expressed as t [ton] or kg [kilogram]



per day) showed that the main sources for outdoor air pollution are industries (37,147 kg/day), domestic fuel burning (8,455 kg/day), and vehicles (8,172 kg/day) (Supplementary Files 1, 2, 3).

Of total 7.6 t/day SO₂ emissions, industrial sources accounted for nearly 50% of total emission and the remaining 50% is attributed to other sources such as domestic fuel burning, vehicles, etc. (Supplementary File 1).

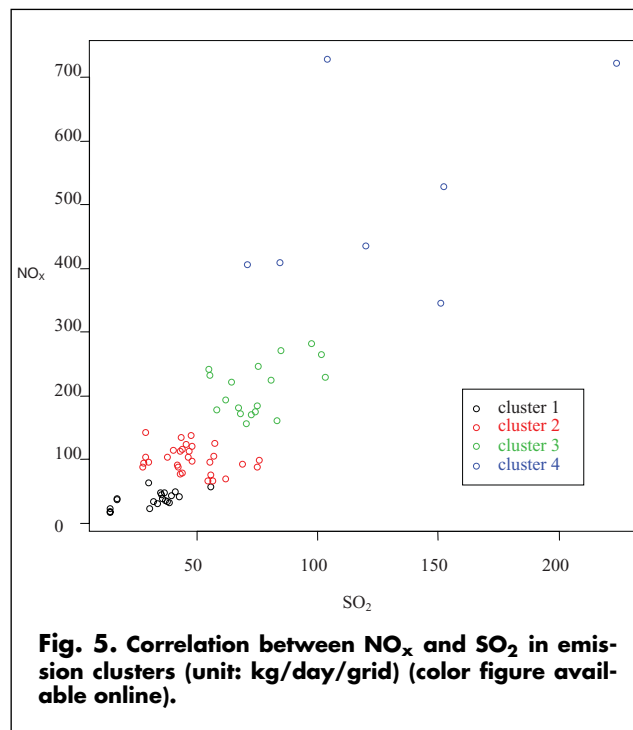
PM emissions accounted for 7.0 t/day. Forty-five percent of these emissions are attributed to domestic fuel burning. This source is followed by vehicles (20%), soil-road dust (18%), garbage burning (8%), and others (9%) (Supplementary File 2).

A total NO_x emission load of 19 t/day has been estimated within the city. The breakdown of emissions is as follows: industrial point sources (43%), vehicles (33%), domestic fuel burning (11%), industry area source (6%), diesel generator set (6%), and others (1%) (Supplementary File 3).

SO₂, NO_x, and PM emissions in grids are highly correlated as an artifact of the methodology, due to the fact that all 3 pollutants are emitted from most of the sources, and because each grid, even if classified into one land use type, usually has a mix of sources (Figure 4). From Figures 4 and 5, we can see that the values of SO₂ and NO_x are much higher in the industrial regions than in the institutional regions.

Emission clusters

The cluster analysis showed that the optimal number of clusters is either 2 or 4. For more exposure resolution, we chose to use 4 clusters. Table 4 provides emission levels for each variable of SO₂, PM, and NO_x within each of the 4



clusters. From Figure 5, we can see that the values of SO₂ and NO_x are much higher in the cluster 4 than in other clusters. Of the 154 grid cells, 78 that lie within the city limits were classified into 4 distinct pollution groups (ie, cluster) are seen in Figure 6.

Health assessment

Total Population in Each Emission Cluster

The spatial variation of number of inhabitants in each cluster is shown in Figure 7. Population is slightly lower in the very highly polluted regions (eg, a total of 232,224 people live in the regions within emission cluster 4). The highest number of inhabitants (748,457) lives in moderately highly polluted areas (ie, cluster 2; Figure 7).

Correlation Between Air Pollution and Respiratory Disease

In each level of emissions, the total populations, the total number of people that have visited hospital, and the total

Table 4.—Emission of SO₂, PM, and NO_x in Each Emission Cluster

Cluster number	SO ₂ (kg/day/grid)	PM (kg/day/grid)	NO _x (kg/day/grid)
1	36.08	44.57	39.00
2	46.57	75.72	104.23
3	62.19	134.76	194.15
4	120.16	259.34	434.97

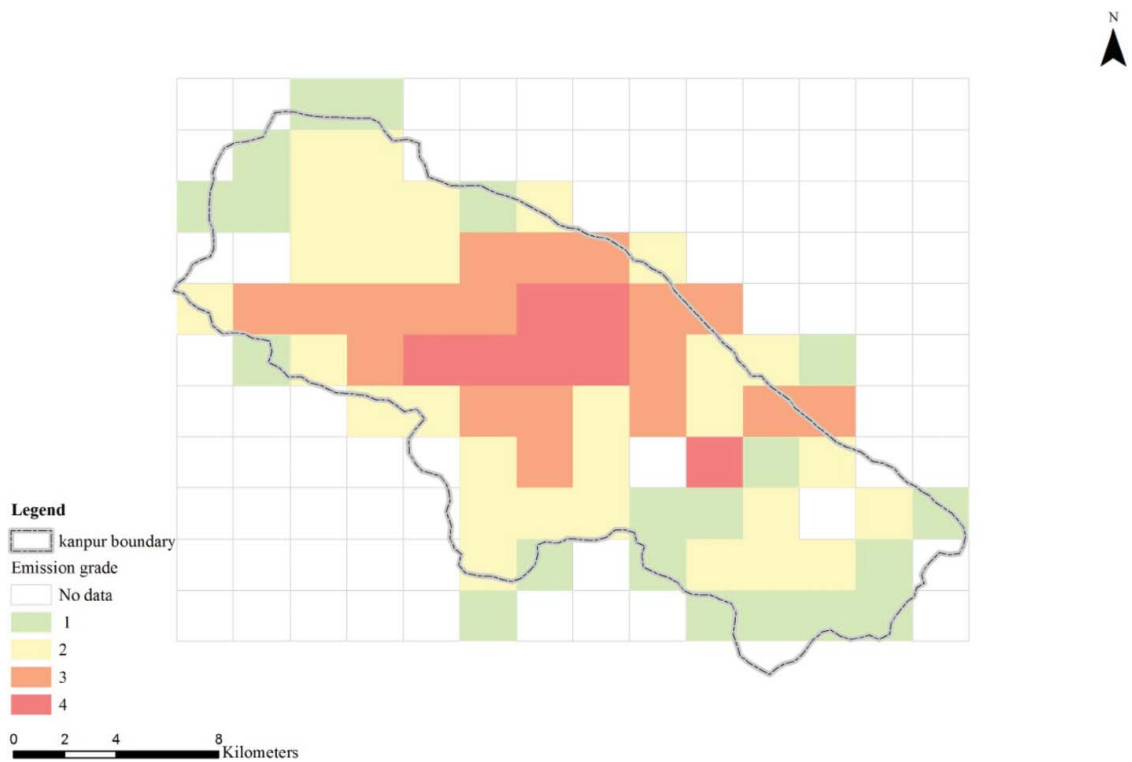


Fig. 6. Grid squares with indicated emission clusters (1 = less polluted, 2 = polluted, 3 = highly polluted, 4 = very highly polluted; refer to Table 4) (color figure available online).

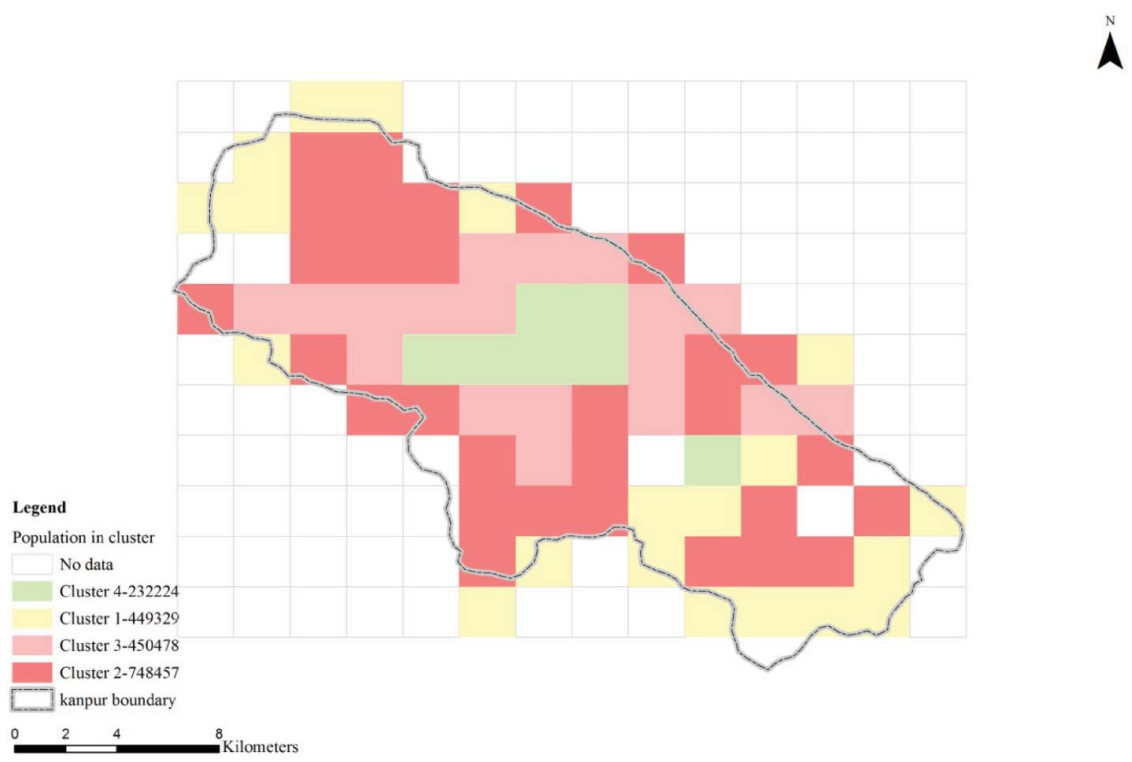


Fig. 7. Total number of inhabitants in each level of emissions (1 = less polluted, 2 = polluted, 3 = highly polluted, 4 = very highly polluted) (color figure available online).

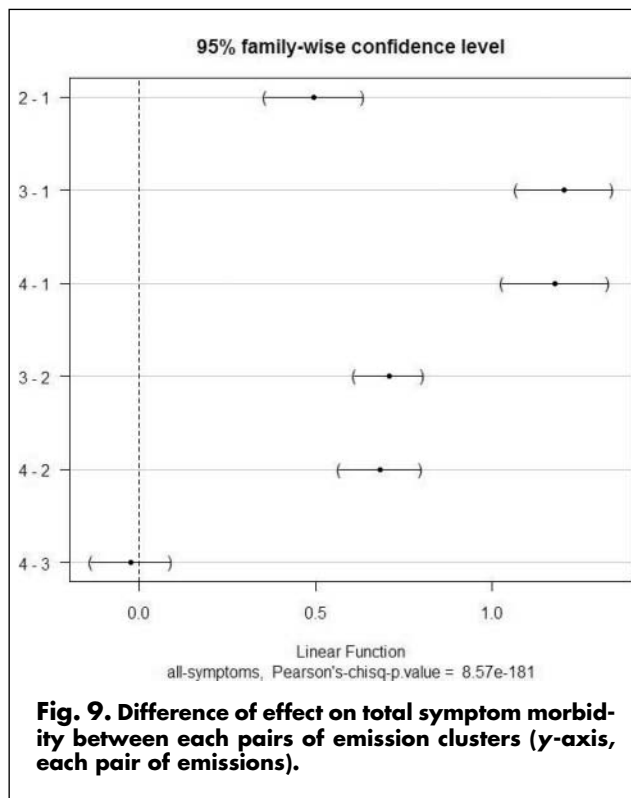
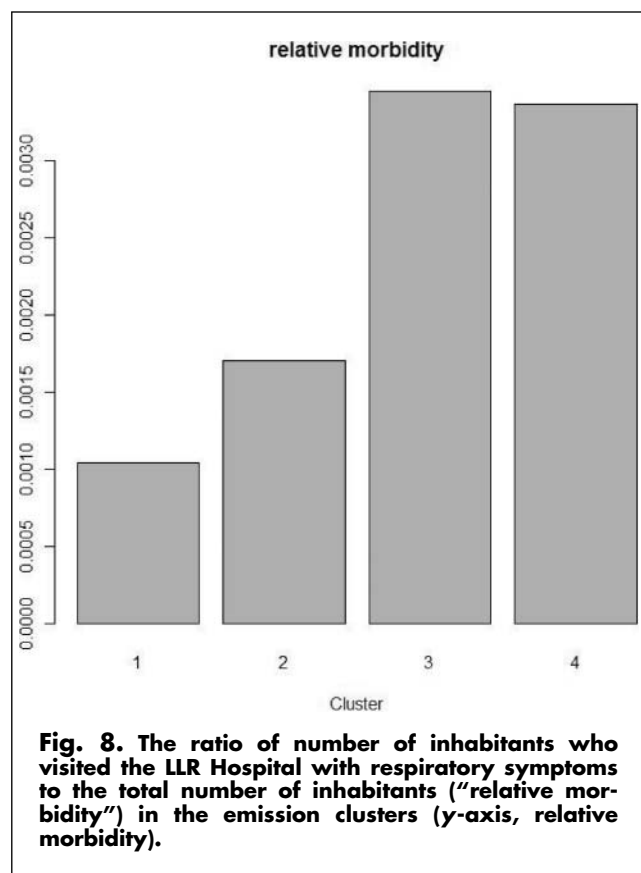
Table 5.—Total Number of Inhabitants in Each Cluster Who Visited the LLR Hospital and the Total Number of the Control Group (see Data Analysis)

Patients	Cluster			
	1	2	3	4
Yes	466	1,274	1,553	781
No	448,863	747,183	448,925	231,443

number of people that have not visited the hospital are incorporated into this analysis (Table 5).

Pearson's chi-square test ($df = 3$, chi-square = 835.52, $p < .0001$) showed that the relative number of patients who visited the hospital per number of inhabitants in each cluster is much higher in the highly polluted regions (clusters 3 and 4; Figures 8, 9) than in the less polluted regions (cluster 1); the ratio in the polluted cluster 3 and 4 is higher than 0.003 (Figure 8).

To see to what extent the type of analysis affects the results, we have also used a logistic regression to model visits to the respiratory hospital in relation to the level of emissions. Cluster inhabitants not having visited the hospital represented the control group. The results were consistent: independent of the cluster variable type (eg, nominal, ordinal, or quantita-



tive), the level of emission significantly affects the probability of visit to the hospital on any reasonable level ($p < .0001$; Table 6).

The 95% simultaneous confidence interval (CI) ("family-wise") for the difference of effect on hospital visits between all the pairs of emission clusters indicated that this probability significantly differs between each pair of emission clusters (pairwise Pearson's chi-square test, $p < .001$), except between the highly polluted cluster 3 and very highly polluted cluster 4 (Figure 9; Pearson's chi-square test, $p = .59$). There is no discernible difference in effect between emission levels of clusters 3 and 4; it can be attributed to a saturation effect that beyond a certain pollution level, there is no significant increase in the probability to visit to the hospital.³⁷⁻³⁹

Table 7 provides further quantification of the above. It provides odds ratios (the value by which the relative risk of having respiratory disease is multiplied when we changed from one emission level to another), and 95% CIs of odds ratios. For instance, comparing emission clusters 1 (less polluted) and 3 (highly polluted), in the grids where the average pollution of SO₂ increases from 36.08 to 62.19 kg/day/grid, PM from 44.57 to 134.76 kg/day/grid, and NO_x from 39.00 to 194.15 kg/day/grid (Table 4), the relative risk of increasing respiratory diseases of the inhabitants is higher than 3.33 (95% CI: 2.91, 3.81) (Table 7), which is a very high increase. This indicates that the respiratory disease morbidity is much higher in the highly polluted regions. This is consistent with findings that the levels of air pollution make a significant

Table 6.—Summary Results From Testing the Effect of Emission Classification Method (Quantitative, Ordinal, and Nominal Values for Exposure) on the Resulting Relationship With Hospital Visits Using Logistic Regression

Cluster (1, 2, 3, 4)		Estimate	SE	z value	Pr (> z)
Quantitative variable	c(1, 2, 3, 4)	0.42470	0.01599	26.57	<2e-16***
Ordinal variable	as.ordered(c(1, 2, 3, 4)).L	0.94894	0.04020	23.603	<2e-16***
	as.ordered(c(1, 2, 3, 4)).Q	-0.26049	0.03488	-7.469	8.07e-14***
	as.ordered(c(1, 2, 3, 4)).C	-0.21101	0.02857	-7.386	1.52e-13***
Nominal variable	as.factor(c(1, 2, 3, 4))	df	Deviance	Residual deviance	Pr (>Chi)
		3	830.48	0.00	2.2e-16***

Note. The null hypothesis is that all of the regression coefficients in the model are equal to zero. The z value is the Wald statistics; Pr (>|z|) is the probability level of 2-tailed test; df is degrees of freedom; Pr (>Chi) is p value that define the probability of observing a chi-square statistic at least as observed under null hypothesis. c = cluster; L = linear; Q = quadratic; C = cubic; *** = the probability level of 2-tailed test or chi-square test is significant.

contribution to the variation in daily hospital administration for respiratory disease.^{1,2,3,39,40}

Similarly, by analyzing separately the individual groups of respiratory symptoms, we got the same result that emission levels 1 and 3 differ significantly for all symptoms, and there is no difference between emission levels 3 and 4 for any of the respiratory symptoms (Figure 10).

Analysis of Seasonal Differences

The aim of this analysis is to assess the effect of a certain time period (ie, months and seasons) on the distribution of relative number of inhabitants that visit hospital on each level of emissions, or an effect of each level of emissions on the distribution during the year. To avoid multiple testing problem and to clearly state what hypothesis we test, we chose month as time period (because this period could be appropriate, not too short or not too long, to capture seasonal effect on morbidity). We performed Pearson's chi-square test for independence in the hospital visits (Table 7) and obtained a p value of .29. Thus, there is not strong enough evidence to claim that the distribution of morbidity in the different emission levels depends on a certain month or that the distribution of morbidity during the year depends on a certain

emission level. Table 8 presents total number of inhabitants who visited the LLR hospital in each month with residence in each of the emission clusters.

Another question we can ask is: Does the morbidity change during the year regardless of the emission level? Table 9 presents the number of patients for each month without considering the emission level. We divided 12 months into 2 samples. The first sample consists of the summer months (April to September) and the second sample consists of the remaining winter months. The Wilcoxon 2-sample test was conducted, with the result ($p = .015$) showing that there is a significant difference for respiratory disease morbidity between summer and winter months. It remains, however, not clear what seasonal factors affect the hospital visits (eg, extreme weather conditions in summer months, high pollution load in winter months), or if the hospital visits are mainly related to specific respiratory symptoms.

Table 7.—Odds Ratios Quantifying Increased Risk of Visiting the LLR Hospital Between the Emission Clusters

Contrasts between clusters	Estimate	95% CI	Odds ratio	95% CI
2 and 1	0.50	0.36, 0.63	1.64	1.43, 1.89
3 and 1	1.20	1.07, 1.34	3.33	2.91, 3.81
4 and 1	1.18	1.03, 1.33	3.25	2.80, 3.78
3 and 2	0.71	0.61, 0.80	2.03	1.84, 2.24
4 and 2	0.68	0.57, 0.80	1.98	1.76, 2.22
4 and 3	-0.02	-0.14, 0.09	0.98	0.87, 1.09

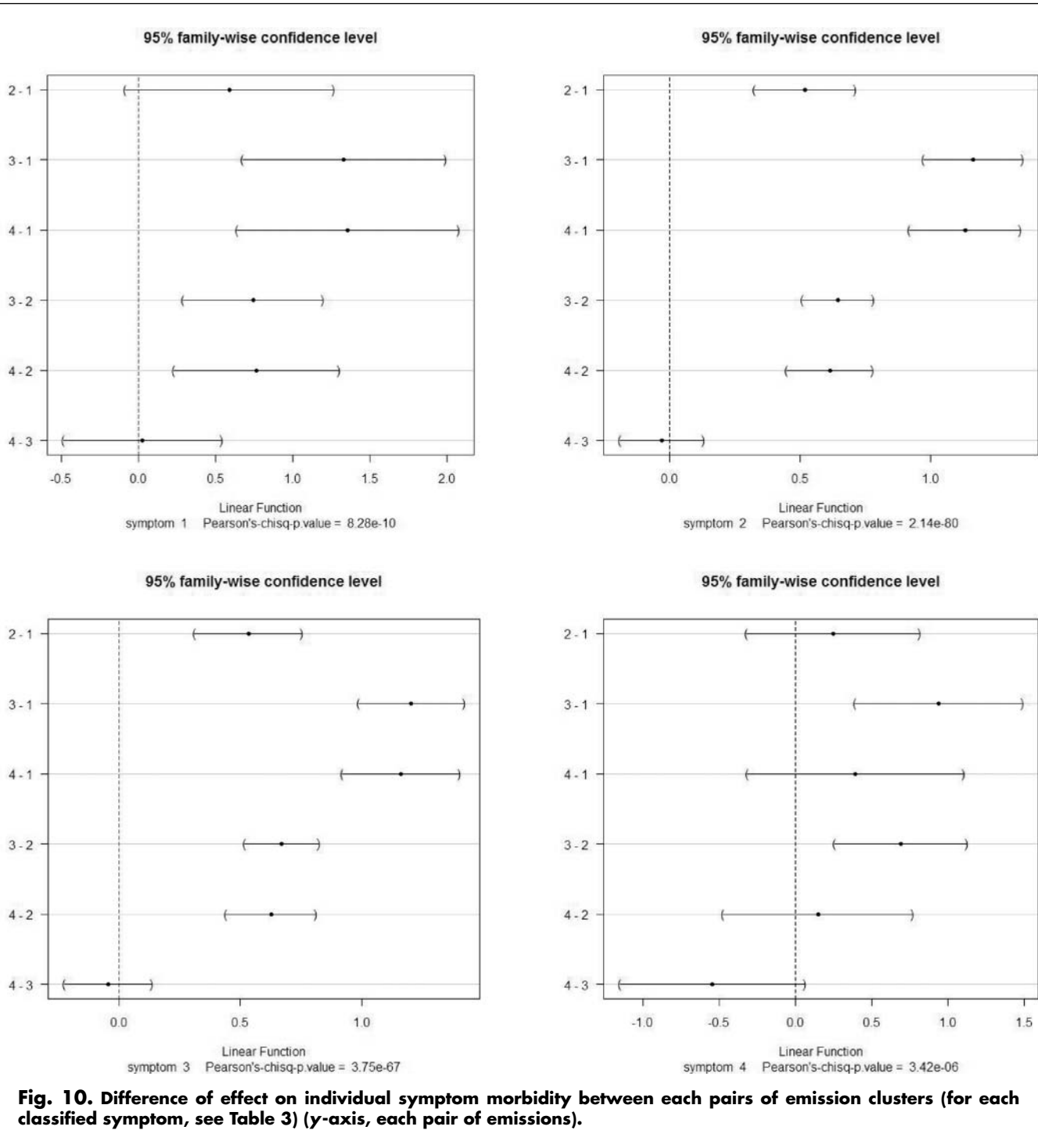
Note. CI = confidence interval.

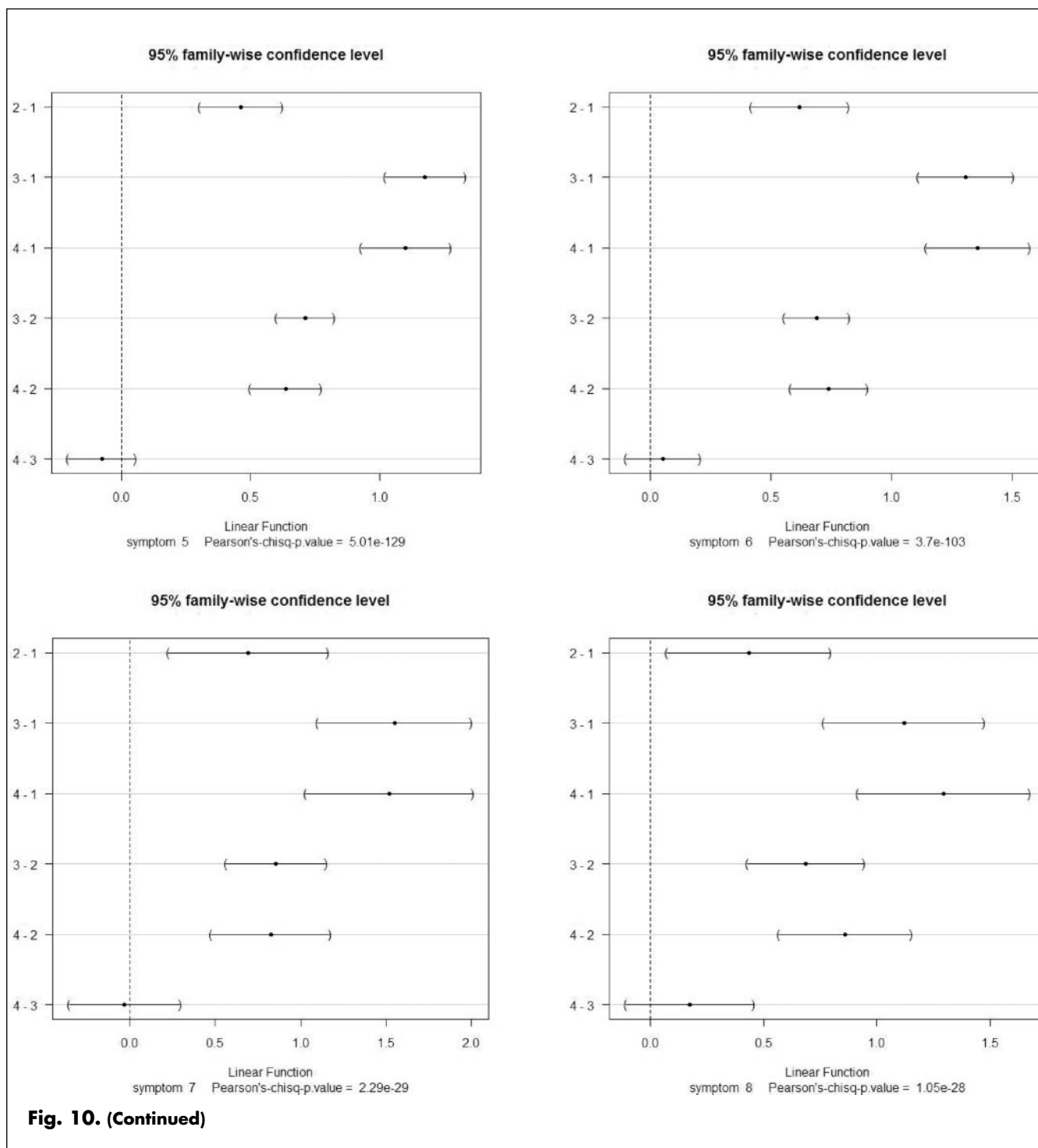
Table 8.—Total Number of Inhabitants Who Visited the LLR Hospital in Each Month, With Residence in Each of the Emissions Cluster (for Patients With Identified Address in the Urban Area—78 Clusters)

Month	Cluster			
	1	2	3	4
1	30	95	129	57
2	44	99	128	71
3	45	111	161	66
4	44	106	139	55
5	45	98	121	73
6	36	107	131	71
7	32	106	133	75
8	47	126	127	69
9	29	119	131	77
10	28	71	109	62
11	48	113	117	52
12	19	70	88	38

Table 9.—Total Number of Patients in Each Month

	Month											
	1	2	3	4	5	6	7	8	9	10	11	12
Total number of patients	555	684	738	680	747	784	772	837	768	581	732	462

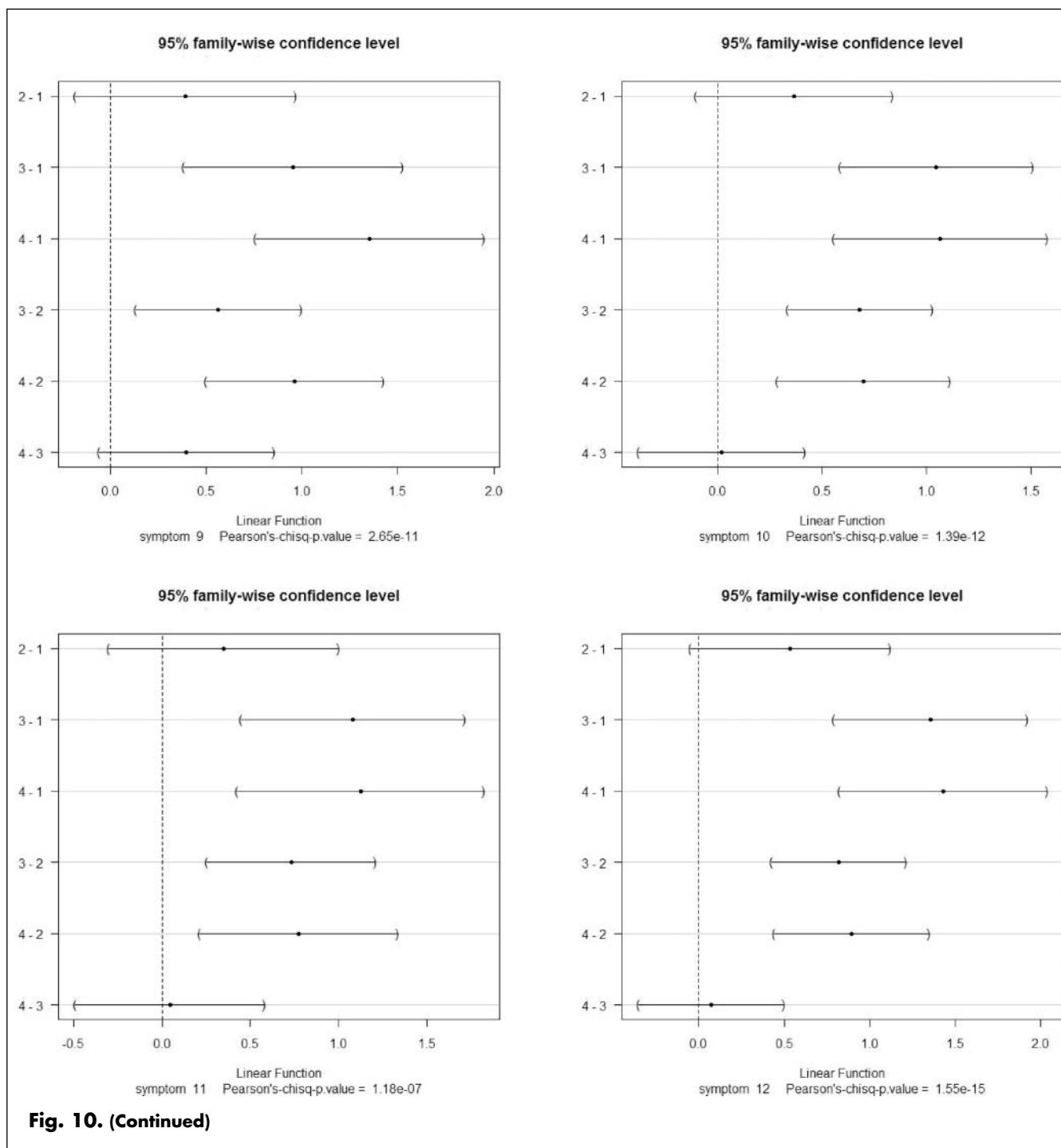




Analysis of Occurrence for a Respiratory Disease Symptom

A logistic regression model with the occurrence of the symptom as the response and the variables cluster, sex, and age as the regressors showed that only the symptoms 4 (common cold), 5 (cough), and 6 (fever) are significantly

impacted by the emission level. Common cold and cough are less frequent in the higher polluted regions, whereas fever occurs more likely in the higher polluted regions. However, symptom recording and classification is perhaps the part of the retrospective data collection that is most subjective and thus least rigorous, and this may affect the result.



Conclusions and recommendations

The main sources for outdoor air pollution in Kanpur are industries, domestic fuel burning, and vehicles. An emission inventory for the urban area was established, and local emissions in the 2 km × 2 km grid square representing the home address of Kanpur inhabitants were used as a surrogate measure of exposure to outdoor air pollution.

There is clear evidence that outdoor air pollution is associated with cardiopulmonary diseases. We did not investigate the effects on cardiovascular disease in this study, but we have shown that people living in the more polluted regions had a higher risk of hospital visits related to respiratory diseases than those living in the less polluted areas. This phenomenon is in accordance with other study results.^{38,40-45}

Our study has several limitations. The exposure is represented by emission category (cluster) for each individual home. This has both advantages (being a more robust method), and disadvantages; it forces the analysis into a cross-sectional mode, considering a cumulative or long-term effect of pollution on respiratory health.⁴⁶ The retrospective data collection, especially to record respiratory symptoms, poses also some difficulties.

Our study could not consider time lags between air pollution and the occurrence of respiratory disease morbidity^{47,48} due to a lack of temporal data on air pollution. Despite these shortcomings, we did show a clear relationship between pollution and respiratory disease. Clearly, more information is available in the data than we have used in this analysis, but we feel that our result is robust, and should be sufficient to trigger further work. In the future, this analysis can be supplemented by adding daily variability in pollution concentrations, allowing an analysis of short-term effects.

All the findings from this study suggest that long-term, systematic, prospective epidemiological studies on exposure to air pollution and its respiratory health effects are needed.⁴⁹

This paper indicates that the polluted air was a clear threat to human health in Kanpur in 2006. This situation is alarming. Mitigation will require a combination of technical measures on all sources (this study was conducted before the massive conversion of the public transport to compressed natural gas) and urban planning. Also, it is necessary to establish adequate monitoring systems both for air quality and for human health, to be able to assess the trends, and the effectiveness of measures taken.

This study has been carried out under the project "Environmental Health Assessment: Respiratory Disease in relation to Air Pollution in Kanpur, Uttar Pradesh," which was an 18-month cooperation project between the Indian Institute of Technology Kanpur (IITK), Ganesh Shankar Vidyarthi Memorial (GSVM) Medical College in Kanpur, State Pollution Control Board (SPCB) in Kanpur, and Norwegian Institute for Air Research (NILU), funded under Royal Norwegian Embassy New Delhi grant (IND 3025 05/051). In addition to the partners funded by this grant, the Central Pollution Control Board, Agra, participated in the project's intercomparison exercises and preparation of standard operating procedures (SOPs).

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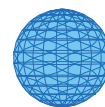
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Attachment 5

Liu HY, **Bartonova A**, Neofytou P, Yang A, Kobernus MJ, Negrenti E, Housiadas C: Facilitating knowledge transfer: decision support tools in environment and health. *Environmental Health* 2012, **11**(Suppl 1):S17
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METHODOLOGY

Open Access

Facilitating knowledge transfer: decision support tools in environment and health

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Abstract

The HENVINET Health and Environment Network aimed to enhance the use of scientific knowledge in environmental health for policy making. One of the goals was to identify and evaluate Decision Support Tools (DST) in current use. Special attention was paid to four "priority" health issues: asthma and allergies, cancer, neurodevelopment disorders, and endocrine disruptors.

We identified a variety of tools that are used for decision making at various levels and by various stakeholders. We developed a common framework for information acquisition about DSTs, translated this to a database structure and collected the information in an online Metadata Base (MDB).

The primary product is an open access web-based MDB currently filled with 67 DSTs, accessible through the HENVINET networking portal <http://www.henvinet.eu> and <http://henvinet.nilu.no>. Quality assurance and control of the entries and evaluation of requirements to use the DSTs were also a focus of the work.

The HENVINET DST MDB is an open product that enables the public to get basic information about the DSTs, and to search the DSTs using pre-designed attributes or free text. Registered users are able to 1) review and comment on existing DSTs; 2) evaluate each DST's functionalities, and 3) add new DSTs, or change the entry for their own DSTs.

Assessment of the available 67 DSTs showed: 1) more than 25% of the DSTs address only one pollution source; 2) 25% of the DSTs address only one environmental stressor; 3) almost 50% of the DSTs are only applied to one disease; 4) 41% of the DSTs can only be applied to one decision making area; 5) 60% of the DSTs' results are used only by national authority and/or municipality/urban level administration; 6) almost half of the DSTs are used only by environmental professionals and researchers. This indicates that there is a need to develop DSTs covering an increasing number of pollution sources, environmental stressors and health end points, and considering links to other 'Driving forces-Pressures-State-Exposure-Effects-Actions' (DPSEEA) elements. Of interest to both researchers and decision makers should be the standardization of the way DSTs are described for easier access to the knowledge, and the identification of coverage gaps.

Background

Additional knowledge of the complex problems surrounding environment and health (E&H) increasingly highlights questions regarding the relation between policy and research [1]. In environmental risk assessment, Linkov et al [2] illustrate how decision making has moved from

an *ad hoc* process towards working within an integrative decision analysis framework. They propose to integrate environmental management within an adaptive management framework, supported by tools, and integrated with methods for management of uncertainty, including the uncertainty of mitigation options. Taking the perspective of environment and health, we have to define a suitable framework, and to find adequate tools that would provide information that is both easy to understand and of sufficient depth to support decision- and policy making.

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Decision support tools (DSTs) (also known as decision aids or decision support technologies) permit the making of the decisions based on complex and wide-ranging information. DSTs can take the form of written guidance, data, models and/or software. They aim not only to facilitate decision making, but to help ensure that the process is transparent, documented, reproducible and robust.

The need for decision support is widely recognised. In recent years, a large number of DSTs have been developed, with varying degrees of success in their practical use [3-5]. However, with the growth of DSTs, the resulting advice can be contradictory, as the different DSTs are based on different data sets and models. Thus, information that would permit the evaluation of the DSTs as well as their inputs is important. As a start, an overview of current DSTs is required.

The HENVINET project (Health and Environment Network) had a general aim to create a “permanent network of professionals”. One line of work supporting this aim was to make publicly available information about DSTs providing qualitative or quantitative assessments that underpin decision making in the field of E&H. This could increase the use of DSTs, leading to their better validation, and more discussion on their use.

Decision support tools are undeniably an important mechanism for transfer of knowledge from researchers to decision makers. The goal of the DST Meta database (MDB) is to make available the vast richness of tools to the management process of environmental health. The main objectives of the work included to 1) define a concept of DSTs in E&H fields; 2) identify available DSTs 3) create an open access web-based DSTs MDB; and 4) carry out categorisation, evaluation, validation and application of DSTs. This paper provides an overview of the work undertaken, with the aim to encourage and facilitate additional effort in making DSTs better known, more used, and therefore, more useful.

Concept of decision support tools

In the broadest sense, a DST is any guidance, procedure, or analysis tool that can be used to help support a decision [6-9]. Within HENVINET, a DST is a tool that supports decision makers to make decisions in the E&H sector, in particular to propose actions and policies for reducing the burden of environmental stressors on human health. HENVINET defines DSTs as: *any tool based on E&H knowledge that can be used in different decision making contexts: from every day operation of health practitioners to strategic long term planning and implementation of policies for reducing the negative effects of environment on health*. Most often, DSTs are in the form of written guidance, or software. Written guidance

is frequently provided by regulatory agencies as a means of ensuring a standardized, reproducible approach to reaching a decision. In many cases, this guidance is translated into computer software. Software tools are also developed to assist in the decision process for computationally intensive analysis (e.g., geo-statistical modelling and multi-criteria analysis), and for mapping the spatial relationship between environmental stressor data and physical features such as buildings, roads (e.g. ArcGIS). Software tools are categorized as data-driven or model-driven DSTs depending on the output of the tools [10].

In HENVINET, a reference concept is the World Health Organisation (WHO) full chain DPSEEA (Driving forces-Pressures-State-Exposure-Effects-Actions) approach, which is identified also as one fundamental concept of the EHAP (Environment and Health Action Plan) [11,12]. Therefore we defined an E&H DST to include models and/or data within at least two of the following areas: environmental stressors’ emissions, their transport and dispersion in the environment, pathways to humans, behaviour and exposure of the population, health effects with reference to the four EHAP priority issues: asthma and allergies, cancer, neurodevelopment disorders and endocrine disruptor mediated-diseases.

Methods

Database concept

The database has been designed as a system of “attributes”, or descriptors, with either pre-described categories or free text (see Additional file 1). The development of the attributes took more than one year. The DPSEEA framework permits the description of both the different elements (drivers, pressures, status, exposure, effect, action), and their links. We have developed different kinds of categorisation for several of the elements. We have gathered contact information, and quality control and assurance information. Several trial runs and a review of different classification systems helped to define which attributes should have prescribed categories, where to allow free text, and where to combine these types. The resulting database permits the user to find information using a search for pre-defined categories and free text. The system also allows commenting on each DST.

Formal validation of each individual DST is the responsibility of its owner or designer (information about such validation may be provided as part of the DST description). We have designed evaluation criteria regarding user friendliness, the design of the DST in relation to the concept of the “causal chain” of DPSEEA, robustness of the tool, user application history and applicability of the tool, and whether or not information about uncertainty is available as part of the output. This information is included in the database.

Database functionalities

The database offers the four following functionalities: add information on new tools and edit it, search for information on available DSTs, and provide reviews or comments.

1. Adding DSTs: in order to upload a DST, registration is required. An online guideline is provided for new users.
2. Editing existing DSTs: only the provider of the given DST is allowed to edit the already uploaded information.
3. Review and comment: each DST has a free text space for providing comments of any kind that can contribute to the improvement of the tool or to improve the description within the database.
4. Search engine: two search options are available: free text search by the user's own selected keywords, and search by (fixed) categories.

Populating the database and controlling the quality of entries

In order to identify the available DSTs, we have formulated a procedure that allowed for both information gathering and content control. These steps were followed:

1. Identify available DSTs through the HENVINET partner network and through literature review by the DST team.
2. Contact DSTs provider or user to collect initial DSTs information in a standard initial contact form.
3. Identify 'tutors', or experts providing initial information, to compile and upload the database entries.
4. Identify 'supervisors', or experts knowledgeable on the DST subject, to review and complete the DSTs information, to authorise release of the DSTs to the public.
5. Undertake coverage assessment of the DSTs using predefined criteria, and provide this information online.

The role of the 'tutors' is solely to review the available information on the DST and enter it into the database. The role of the 'supervisors' is to review the entries, and to assess the DST regarding validation and current application. In this process, both the "tutors" and the "supervisors" are independent of the DST owner/provider.

Access to changes in the MDB is differentiated: read and search access is public, adding records require registration; a registered user can change the entry they have made. During the project (end April 2010), the 'tutors' and the 'supervisors' were authorized to change records. The owners of the DST, as far as they were known, were notified about the entry.

Information gathering on existing decision support tools – initial contact

For initial contact, an entry form (see Additional file 2) was designed and distributed to either DST providers or DST users, or even simply to people with potential information about a DST. This initial contact form consisted of two parts, namely the contact person information and

DST information. The first part included details on the contact person and the person's organization, whereas the second part included details on a DST such as its title, category, web link and a short description. A total of 34 completed forms were received through direct contacts.

In addition to the directly identified DSTs, a literature review and an online search were undertaken to identify further DSTs. For each DST, a HENVINET partner completed the contact form. 76 additional DSTs were identified through this process, a total of 110 DSTs with brief descriptions as a basis for further work.

Uploading information

The contact persons were asked to upload full DST information to the DST entry template. In a few cases, the initial contact person did not wish to upload the information due to a limited knowledge of the details, and was replaced by a more expert colleague, either internal or external to the HENVINET partnership. A total of 78 DSTs were uploaded into an online MDB.

Quality control of entries

After uploading DSTs, the information was reviewed. Each DST was assigned to a HENVINET partner with experience in the sector (a 'supervisor'). The review also included an evaluation of the DSTs regarding their use. The following six evaluation criteria were applied: 1) user friendliness (how easy is it for the user to use the DST?); 2) causal chain approach (how does the DST relate to the causal chain?); 3) robustness (how reliable is the DST?); 4) user application history (how often has the DST been used and by whom?); 5) applicability (how widely can the DST be applied?), and 6) uncertainty (has the DST been given a thorough review with regard to uncertainty?). The assessment of the DSTs was conducted in simple manner with three categories for each criterion. After the review and evaluation, the 'supervisors' had right to publish the contents in the MDB.

Assessment of the coverage

To help identify any gaps in coverage of DSTs and as a basis for recommendations for further research and development of DSTs, we have summarized the database entries. The following six categories of DSTs are recognized: database, guideline, handbook, indicator, methodology and software model [12].

Results

Contact information is available for 110 DSTs. After 'tutors' uploaded and 'supervisors' reviewed the entries, a web-based MDB with 67 DSTs (Additional file 3) is accessible through the HENVINET networking portal <http://>

www.henvinet.eu and the HENVINET project website <http://henvinet.nilu.no>.

Categorization results showed that the majority of the DSTs are software models (Fig. 1). Most DSTs 1) are for wider use (Fig. 2a); 2) are multi-level (Fig. 2b); 3) show either medium or high robustness (Fig. 2c); 4) provide some analysis on uncertainty (Fig. 2d); 5) are characterized by frequent use (Fig. 2e); 6) are about equally divided between two levels, i.e., easy to use (37%) and medium difficulty to use (36%) (Fig. 2f).

Validation results showed that 1) most DSTs are designed to address the most common pollutants found in the atmosphere, e.g., PM, NO_x, VOCs and poly-aromatic hydrocarbons (Fig. 3a); 2) 25% of the DSTs address only one environmental stressor. The majority of DSTs (52%) are relevant for 4 to 11 stressors, whereas 3% are relevant for all the specified 36 stressors (Figs. 3a, 3b); 3) most DSTs address road transport, followed closely by industrial production processes and combustion in energy and transformation industries (Fig. 4a); 4) more than 25% of the DSTs address only one pollution source. A large proportion of DSTs (42%) cover from 1 to 3 sources, whereas another large proportion (46%) cover 10 or more stressors (Fig. 4b); 5) the four priority issues - asthma and allergies, cancer, neurodevelopment disorders and endocrine disrupting effects - are quite evenly addressed (15-23%) by the DSTs (Fig. 5a). Slightly more DSTs (28%) cover the topic of toxicology; 6) almost 50% of the DSTs cover only one disease or issue (Fig. 5b).

Application results showed that 1) most DSTs are designed to address the most common decision making

areas in environment and health, namely public health protection and air quality management, whereas the least addressed areas are agriculture and waste management (Fig. 6a); 2) 41% of the DSTs cover only one decision making area, whereas 86% of the DSTs cover from 1 to 6 areas (Fig. 6b); 3) the most frequent user is the national level authority (Fig. 7a); 4) 60% of the DSTs cover one or two decision-making levels (Fig. 7b). Most of DSTs combine either a single or two neighbouring levels, e.g., regional and national authority levels; 5) most DSTs are developed for use by environment professionals (Fig. 8a); 6) almost half of the DSTs can be used by professionals in two areas, whereas only 12% of DSTs can be used by all professionals. About 20% of DSTs may be used either by professionals in one or three areas (Fig. 8b). It is important to note that DSTs that can be used by professionals in two areas usually refer to the environmental professional combined with a professional from another of the three remaining areas, whereas a combination of administrator and researcher rarely occurs.

Discussion

A number of DST repositories exist on-line, such as those by the US EPA (Environmental Protection Agency); however they usually target narrower communities, and do not offer the kind of access to information that would promote the "full chain" or DPSEEA thinking.

The HENVINET DST MDB can constantly be updated with information on additional DSTs. It provides easy access to information, is easy to manage, and

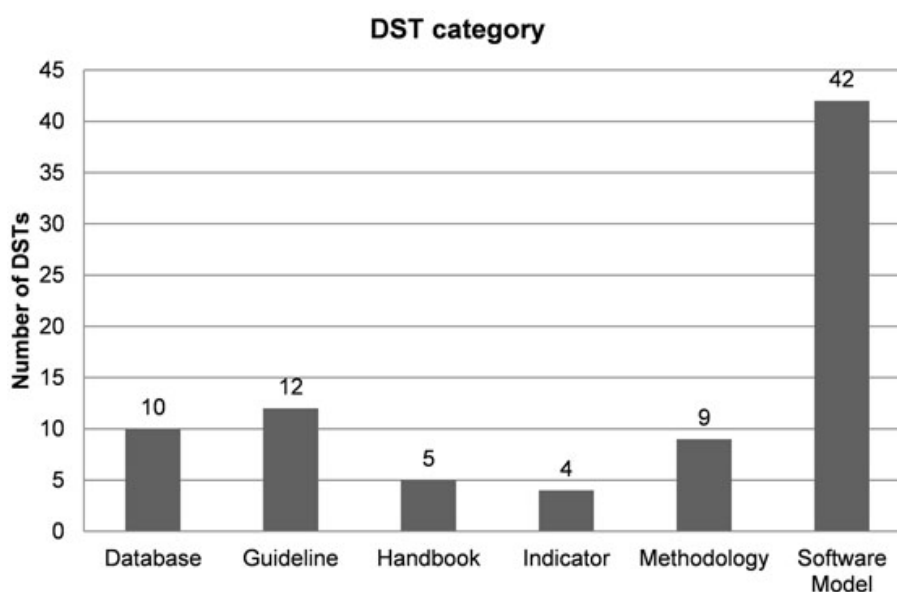
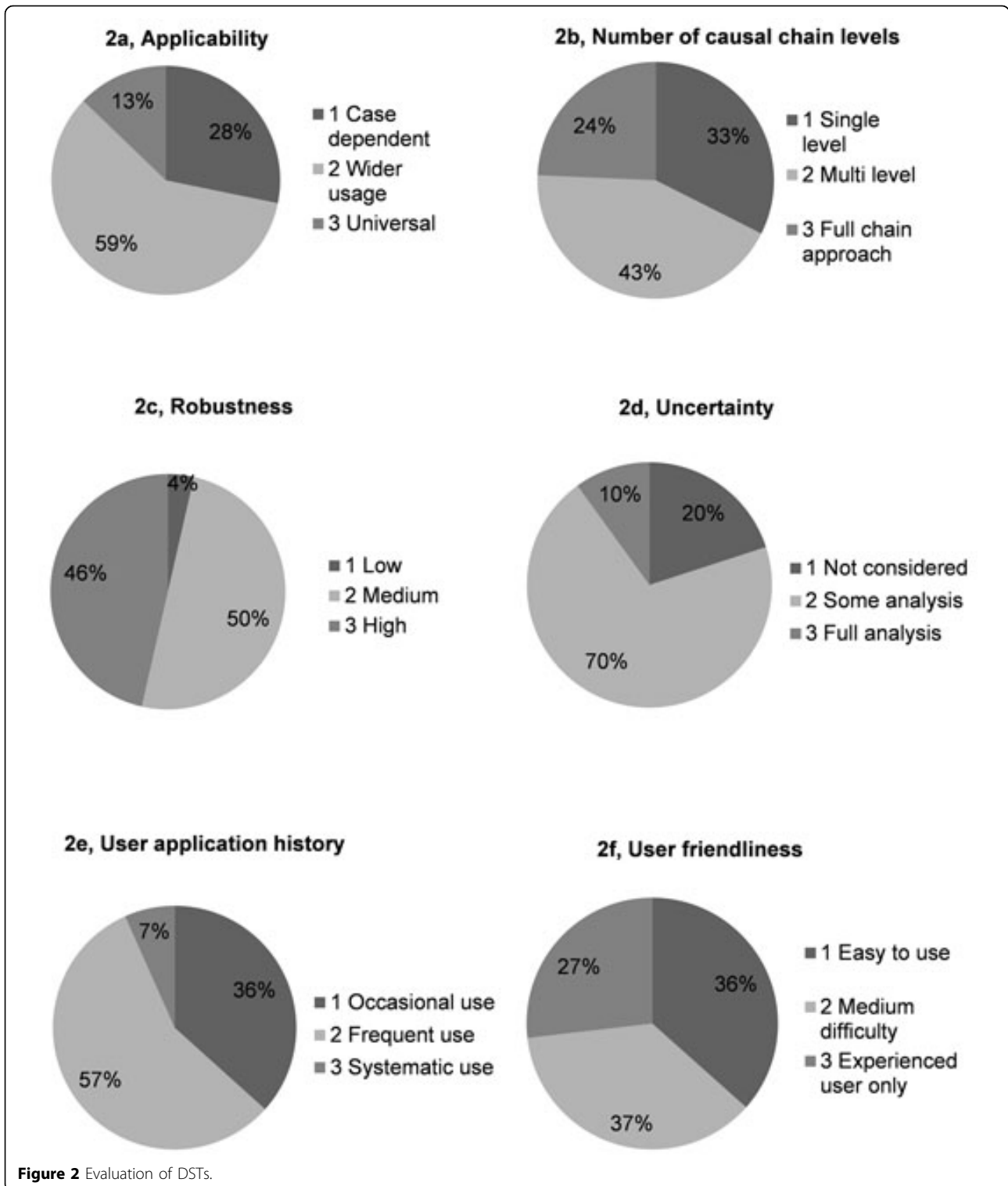


Figure 1 Overview of the different DSTs categories.



it allows the user to browse data on identified DSTs, to input data on a new DST, to update the information, correct errors, or search for DSTs with specific characteristics. The MDB in particular permits the description

of the purpose of the DST, its application areas, the expected users, the considered stressors and health outcomes. Where available, it provides information about how the DST was validated.

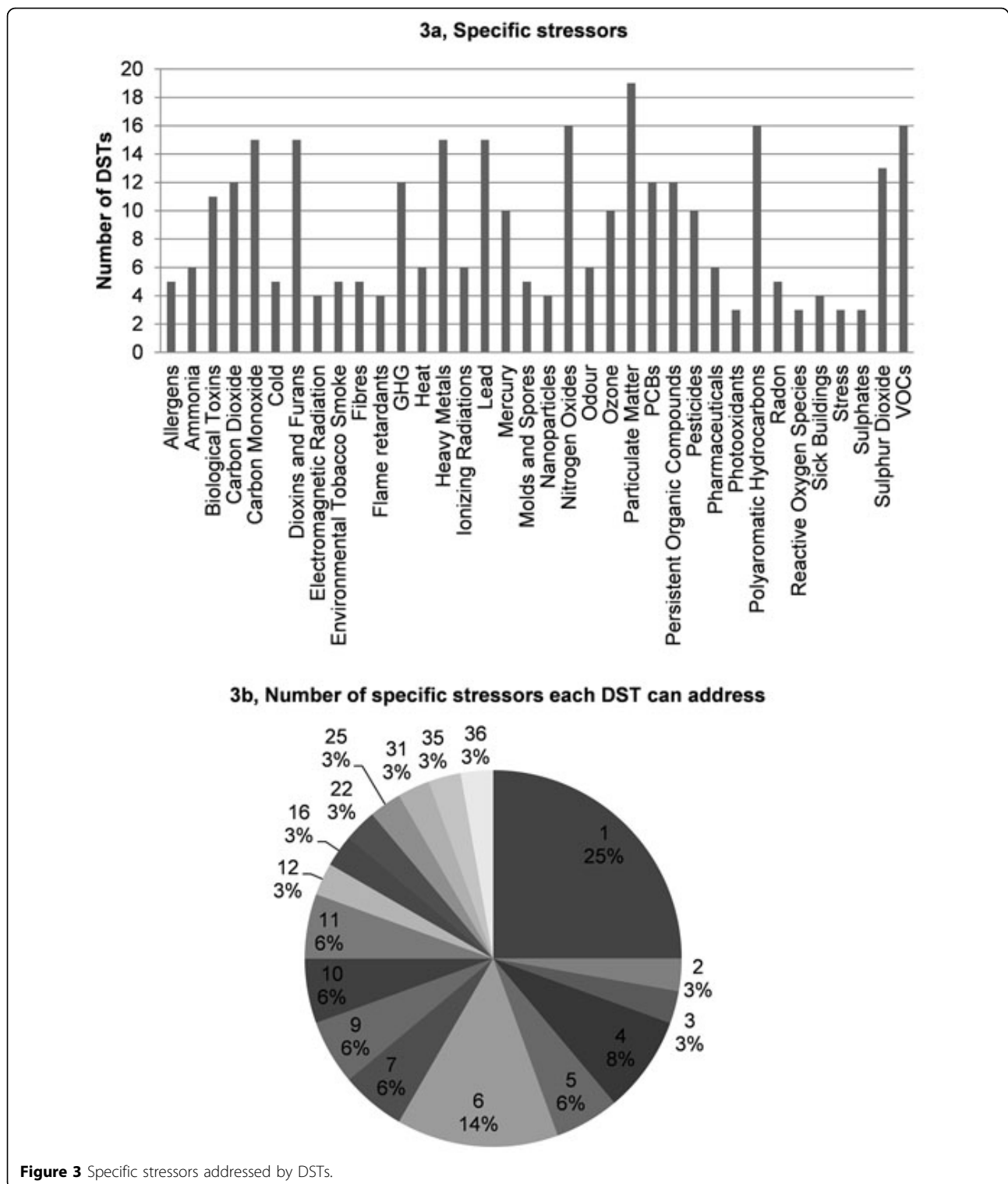
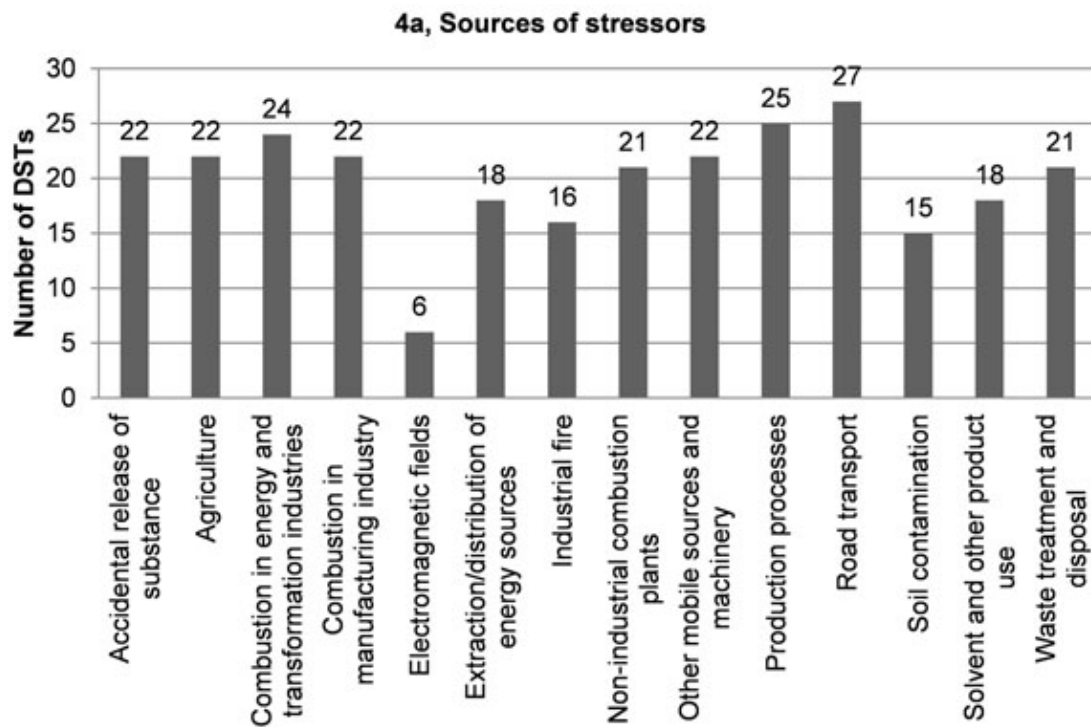


Figure 3 Specific stressors addressed by DSTs.

Similar review and classification of DSTs have been carried out in other fields. For instance, McLellan et al [13] have reviewed tools and methodologies “used for incorporating sustainability considerations in the design of mineral processing operations”. They note that a systematic

approach is lacking, and while their framework is to support a specific industry (having in mind specific industrial process); it does have an element of the DPSIR (Driving Force–Pressure–State–Impact–Response) framework/ DPSEEA in the element “understanding the effect of design



4b, Number of sources of stressors each DST can address

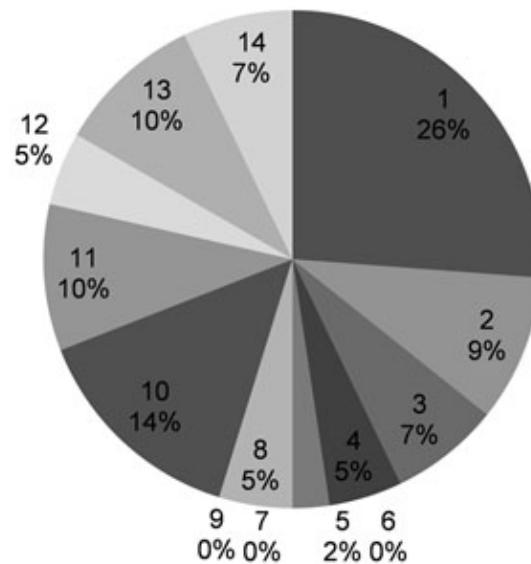
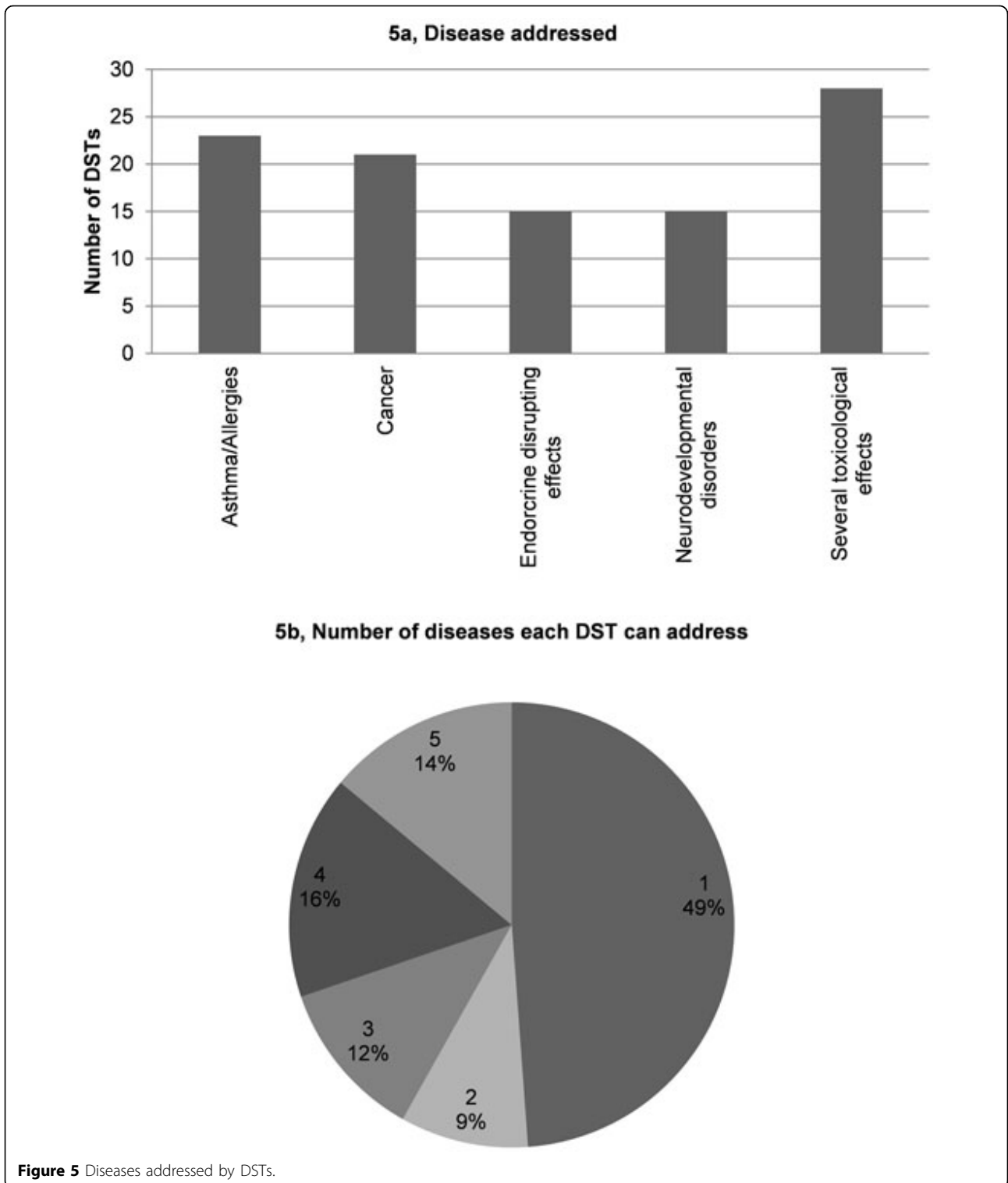


Figure 4 Sources of stressors addressed by DSTs.

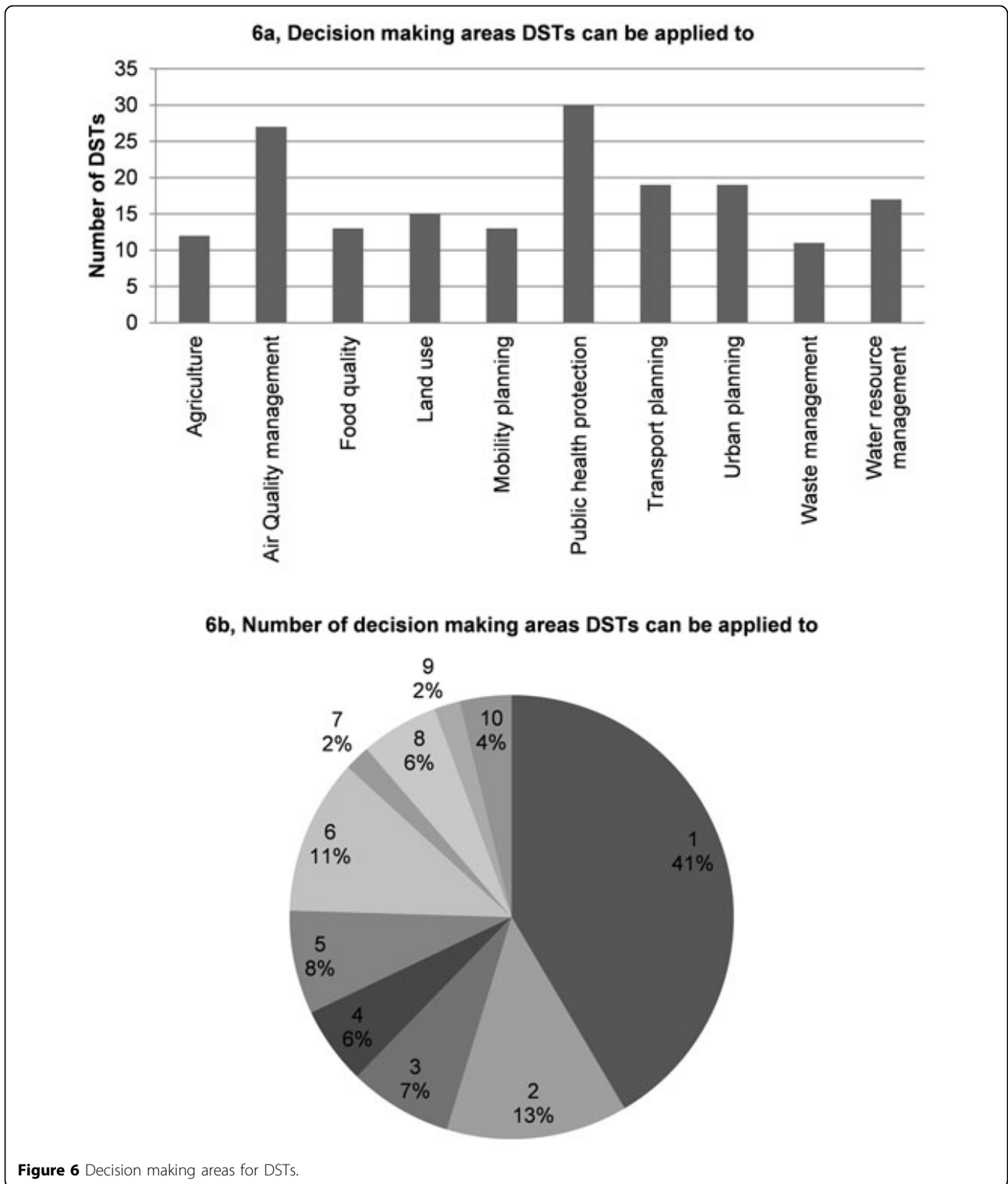
choices [13]". Hamouda et al [14], having reviewed decision support systems for water and wastewater treatment processes point out that there is a need to develop integrated systems that consider a system analysis approach. Chang et al [15] analyzed systems for solid waste management,

looking at systems engineering models (e.g., cost benefit analysis, forecasting analysis), systems analysis platform (e.g., decision support tools, expert system), and assessment tools (e.g., scenario development or environmental impact assessment). Their work provides a possible framework to



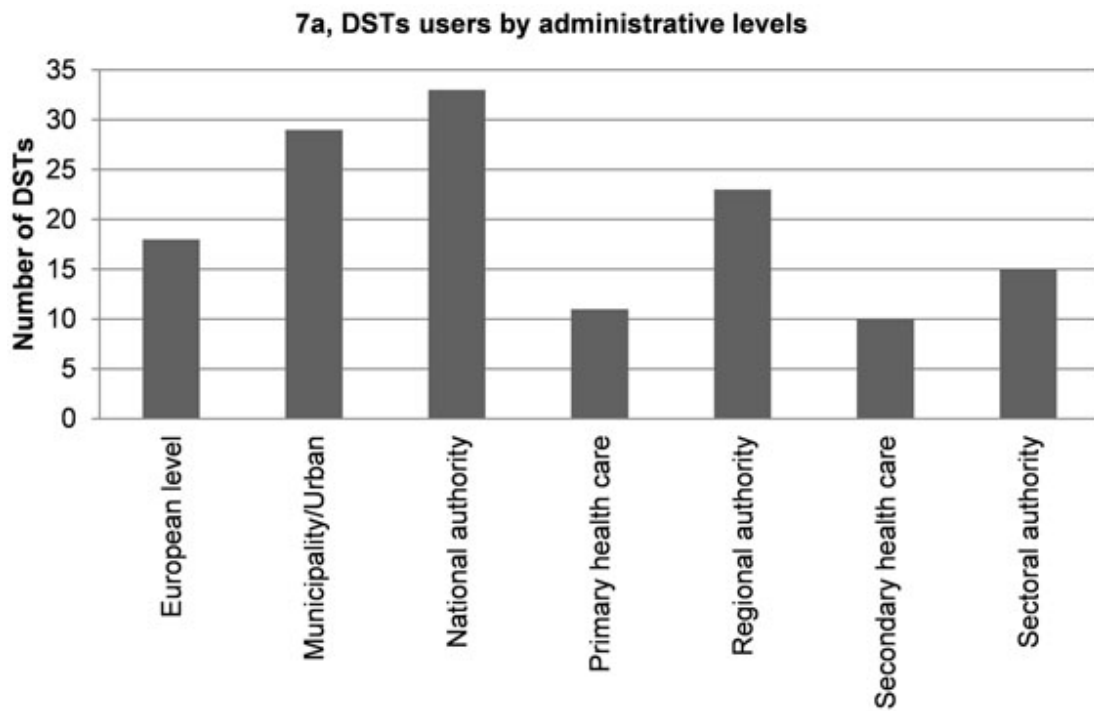
build on, for which there was no capacity in the current project. From this point of view, HENVINET has undertaken the first step in classifying DSTs in the area of health and environment.

From the point of view of supporting system analysis, many of the existing DSTs are classified as 'software models', with a majority having a 'single type' characteristic (e.g., one environmental stressor, one type of



disease). Only a few have a more universal character. In addressing the natural complexity of E&H issues and using the most suitable methodology, there is a need to define or identify a universal framework encompassing

this variety of tools. As a preparation for such activity, the achievements of existing health impact assessment (HIA) frameworks, e.g., the HIA framework defined by WHO, should be investigated. Currently, more general



7b, Number of administrative levels who can use a DST

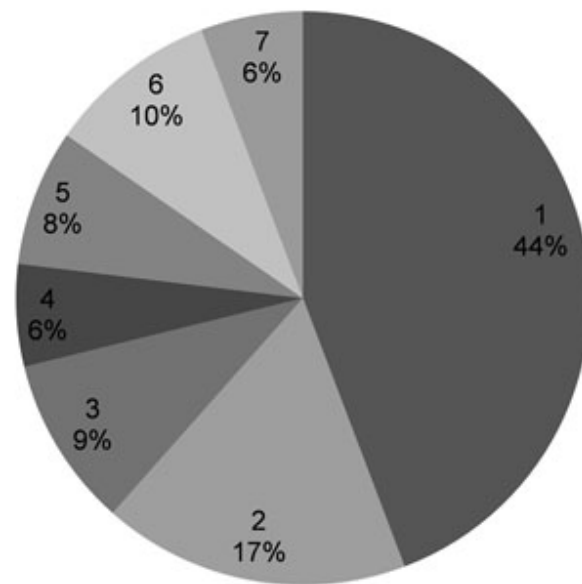
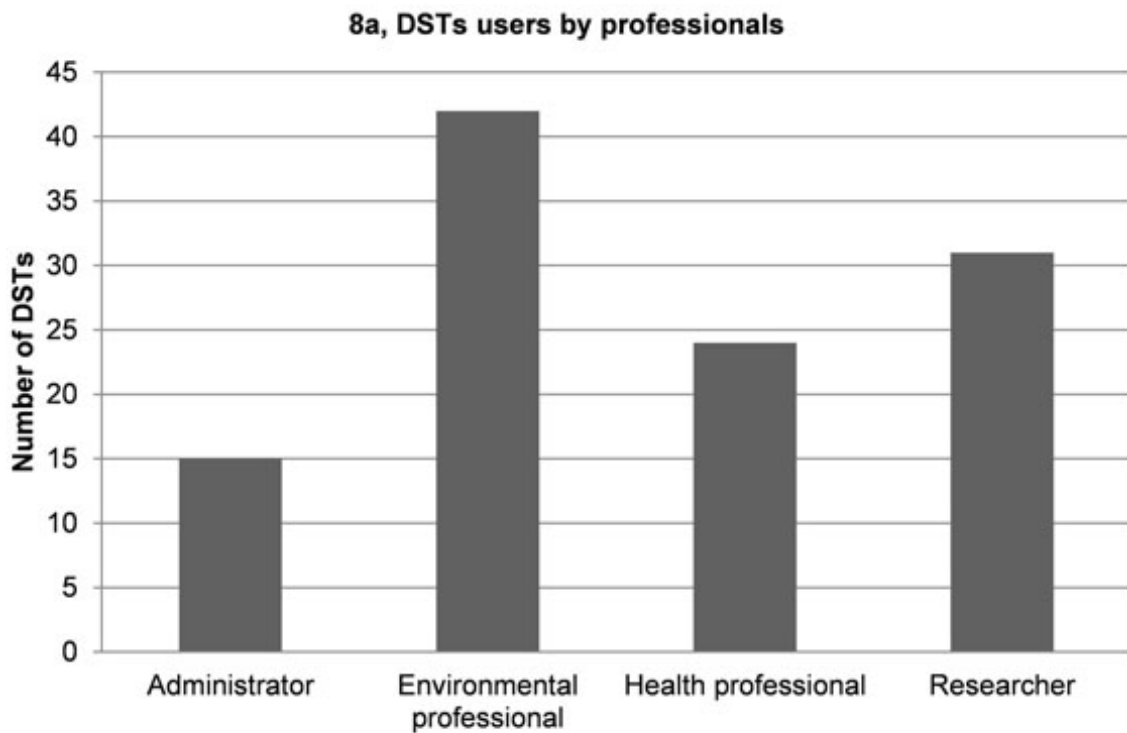


Figure 7 The intended administrative levels users for DST.

methodologies are being developed, amongst them is the toolbox on integrated environmental health impact assessment system (<http://www.integrated-assessment.eu>) developed by EU FP6 projects HEIMTSA (Health

and Environment Integrated Methodology and Toolbox for Scenario Assessment) (<http://www.heimtsa.eu>) and INTARESE (Integrated Assessment of Health Risks of Environmental Stressors in Europe) (<http://www.>



8b, Number of different types of professionals who can use a DST

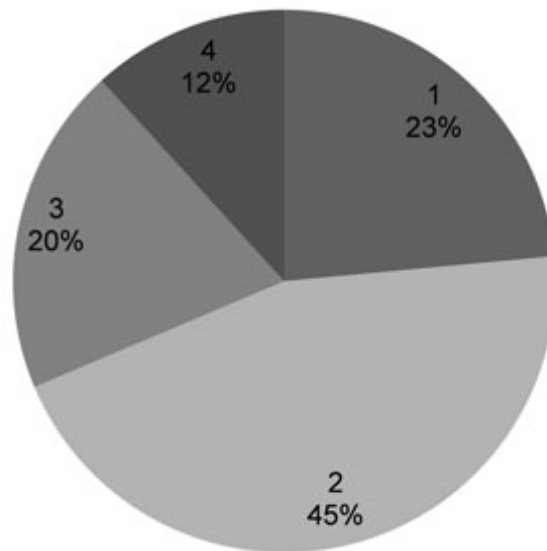


Figure 8 The intended professional users for DSTs.

intarese.org), as well as an interactive wiki-based platform for communication - the Open Assessment Network (<http://www.opasnet.org>), which is mainly supporting open environmental assessments.

The present evaluation of E&H DSTs aimed to provide an overall and general idea of the quality and usability of the tools, based on six aspects (applicability, causal chain approach, robustness, uncertainty, user

application history and user friendliness, Fig.2). This choice of aspects represents a compromise between the academic-scientific approach and the expected difficulties for users to reply with high confidence and credibility to the questions included in the online MDB.

In terms of the DST validation, the most striking points emerging from the analysis are: 1) only 3% of DSTs claim to deal with all 36 stressors; while 2) 25% of DSTs deal with only one stressor; and 3) 50% of DSTs deal with only one disease/issue. This leads to the question whether it is feasible or useful to stimulate the creation of DSTs covering more stressors and more diseases/issues. Such an integrative trend seems desirable. In designing a policy, it is essential to know the impacts on a given aspect e.g., of local importance, but limiting ourselves to a single issue, albeit perceived as the most important one at a given time, will lead to unbalanced decisions and possible long-term harm. The goal of a 'multi diseases tools' is evident, as is the need for 'all stressors based' DSTs. How can we assess environmental health if we do not consider the known or suspected stressors and effects? The development of methodologies and software tools covering increasing numbers of environmental stressors and health end points should be pursued, notwithstanding the inevitable difficulties that this implies.

Half of the DSTs are applicable for only one decision making area. What is the effect of this? We have identified 10 decision making areas (Fig. 6a), and 50% of DSTs cover only 1 of them. This is a consequence of the high number of DSTs covering only few stressors and dealing with only few diseases.

Regarding the administrative levels and the type of users using E&H DSTs, we noticed a remarkable dominance of environmental scientists and researchers compared to administrators and health professionals using DSTs. As a consequence, there is a need to develop DSTs for a wider application context, relevant to more decision making areas, and in particular, suitable for use by administrators and health professionals.

The project has identified 110 DSTs, but despite considerable effort, has managed to get structured information on only 60% of those. Better recognition of the need to identify the multiplicity of the tools, and their wider review, seems to be necessary.

Conclusions

We have developed a common framework for DSTs in the E&H field that allows for "issues" or "systems" thinking rather than "discipline" thinking, and we have started information gathering, classification and evaluation. We have delivered a product – an operational web-based searchable DSTs MDB. The framework for DST information gathering is general, and in our opinion can cover many more areas of use and application

of DSTs. The categorisation, evaluation and application descriptors are a workable compromise of our ideas of what is useful for the user to know, in order to choose an appropriate DST.

It has not been the aim to formally validate each individual DST. This is the task of any responsible DST provider, who should document their tools in a manner that would provide the user with confidence in the product.

Different DSTs that are relevant to any single disease/issue may have different inputs. This indicates that they use different determinants to achieve the same outcome, and are based on different partial understanding of underlying mechanisms. Since recommended actions are directed at changing/reducing the determinants, different DSTs will provide different advice to address the same disease/issue. Therefore there is a bias resulting from the uneven availability of information, favouring information that is readily available over perhaps more relevant but not so easily available information. This stresses the importance of the initiatives at both European and global levels that aim to secure comparable information on DSTs in the area of health and environment, and for more research on the issues linking environment and health. It also underlines the need to maximise thorough and systematic documentation of existing DSTs, using common criteria. This current work is one step on the way.

Additional material

Additional file 1: Questionnaire for information gathering on decision support tools

Additional file 2: Contact person information and decision support tools information

Additional file 3: Overview of 67 DSTs with their name, category, contact person, location, and web link (— means no available information on contact person, location or web link).

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Authors' contributions

HYL and AB planned this work. HYL wrote the manuscript, revised data analysis. All authors contributed to the concept development and implementation. PN, CH, EN, HYL and AY were in charge of the implementation and data gathering. MJK was in charge of the design of the technical solutions, MJK and AY were responsible for technical implementations and support. PN and CH did data analysis. AB thoroughly revised the manuscript. EN was responsible in the project for the DST work, AB was the project coordinator. All authors approved the final version.

Competing interests

The authors declare that they have no competing interests.

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Attachment 6

Bartonova A, Jovasevic-Stojanovic M: Integrated assessment and management of ambient particulate matter – international perspective and current research in Serbia. *Chemical Industry and Chemical Engineering Quarterly* 18(4/II), 605-615, (December 2012)

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REVIEW PAPER

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INTEGRATED ASSESSMENT AND MANAGEMENT OF AMBIENT PARTICULATE MATTER - INTERNATIONAL PERSPECTIVE AND CURRENT RESEARCH IN SERBIA

Air pollution mitigation is a necessity in Serbia, due to its high levels of criteria pollutants in ambient environment. Successful implementation of mitigation measures requires access to sufficient information from national research, and well running and efficient local participatory processes. To support air pollution mitigation in the West Balkan region, the WeBIOPATR project started a series of bi-annual conferences in 2007. They bring together an inter-disciplinary research community and local and national administrations from Serbia and its neighbourhood, to present research results from Serbia and countries all over the world, and to share knowledge and best practices of mitigation. The conferences promote research that may support integrated assessment of particulate matter, and further refinement of the "Pressures-State-Impact" (PSI) part of the "Drivers-Pressures-State-Impact-Response" (DPSIR) framework. Integrated approach needs to be underpinned by solid disciplinary research covering, e.g., air quality monitoring technologies, atmospheric and further ambient composition, atmospheric modelling, biological effects and human health. WeBIOPATR conferences report on recently performed studies of particulate matter in Serbia and abroad. Through the breadth of subjects and audience, they bring together a wide inter-disciplinary and cross-sectoral expertise in support of translation of research to practice. They also allow to present examples of successful mitigation achieved with the help of strong local participatory environmental governance, demonstrating the increasing recognition of the need to involve both public and private actors. This paper gives the main features of a full chain approach and elements of integrated approach to particulate matter research, summarizes the proceedings of the 3rd WeBIOPATR conference, and in addition, reviews the results of particulate matter monitoring and source identification studies in Serbia since the monitoring start ten years ago.

Keywords: particulate matter; integrated assessment; sources; modeling; exposure; health effects.

BACKGROUND AND AIM OF THE CONFERENCE

In Europe, air quality is regulated by legislative instruments developed in broad consensus process going back several decades. The legislation aims at protecting human health and natural ecosystems. Particulate matter (PM) is one of the main air pollu-

tants, receiving attention due to its documented adverse effects on human health. Despite the long-term focus, levels of particulate matter remain above the set limit values in many areas. This is due to increasing activities in economic sectors that contribute to particulate pollution, as well as to natural processes and events. Mitigation requires thorough scientific understanding of the issues, and a wide collaboration of legislators and administrators with the society, including economic actors, civil society and research.

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PM arising both from primary emissions and as a result of secondary formation in the atmosphere is an extensively studied, but still not sufficiently understood, atmospheric pollutant. In the EU, the legislation development, implementation, societal acceptance and the underlying research on PM in outdoor and indoor environment have long tradition. In the West Balkan countries, including Serbia, only total suspended particles (TSP) were recognized as a criteria pollutant for a long time, and smaller fractions of PM, measured and regulated elsewhere, have received less attention. In the last decade, superposition of the EU legislation and the need to find practical ways to implement it changed focus from TSP to PM and its fractions, and has brought about a number of activities [1]. The WeBIOPATR project (2006-2009) aimed at generating data on PM, and at supporting communication between all actors in Serbia through workshops/conferences. The third conference (2011) continued the bi-annual cycle, after the initial project was completed.

The conferences [1-4] address atmospheric PM, the air quality constituent that is currently responsible for most instances of non-compliance with air quality directives in Europe. They aim to provide insight into integrated assessment and to support successful PM mitigation. They also provide the much needed communication platform for exchange of views and perspectives between the regulatory and the research community in Serbia. Such platform can serve as a link and a mediator that provides for the necessary discussions [5], thus facilitating uptake of research results by the decision making community and increasing the understanding by the research community of the decision-makers perspectives.

This article defines the framework for management of PM, summarises the conference contributions that include results of all recent relevant Serbian research projects, and provides an overview of PM levels measured in Serbia since the start of PM monitoring in 2002.

INTEGRATED ASSESSMENT FRAMEWORK WITH DETAILED EXPOSURE ASSESSMENT

Air quality management was introduced in a keynote lecture outlining practical steps in air quality management and giving a summary of European current practice [6], and providing a methodological background and an integrating framework. Successful mitigation of PM problem requires understanding from many disciplines, and this poses great challenges to both disciplinary skills and communication between different participants. Insights into problems that arise

in the communication process are provided by Keune *et al.* [7]. The authors illustrate the different perspectives of the scientists and of the decision-makers, and offer guidance on how these perspectives can be taken into account for the benefit of providing lasting solutions. A common framework helps both to define an understandable structure within which to address each problem, and to effectively communicate across professions [6].

Frameworks used for assessments that support mitigation of air pollution were reviewed e.g. by Liu *et al.* [8]. The authors put weight on the need to protect human health, and identify the necessary information and knowledge elements and available technical tools. Several examples of integrated assessment as a support to design strategies for mitigation of air pollution can be found in the literature, perhaps starting from the Rains model [9] and the ExternE project [10] that have laid basis for modern European air quality legislation. This kind of “integrated assessment” is closely linked with economic assessment of the costs and benefits of mitigation measures. The “integration” follows the “Drivers-Pressures-State-Impact-Action” [11] approach that allows building an operational model to address the expected effects of pollution mitigation scenarios on human health and ecosystem status. To assess the links between environment and health requires further refinement of the “Pressure-State-Impact” part of the framework, and more emphasis on the societal involvement. This can be done in a framework of Integrated Environmental Health Impact Assessment (IEHIA) [12].

In the recently completed HEIMTSA project [13], the research basis for outdoor air quality management was reviewed and complemented. HEIMTSA suggests using a methodology closely linked to the IEHIA, the “full chain approach”, *i.e.*, strengthened “people”- related element in the assessment: the social and economic context, individual and group behaviour, and perceptions of risk. In common with the IEHIA approach, this extension of integrated assessment highlights the development of an exposure assessment. Exposure links the environmental status (air quality) and effects. Allowing for differences in exposure patterns and health responses between groups or individuals allows development of mitigation strategies that protect vulnerable groups. Controlling the levels to which individuals are exposed by limiting the contact of individuals or special groups with air pollution, *e.g.*, by providing air pollution warnings or by suggesting alternative behaviour, is a widely used approach that complements the control of pollution through minimizing emissions at the source.

The HEIMTSA team has also developed an example [14,15] that quantifies the effect of concentration gradients of gaseous compounds between background and “hot spots”, and the effect on the overall exposure of different time spent by different population groups in certain micro-environments (outdoors, in traffic, at home and at work). An exposure scaling factor, ESF, is calculated based on a combination of data on time spent in the selected micro-environments by different demographic groups (by gender, age groups, employment status); it is a weighted average of concentrations in given micro-environments, with weights corresponding to the time spent in each microenvironment, specific for each population group. The population data are derived from European-level datasets from the Harmonized European Time Use Survey, HETUS [16], and the Multinational Time Use Study, MTUS [17]. Furthermore, the ESF utilizes the fact that both HETUS and MTUS provide individual level data, and allows a presentation as a probability distribution. Gerharz *et al.* [14] estimated that seniors (65 years of age and older) have clearly the lowest exposure values, while children are exposed the most: their median exposure is about twice as high as that of seniors. This has wide implications for public health, and should lead to special mitigation measures: children are considered an especially vulnerable population group with respect to air pollution, and this result indicates that they are the most highly exposed.

The example of exposure scaling factor also illustrates how exposure assessment often needs to draw on different kinds of information sources and techniques, ranging from sociological data on population behaviour to modelled data on future air quality derived from advanced European-level dispersion modelling. Linking these data is not trivial. A number of sources of data exist, not least the European database ExpoFacts [18]. Work on exposure scaling factor provides a good insight into the complexities of population exposure, and it clearly illustrates the need to differentiate between different population groups when designing mitigation strategies for air pollution.

Indoor air quality

While the relationships between outdoor air pollution levels and health are beyond doubt, the role of indoor environment receives less research attention. A recent EU FP6 research coordination action EnVIE [19] has reviewed the state of knowledge as well as means to address the issue. One of the challenges is an understanding of formation of secondary aerosols in indoor air [20].

The indoor environment is legislatively a difficult one due to the many public and private actors involved [21]. In addition, information about indoor air quality is generally lacking, and there are almost no attempts to set up systematic monitoring programs. A recently funded European Observatory on Indoor Air SINFONIE [22] is developing a monitoring framework and collects data for assessment of health-related aspects of European schools. Several related projects are also in place in Serbia. The ratio of concentrations in indoor and outdoor kindergarten micro-environment located in the city centre of Belgrade next to a busy street was investigated for pollutants specific for traffic urban environment (PM_{10} and $PM_{2.5}$, priority PAHs and metals and metalloids) [23] while metals, metalloids and secondary aerosol were analysed representing exposure in kindergarten located in a vicinity of a copper smelter in the city of Bor, and in a traffic exposed area of Niš [24,25].

ATMOSPHERIC MONITORING AND MODELLING AS A BASIS FOR MITIGATION

Air quality monitoring and modelling are the two main methods used to assess the levels and trends in air pollution. On regional basis in Europe, the European Monitoring and Assessment Program [26] provides an assessment framework for PM that combines monitoring and atmospheric dispersion modelling in an integrated assessment framework [27]. The program is in operation since 1972, with PM (as PM_{10} and $PM_{2.5}$) measurements going back to mid-1990s [28]. The modelling done in this program was presented by Tsyro [29]. In urban areas, monitoring is done on the basis of the Clean Air for Europe thematic strategy resulting in the Directive 2008/50/EC [30] on ambient air quality and cleaner air for Europe that specifies standards for both PM_{10} and the potentially more health relevant fraction $PM_{2.5}$. A comparison of the regional background measurements of EMEP with the urban background $PM_{2.5}$ data reported in the European Air Quality Database - AirBase [31] shows that more than 60% of the urban background concentration is likely to be attributed to the rural background contribution [32]. While regional levels of PM have been somewhat reduced over time [27], there is a wide non-compliance with the air quality standards for both PM fractions in urban areas [33]. In Serbia, the recently finished twinning project “Strengthening Administrative Capacities for Implementation of Air Quality Management System” (autumn 2009-spring 2012) will undoubtedly contribute to the improvement of implementation of Air Quality legislation [34,35].

PARTICULATE MATTER LEVELS AND SOURCE CONTRIBUTION IN SERBIA

Serbian ambient PM monitoring at state and local level and research projects that measured PM on campaign basis were reviewed in connection with the 2nd WeBIOPATR workshop [1]. Currently, automatic monitoring networks in Serbia operate at national level under the Serbian Environmental Protection Agency (SEPA) [36], and at local level in two areas under the Province of Vojvodina Secretary of Urbanism, Construction and Environmental Protection [37] and under the Municipality of Belgrade [38]. The number of PM₁₀ monitors is similar in 2012 as in 2009 [1]. Table 1 summarizes 24 h levels and number of exceedances of limit values at automatic monitoring stations in Serbia in 2010 and 2011 [39,40]. Since 2010, three additional PM monitoring stations were established in industrial areas. In the southern and western part of Serbia, there are no urban sites equipped with PM automatic monitors.

Table 2 presents levels of PM fractions PM_{2.5} and PM₁₀ on available urban automatic monitoring sites (Zrenjanin and Novi Sad) or during campaigns (Zrenjanin, Bor, Vršac, Kikinda and Belgrade) performed in Serbia during the last decade [23-25,41-48].

Compared to EU countries, there is a lack of PM data from Serbian rural areas. Tasic *et al.* [49] compare PM₁₀ and PM_{2.5} in urban industrial area and in its rural surroundings. There is a significant seasonal

difference in PM_{2.5} levels on all rural sites, because they are affected by domestic heating emissions in cold periods. PM levels in the urban area of Bor are more influenced by the air pollution from the Copper Smelter Complex than by rural settlements.

Source contribution, regional transport and health effects can be determined from a more detailed analysis of PM. Prior to 2002, there is no PM₁₀ data in Serbia. Mijić *et al.* [50,51] present results of receptor modelling based on 10 metals analyzed in PM₁₀ fraction collected on 3 sampling sites in Belgrade in 2003-2006. Using the Unmix model, they identified 4 factors, representing contribution to PM concentrations from fossil fuel combustion, traffic exhaust, regional transport from industry in the surroundings of Belgrade and mineral/crustal matter. A PM database with metals, cations and anions from a later period was similarly analyzed applying Unmix by Joksic *et al.* [52] and applying PMF by Cvetkovic *et al.* [53]. For the first time in Serbia, the later assessed source contribution to PM₁₀ and PM₁ of 16 EPA PAHs in winter and summer period of 2009 [54].

Milutinović *et al.* [55] present a method for assessment of contribution to local PM levels of thermal power plant landfills. They combine concentration monitoring and Gaussian modelling to estimate ash resuspension and a dust cloud occurrence and location in real-time. This enables the landfill operator to take measures to reduce harmful effects downwind in the vicinity of the ash dump.

Table 1. Observed PM₁₀ 24 h levels at automatic monitoring stations from national and local networks in Serbia in 2010 and 2011

Automatic station location		Annual average, µg/m ³		Number of 24 h limit value exceedance		Maximum, µg/m ³	
		2010	2011	2010	2011	2010	2011
Belgrade	Bulevar Despota Stefana	37	79	66	181	192	536
	Stari Grad	37	52	152	132	156	250
	Pančevački most	48		115	-	178	-
	Zeleno brdo	47	53	103	134	232	293
	Zemun	47		74	-	385	-
	Mostar	41	51	86	129	162	224
	New Belgrade 1	37	41	57	94	769	216
	New Belgrade 2	-	69	-	175	-	344
Belgrade Metropolitan	Lazarevac	53	-	115	-	226	-
Pancevo	Obrenovac M. Milan 3	-	75	-	164	-	473
	Obrenovac Centar	-	69	-	186	-	278
Smederevo	Starčevo	60	-	149	-	252	
	Vojilovica	40	48	79	107	313	311
Novi Sad	Radinac	60	85	161	258	269	355
	Ralja		69	-	208	-	251
Bor	Dnevnik	36	45	62	102	113	147
Niš	Municipal Park	31	-	36	-	80	-
Kosjerić		51	67	123	167	197	255
		-	63	-	159	-	270

Table 2. Overview of monitoring instruments, sampling periods and levels of PM₁₀ and PM_{2.5} observed at automatic stations or during campaigns in cities in Serbia; μ - average value ($\mu\text{g}/\text{m}^3$), σ - standard deviation

Sampling site(s)	Sampling period and duration	Sampling instrument and flow	Main results and remarks	Ref.
Belgrade, 3 sampling sites in city center	June-December 2002; 24 h data sets; 47 of PM ₁₀ and 49 of PM _{2.5} samples	Mini-Vol LVS Airmetrics, Co. Inc. / 5 lpm	PM ₁₀ : $\mu = 56$ summer, $\mu = 96$ winter PM _{2.5} : $\mu = 35$ summer, $\mu = 75$ winter	41
Belgrade, 2 sampling sites in city center	June 2003-July 2005, 209 PM ₁₀ and 64 PM _{2.5}	Mini-Vol LVS Airmetrics, Co. Inc. / 5 lpm	PM ₁₀ : $\mu = 68$ ($\sigma = 46.4$); PM _{2.5} : $\mu = 61.4$ ($\sigma = 52.2$)	42
Belgrade, 1 sampling site	November 2007-May 2008, PM ₁₀ , PM _{2.5} and PM ₁ 4 seasonal campaigns each 20 days, 24 h data sets	LVS Leckel / 37,3 lpm	PM ₁₀ : $\mu = 96$ autumn, $\mu = 89$ winter, $\mu = 40$ spring, $\mu = 40$ summer PM _{2.5} : $\mu = 73$ autumn, $\mu = 66$ winter, $\mu = 22$ spring, $\mu = 32$ summer PM ₁ : $\mu = 48$ autumn, $\mu = 38$ winter, $\mu = 14$ spring, $\mu = 11$ summer	43,44
Belgrade, 1 sampling site	November 2008-November 2009, PM ₁₀ , PM _{2.5} and PM ₁ 4 seasonal campaigns each at least 20 days, 24 h data sets	LVS Leckel / 37,3 lpm	PM ₁₀ : $\mu = 23.1$ summer, $\mu = 69.7$ winter PM _{2.5} : $\mu = 12.8$ summer, $\mu = 49.8$ winter PM ₁ : $\mu = 8.8$ summer, $\mu = 28$ winter	45
Belgrade, 1 sampling site, city center	March-May 2010, PM ₁₀ and PM _{2.5} 40 days, 24 h data sets	LVS Leckel / 37,3 lpm	Belgrade (traffic-residential) PM ₁₀ : $\mu = 44.84$ PM _{2.5} : $\mu = 40.04$	23
Novi Sad, AMS, state network	November 2009-July 2011, PM ₁₀ continuous monitoring	GRIMM	$\mu = 38.35$, $\sigma = 26.27$ Rush hours: 7-10 h and 18-22 h slight increase, while slight decrease over weekend -heating period $\mu > 40$, nonheating $\mu < 40$	46
Zrenjanin, AMS, regional network	2005-2007, PM ₁₀ continuous monitoring	MP101 Teom	Daily average calculated for 676 days: $\mu = 33.76$; nonheating period 417 samples $\mu = 27.95$, exceedance 7.43%; heating 263 samples $\mu = 42.68$ exceedance: 28.51%	47
Bor, Niš	September 2009-July 2010, PM ₁₀ and PM _{2.5} 4 seasonal campaigns each 20 days in both towns, 24 h data sets	LVS Leckel / 37, 3 lpm	Bor (residential-industrial): PM ₁₀ : $\mu = 34.1$ summer, $\mu = 53.4$ winter PM _{2.5} : $\mu = 22.8$ summer, $\mu = 42.5$ winter Niš (residential-traffic): PM ₁₀ : $\mu = 31.8$ summer, $\mu = 57.7$ winter PM _{2.5} : $\mu = 23.8$ summer, $\mu = 42.5$ winter	24,25
Pančevo, Vršac, Zrenjanin, Bor, Kikinda, 1 sampling site per city	Summer and autumn 2011, PM ₁₀ 6 days	LVS 24 h gravimetric data set and/or TSI-DRX Dust Track, continual data, 10 sec resolution	Pančevo (urban): TSI: $\mu = 40.91$ ($\sigma = 3.02$), LVS: $\mu = 40.40$ ($\sigma = 4.40$) Vršac (urban): TSI: $\mu = 43.34$ ($\sigma = 6.07$), LVS: $\mu = 47.04$ ($\sigma = 4.55$) Zrenjanin (urban): TSI: $\mu = 43.75$ ($\sigma = 6.87$) Bor-Krivelj (industrial): TSI: $\mu = 41.48$ ($\sigma = 7.46$) Kikinda-Banatsko Novo Selo (rural): TSI: $\mu = 12.87$ ($\sigma = 2.17$), LVS: $\mu = 13.61$ ($\sigma = 2.17$)	48

Table 3 presents an overview of receptor studies using PM fractions collected in Serbia (Belgrade, Niš and Bor), analyzed for species including heavy metals, cations and anions and/or PAHs [42-44,49, 51,53,56-58].

PARTICULATE MATTER AND HUMAN HEALTH

Human health has been the main driver of European air quality legislation. Katsouyanni [59] and Jovanovic Andersen [60] summarize current findings on respectively, long-term and short-term effects of particulate matter on human health. Despite the large number of studies μ and the undisputable observed ef

Table 3. Overview of receptor modelling studies for PM in the Belgrade region; LVS - low volume sample; lpm - liter per minute; Dp - particle diameter; FAAS - flame atomic absorption spectrometry; AA - atomic absorption spectrometry; GFAAS - graphite furnace atomic absorption spectrometry; SEM/EDX - scanning electron microscopy/energy dispersive x-ray, OC/EC - organic/elemental carbon; HPLC - high performance liquid chromatography; HRMS-TOF - high-resolution mass spectrometer time of flight; ICP-MS - inductively coupled plasma-mass spectrometer; IC-OES - inductively coupled plasma - optical emission spectrometer; PSCF - potential source contribution function; CWT - concentration weighted trajectory; N, NW, W, SW, S, SE, E, NE - geographic directions, PCA - principal component analysis; UNMIX - multivariate receptor model; PMF - positive matrix factorization

Sampling site(s) location	Period of collecting and no. of samples	Sampling instrument(s)/sampling flow	Analyses	Main results and remarks	Ref.
Belgrade, 3 sampling sites in the city centre	Jun 2003 -Jul 2005 50 PM ₁₀ samples	Mini-Vol LVS Airmetrics, Co. Inc. sampling flow 5 lpm; Teflon and Quarz filters, PM _{2.5} , PM ₁₀	Perkin Elmer FAAS, AA 200 and GFAAS AA 600: Pb, Cu, Zn, Mn, Fe, Cd, Ni, V, Al, Cr	UNMIX modelling-PM _{2.5} ; Fossil fuel 40%, metallurgical industry 13%, resuspended road dust 47%. PSCF and CWT: PM ₁₀ high probability for NW and W; V similarly distributed in NE, Al and Mn dominant from local sources, Mn transport from SE.	56,57
Belgrade, 3 sampling sites, city centre	Jul 2003-Dec 2006, 277 24 h PM ₁₀ samples	Mini-Vol LVS Airmetrics, Co. Inc. sampling flow 5 lpm; Teflon and Quarz filters, PM ₁₀	Perkin Elmer FAAS, AA 200 and GFAAS AA 600: Pb, Cu, Zn, Mn, Fe, Cd, Ni, V, Al, Cr	UNMIX modelling-PM ₁₀ ; Fossil fuel 34%, regional transport mainly from steel and petrochemical industry 26%, resuspended road dust (19%) and traffic exhaust (21%). PSCF and CWT: PM ₁₀ high concentrations probability W-SW and S pathway.	50
Belgrade, 3 sampling sites, city centre	2004-2008, 24 h PM ₁₀ and PM _{2.5} samples	Mini-Vol LVS Airmetrics, Co. Inc. sampling flow 5 lpm; Teflon and Quarz filters, PM _{2.5} , PM ₁₀	Perkin Elmer FAAS, AA 200 and GFAAS AA 600: Pb, Cu, Zn, Mn, Fe, Cd, Ni, V, Al, Cr; SEM/EDX, JEOL 840A with INCAPentaFETx3	PSCF, CWT modelling: most frequently arriving directions W, NW, SW, during winter period N and SE; major contribution of PM ₁₀ from local and regional sources; PM _{2.5} in heating period mean size value 1.32 µg (σ = 0.52), while 0.44 µg (σ = 0.27) in non-heating period	57
Belgrade, city centre, 1 sampling site	Jun-Dec 2008; 36 samples, every 6 th day	HV Cascade Impactors, Model TE-236, collected particles size range; Dp < 0.49, 0.49 < Dp < 0.95, 0.95 < Dp < 1.5, 1.5 < Dp < 3.0, 3.0 < Dp < 7.2 and Dp < 7.2 µm	IC system Metrohm, type 761 Compact IC, conductometric detector: Na, NH ₄ , K, Mg, Ca, Cl, NO ₃ , PO ₄ , SO ₄	Mean mass concentration show maximums in 0,49 < Dp < 0,95 and Dp > 7,2 µg/m ³ range. The absolute highest concentration is SO ₄ ²⁻ in the range 0,49 < Dp = 1.55 µg/m ³ . Main sources for the generation of the particles were the gas precursors SO ₂ and NH ₃ over Belgrade urban area. PCA suggested the influence of marine aerosol	58
Belgrade, 1 sampling site	2007-2008	LVS Leckel/37.3 lpm	ICP-OES: Al, Ba, Ca, Fe, K, Mg, Na, Ti, Zn ICP-MS:As, Cd, Co, Cr, Cu, Mn, Mo, Ni, Pb, Sb, Se,V; IC:NO ₃ ⁻ , SO ₄ ²⁻ , NH ₄ ⁺ , K ⁺ , Ca ²⁺ , Na ⁺ . TOT: OC/EC, HPLC and HRMS-TOF: biomass burning tracers	UNMIX modelling PM ₁₀ : winter: Biomass burning (52%), crustal/soil (36%), gasoline (5%), diesel (5%), secondary aerosols (2%) source; summer: soil/crustal (28%) and secondary aerosols (27%) dominant sources, diesel (14%), gasoline (11%), wood burning (20%); Diesel and gasoline contribution was higher during the summer (25%) than during the winter period (10%).	43,44,52
Belgrade, 2008-2009, 1 sampling site	2008-2009, 24 h about 40 samples per PM fraction and heating period, total samples	LVS Leckel/37.3 lpm	ICP-OES: Al, Ba, Ca, Fe, K, Mg, Na, Ti,Zn; ICP-MS:As, Cd, Co, Cr, Cu, Mn, Mo, Ni, Pb, Sb, Se,V; IC:NO ₃ ⁻ , SO ₄ ²⁻ , NH ₄ ⁺ , K ⁺ , Ca ²⁺ , Na ⁺ .	PMF modelling metals, cations and PM _{2.5} : winter mixed coal-fired thermal power plant and fuel oil combustion in heating plants (29.9%); diesel and gasoline (27.7%); (secondary aerosol (23.1%); resuspended dust from road (10%); mixed resuspended salt from road and coal combustion from domestic heating (9.2%). Summer: PMF modelling PAH in PM ₁₀ : winter: coal and oil combustion 62.1% (~18 ng/m ³) diesel and gasoline 30.4% (~8.8 ng/m ³), wood burning 7.5% (~2.9 ng/m ³). Summer: coal and oil combustion 29.8 % (~0.7 ng/m ³), diesel and gasoline 37.2 % (~ 0.9 ng/m ³), 33.2 % (~0.9 ng/m ³) wood burning.	45,53,54

fects, the mechanisms of action are not fully understood. Stankovic and Zivkovic [61] provide an overview of current knowledge on mechanisms of action of air pollution related to asthma, one of the most studied types of health end point.

Many studies point out that toxicological characteristics of locally collected PM fractions are necessary as a basis for locally valid health assessment. A study published in this issue [62], details an analysis of impact on human health of urban PM in the largest North Italian city Milan. Molecular markers of exposure were used as characteristics of effects of summer and winter PM₁₀ and PM_{2.5}. Results of in vitro and in vivo testing show the need for a comprehensive knowledge of PM composition and sources in a given region. For Milan, it was shown that the most cytotoxic and pro-inflammatory fraction in summer was PM₁₀ enriched in crustal elements and endotoxins. In winter, the fine fraction PM_{2.5} induced a stronger effect than PM₁₀: genotoxic effects and xenobiotic metabolizing enzymes (like CYP1B1) production increased as a consequence of the higher content of combustion derived particles rich in PAHs and heavy toxic metals.

Several epidemiological results are already available from Serbia for the last decade. For the first time in Serbia, short-term effects of air pollution on cardiovascular hospitalization were quantified on an elderly population in the Niš region [63]. Although the authors report increased risk of total hospitalizations, their results did not support findings from previous studies that showed an increase in number of cardiovascular hospitalizations in elderly in association with increase of 10 µm/m³ of black smoke measured using a refractometry method.

Environmental tobacco smoke (ETS), a source of numerous gaseous and particulate pollutants in indoor environment, poses a recognized health concern. An epidemiological study was done on 708 children aged 11-14 years from the city of Niš [64]. Smoking in the home was associated with an increased respiratory symptoms (dyspnea, wheezing), bronchitis and asthma.

PARTICIPATORY GOVERNANCE AS PART OF MITIGATION SOLUTIONS

Development and implementation of research based mitigation measures requires a wide societal dialogue, where the decision makers, the scientists and a variety of other societal actors are partners. According to Kingdon [65], for a policy to be formulated, a collusion of three factors is to be in place: the research has to recognize a problem and offer its so-

lutions, the means necessary for the solution are to be available, and there is to be a wider political consensus.

The process can be seen as consisting of three stages: consensus within science, consensus between science and decision-makers, and consensus between the three actors - science, decision-makers and society. Recent examples can give some insight.

It is argued that to create a valid science, a dialogue between science and society is necessary. In atmospheric research, the ACCENT Network of Excellence [66] recognized the need to include a societal dialogue in knowledge productions, and argues that the research community is ready to do so [67]: "The dialogue between scientists and stakeholders should not be limited to the dissemination of results, but should involve stakeholders already from the early stages of problem identification" [68].

The issues of how to bring science nearer to decision-making have been studied by many. Recently, the HENVINET network [5,7] investigated how to create a network of all stakeholders to support environmental health decisions, and concluded that the mutual understanding of and respect for different perspectives is essential. This indicates that a participatory process of informing decision makers by science and scientists by the decision making is needed.

Several policy developments, most notably the UN CLRTAP [69], provide examples of successful implementation of research based legislative processes. Davidson and Nordbeck [70] give a historical overview of the development and implementation of the Clean Air Act in the USA, The appendix to this book offers an overview of actions of the Environmental Protection Agencies of individual States. Also, owing to the fact of the special autonomy status of Californian environmental legislation, the most comprehensive actions were taken by the Californian Air Resources Board (CARB). CARB employed a wide variety of approaches to develop and implement air quality legislation, in collaboration with stakeholders including the industries, the civil society groups, and researchers.

A successful example of a local air quality management program, "STOP PRACH" or "Stop Dust is briefly described by *Kotlik et al.* [71,72]. Open pit mining is a very controversial issue, as it affects large districts in a number of ways, and alters forever the local living conditions. In the neighbouring communities of a major open pit mine "Lom Bilina" in North Bohemia, CZ, levels of dust were perceived as extremely high, especially in episodes with atmospheric conditions favourable to dispersion of dust. In response to the public demand, an initiative STOP PRACH

(Stop Dust) was formed as collaboration between the mine owner, the most affected municipalities, local NGOs and the Ministry of Environment. National bodies responsible for air quality monitoring and assessments and public health protection contributed with research. The public was also invited as a partner in the process.

An assessment of the air quality situation and contribution of the main sources to PM₁₀ levels was a first step. The proposed goals of “Stop Dust” and simple municipal-level plans were accepted through a series of conferences, meetings, public consultations and negotiations with all local stakeholders, and recommended for implementation by the elected representatives.

The following factors are considered essential for achieving success [71]:

- A functioning partnership among all of the stakeholders.
- A “critical mass” of energy (interest, determination, time) from key interest groups.
- The existence of a true will to implement the proposed measures by the primary “movers”, the owners of the open pit mine.
- Government support.

The “Stop Dust” activity put an emphasis on providing credible scientific information to the affected parties, and on impartial managing of the discussion. “Stop Dust” produced a minimum of documents, and its support materials were very brief. It was primarily a communication, negotiation and decision-making process. This has contributed to a wide acceptance of the proposed solutions by all stakeholders.

CURRENT TRENDS AND FINAL REMARKS

The WeBIOPATR conference highlighted several issues to be addressed in the near future. First, it is the need to close a number of knowledge gaps in atmospheric sciences, atmospheric modelling and environmental health and social sciences. National data needs to be generated to allow monitoring of trends and of effectiveness of the implemented measures. This information needs to feed into a participatory process of decision making.

In addition, there are several exciting technological and scientific opportunities that may change the research methodologies as well as practice of the air quality management. New monitoring technologies respond to the needs of the environmental health research and allow, *e.g.*, for monitoring of oxidative capacity of combustion particles [73]. New monitoring approaches, including community based monitoring using ubiquitous sensing [74], offer a tool for involving

the public as well as to provide environmentally relevant information that can supplement existing monitoring and other information gathering systems. New activities in this direction are already being developed.

Issues of particulate matter pollution are rather pressing. The conference has further documented that without a broad cross-sectoral and societal alliances, they cannot be solved. It has contributed to common understanding of these issues, and enabled an improvement of tools, methods and measures suitable for use in air quality mitigation in Serbia.

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PREGLEDNI RAD

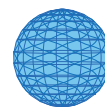
INTEGRALNA PROCENA I UPRAVLJANJE RESPIRABILNIM ČESTICAMA U AMBIJENTNOJ SREDINI - INTERNACIONLANA PERSPEKTIVA I TEKUĆA ISTRAŽIVANJA U SRBIJI

U skladu sa strogim kriterijumima o nivou aerozagađenja u ambijentnoj sredini, neophodno je da se smanji aerozagađenje i u Srbiji. Za uspešnu implementaciju mera za smanjenje aerozagađenja potrebno je da se raspolože sa dovoljno podataka na osnovu domaćih istraživanja i da se uspostavi efikasan proces učešća javnosti na lokalnom nivou. U cilju podrške procesu smanjenja aerozagađenja u regionu Zapadnog Balkana, tokom realizacije WeBIOPATR projekta započeta je serija konferencija koje se počev od 2007. održavaju svake druge godine. One povezuju interdisciplinarnu istraživačku zajednicu sa lokalnim i državnim vlastima Srbije i susednih zemalja, da bi se predstavili rezultati istraživanja u Srbiji i zemljama širom sveta i da se razmenila znanja i najbolje prakse za smanjenje aerozagađenja. Konferencije promovišu integralnu procenu respirabilnih čestica i bliže „Pritisak-Stanje-Uticaj” (PSI) u okviru „Pokretač-Pritisak-Stanje-Uticaj-Odgovor” (DPSIR) koncepta. Integralni pristup treba da se oslanja na istraživanja u okviru disciplina kao što su: tehnologije monitoringa aerozagađenja, sastav atmosfere uključujući i ambijentu sredinu, modelovanje atmosfere, biološki efekti i zdravlje ljudi. Na konferencijama su prikazane najnovije studije o respirabilnim česticama koje su sprovedene u Srbiji i inostranstvu. U interakciji između predavača i auditorijuma, izgrađuje se široka interdisciplinarna i višesektorska ekspertiza za podršku primene rezultata istraživanja u praksi. Takođe je omogućeno da se prezentuju primeri uspešnih akcija smanjenja aerozagađenja koji su ostvareni uz pomoć učešća lokalne uprave za zaštitu životne sredine, što ukazuje na rastuće potrebe da se uključi i javni i privatni sektor. Ovaj rad daje osnovne karakteristike celovitog lančanog pristupa i elemente intergalnog pristupa istraživanja respirabilnih, čestica, sumira naučne radove prikazane na 3. WeBIOPATR konferenciji, a pored toga daje i pregled rezultata monitoringa i identifikacije izvora respirabilnih čestica u Srbiji od početka merenja respirabilnih čestica u ambijentnom vazduhu u poslednjih deset godina.

Ključne reči: respirabilne čestice, integralna procena, izvor, ekspozicija, zdravstveni efekti.

Attachment 7

Bartonova A: How can scientists bring research to use: the HENVINET experience. *Environmental Health* 2012, 11(Suppl 1):S2 (28 June 2012).



METHODOLOGY

Open Access

How can scientists bring research to use: the HENVINET experience

Alena Bartonova

From HENVINET (Health and Environment Network) final conference
Brussels, Belgium. 14 April 2010 - 15 April 2010

Abstract

Background: Health concerns have driven the European environmental policies of the last 25 years, with issues becoming more complex. Addressing these concerns requires an approach that is both interdisciplinary and engages scientists with society. In response to this requirement, the FP6 coordination action "Health and Environment Network" HENVINET was set up to create a permanent inter-disciplinary network of professionals in the field of health and environment tasked to bridge the communication gap between science and society. In this paper we describe how HENVINET delivered on this task.

Methods: The HENVINET project approached the issue of inter-disciplinary collaboration in four ways. (1) The Drivers-Pressures-State-Exposure-Effect-Action framework was used to structure information gathering, collaboration and communication between scientists in the field of health and the environment. (2) Interactive web-based tools were developed to enhance methods for knowledge evaluation, and use these methods to formulate policy advice. (3) Quantification methods were adapted to measure scientific agreement. And (4) Open architecture web technology was used to develop an information repository and a web portal to facilitate collaboration and communication among scientists.

Results: Twenty-five organizations from Europe and five from outside Europe participated in the Health and Environment Network HENVINET, which lasted for 3.5 years. The consortium included partners in environmental research, public health and veterinary medicine; included medical practitioners and representatives of local administrations; and had access to national policy making and EEA and WHO expertise. Dedicated web-based tools for visualisation of environmental health issues and knowledge evaluation allowed remote expert elicitation, and were used as a basis for developing policy advice in five health areas (asthma and allergies; cancer; neurodevelopmental disorders; endocrine disruption; and engineered nanoparticles in the environment). An open searchable database of decision support tools was established and populated. A web based social networking tool was developed to enhance collaboration and communication between scientists and society.

Conclusions: HENVINET addressed key issues that arise in inter-disciplinary research on health and environment and in communicating research results to policy makers and society. HENVINET went beyond traditional scientific tools and methods to bridge the communication gap between science and policy makers. The project identified the need for a common framework and delivered it. It developed and implemented a variety of novel methods and tools and, using several representative examples, demonstrated the process of producing politically relevant scientific advice based on an open participation of experts. It highlighted the need for, and benefits of, a liaison between health and environment professionals and professionals in the social sciences and liberal arts. By adopting critical complexity thinking, HENVINET extended the traditional approach to environment and health research, and set the standard for current approaches to bridge the gap between science and society.

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Background

Human health linked with environmental quality has been on the European agenda for many years, leading to significant improvement in many areas. In 2003, the SCALE process led to the EU Environment and Health Strategy, developing a long-term vision seeking to address the links between poor health and environmental problems, and to “reduce diseases linked to environmental factors”. The following Environment Health Action Plan 2004-2010 (EHAP) [1] brought together current knowledge and identified 13 priority areas, of which four were dedicated to reviewing policies and improving collaboration and communication. The EHAP acknowledges multi-causality in environment and health, identifies priority health endpoints, and calls for a high level of inter-disciplinary knowledge and an ability to communicate within and between science and decision making community. The EU 6th Framework program responded by a call for proposals to “create a permanent network of professionals in environment and health”, specifically asking to address the EHAP health priorities (asthma and allergies, childhood cancer, neurodevelopmental disorders, and endocrine disruption). The call was answered by a 3.5 year HENVINET project.

The project established a wide collaboration between many disciplines and sectors, and it can serve as a comprehensive example of “inter-disciplinary” collaboration [2]. Inter-disciplinarity requires firm commitment from the participants: the complexities of each discipline have to be understood and respected by all. The target – prevention of environmentally related diseases – requires strong policy support, as only those issues recognized by policy makers are addressed. The health and environment community aims to support current policy making, and to point out new threats. In each of the medical and the environmental professions, sectoral mechanisms for policy support are in place. The health and environment field includes both these communities, and has implications to other sectors as well. Creating support mechanisms is thus more difficult.

This paper is an introduction to the in-depth reports on HENVINET in this Supplement. It provides an overview of our activities, and describes our experiences. It reflects on how our approach to inter-disciplinarity led to a shift in focus from traditional research instruments and methods to approaches that better address collaboration and communication.

The HENVINET project

The consortium comprised 25 European partners and five partners outside Europe, with experts from the risk assessment community, environmental and air pollution epidemiology, clinical practice and public health, and

from environmental institutes dealing mainly with air pollution (for partner list, see <http://www.henvinet.eu>). Through an advisory group, HENVINET also involved decision-makers from local and national administrations, and international organizations. The total range of expertise was somewhat broader than in previous activities, such as the AIRNET [3], [4] or the PINCHE [5] networks. The consortium incorporated a social sciences expertise from the 2nd year of the project.

The project was done through several integrated strands of work (Figure 1), all using a common framework. The research-oriented “Knowledge Evaluation” and “Tools for Practitioners” were supported by a technological backbone and a dissemination and communication activity (“Stakeholder Contact”). The Knowledge Evaluation was organized in four topic groups, each addressing one of the EHAP health priorities.

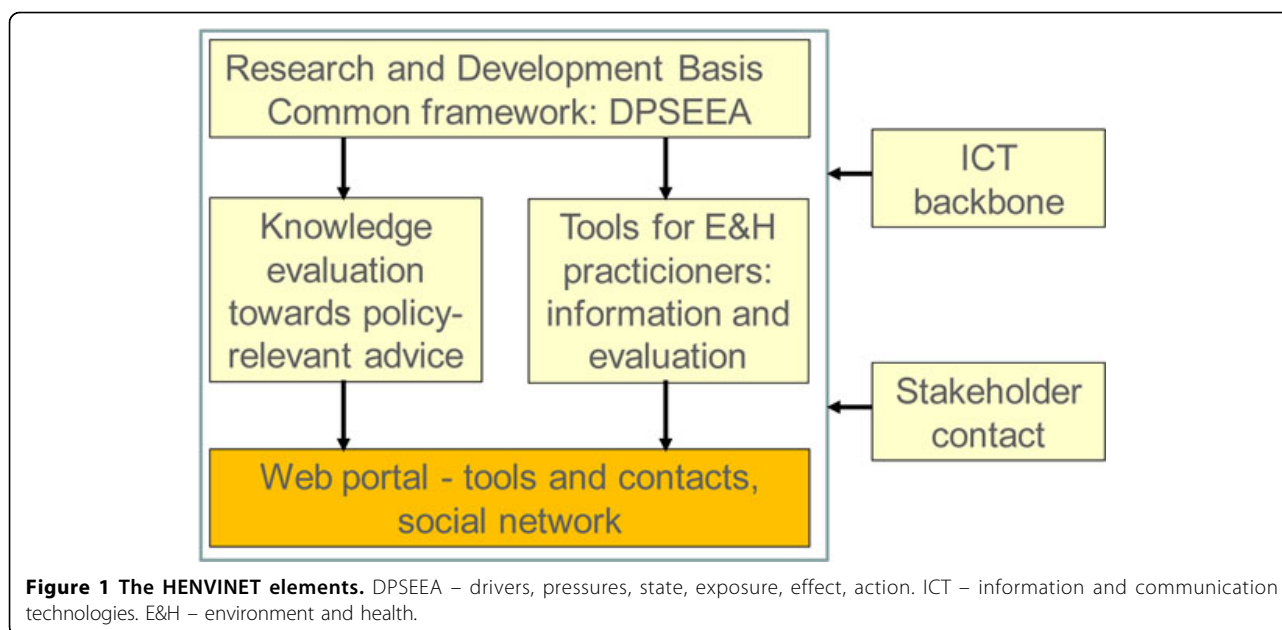
Approach and challenges

In order to “create a permanent network”, we had to solve several methodological issues: (1) develop a tool for collaboration and communication of ideas within the consortium and to the outside, (2) provide a method that would allow assessment of what science “knows”, (3) provide a way to make practical tools available, and (4) decide on how this “network” should operate. We have developed and applied tools that solve all these issues, and in this way, have created a toolbox that can be applied to different aspects of collaboration and communication between science, policy and other stakeholders.

Tools for collaboration and communication: common framework and complexity

The fundamental element of the project was the development of a common framework. The consortium members brought to the project different experiences and traditions, often from single discipline. Such common approach is required to join these expertises for a common purpose to provide policy advice, and to maintaining coherence across the project. In the environmental disciplines, operational frameworks such as the Pressure-State-Impact or the Drivers-Pressures-State-Impact-Response (DPSIR) framework [6] have been used since the 1980s. DPSIR provides an intuitive operationalisation for a large variety of issues. Approaches of integrated environmental assessment [7] expand this concept. A clearly useful framework is the extension by WHO, the Drivers-Pressures-State-Exposure-Effect-Action (DPSEEA [8]). It puts emphasis on exposure and effect; essential factors when dealing with health [9].

Henvinet adopted the DPSEEA framework, informed by developments in integrated environmental health impact assessment[7], and used it also as a communication tool in



all the topical case studies [10-16]. As Fucic et al. [16] note, the diagrams constructed along the DPSEEA to help the experts in the evaluations, provide an excellent visual communication tool, also suitable for discussions with non-experts. The framework has also been used to build a set of descriptors for a database of decision support tools [17]. Theoretical aspects that arise in application of this kind of framework, requiring collaboration of many disciplines to arrive at a common product, are addressed from the critical complexity perspective by Keune [18].

What does science know: the way from review to policy brief

Translating research results for policy requires an understanding of the needs of each stakeholder group. Traditional research outputs such as reviews are obviously not suited for the needs of the public, or the policymakers. The process of translating research results for policy, or for the public, has been studied, but is seldom successfully carried out. The high degree of interdisciplinarity required in the health and environment makes it difficult even for the research actors to understand each other.

A common framework is a necessary but not a sufficient requirement for such collaboration. There is also a need to reach a broad scientific consensus, and to reach an understanding of areas where the consensus cannot be attained with present knowledge. Further, the consensus or the lack of it needs to lead to appropriate actions. These needs are addressed by an expert elicitation methodology described by Keune et al [19], applied in the case studies [10-16].

What does science know: assessing knowledge and measuring consensus

One of the starting points of the project was a search for a methodology for knowledge assessment. The consortium considered to develop a series of reviews as tools for knowledge evaluation. We soon realized that this would not provide the wide consensus needed, but only one more additional piece of evidence. We decided instead to provide only an initial knowledge status assessment (a review), and to ask experts outside the consortium for their views [19].

A specific methodological element was missing: how to evaluate consensus on the state of knowledge. The starting set of criteria for knowledge evaluation was based on nine theoretical properties of information and knowledge (such as robustness or fitness for purpose), each with a 1-5 scale of evaluation, with a description of requirements for each score. Such a complex methodology turned out difficult to apply, and led to a fragmented assessment, nearly impossible to summarize. A simpler concept was adopted [19], using a scale similar to the one used by the International Panel on Climate Change for assessment of uncertainty. In most cases, this concept is implemented through a set of questions “What is your level of confidence in the scientist’s ability to...”, with answers on a scale 1 (very low) to 5 (very high), each number on the scale described as a probability value.

To interpret the results, we need to define what constitutes consensus, or the lack of it. A methodology was adopted from [20]. They propose a mathematical measure, developed to yield a logical determination of dispersion around a category value. A Likert 5-category scale was

constructed (Very High confidence (VH), High Confidence (H), Medium confidence (M), Low confidence (L), and Very Low confidence (VL)), assigning these categories ordinal values (scores): VH=5, H=4, M=3, L=2, VL=1. This allows the calculation of a "Consensus value" for each question. A complete lack of consensus generates a value of 0, and a complete consensus of opinion yields a value of 1. The consensus value is then interpreted together with the mean score for each question (for formulas, see [20] or [12]).

In the case studies, this method was applied to every "What is your level of confidence ..." question asked. The numbers of questions in case studies varied between 27 (Chlorpyrifos, [11]) and 63 (HexaBromoCycloDodecane, [13]). To identify areas that merit interest, we ranked the consensus values and then further explored the questions that ranked lowest, or highest.

We can compare the consensus values and scores across the different case studies (Figure 2). It appears that lowest average ranking (i.e., least average confidence that science has the knowledge) is for Brominated Flame Retardants, but on most questions, there is a relatively high level of agreement. In Climate Change [10], there is on average high confidence in available knowledge (high score), but a comparatively large spread in consensus. On Cancer, there is a large spread of confidences (scores), and the largest spread of consensus values. No data have been found in the literature that would allow us to compare these findings, and to interpret them in relation to other studies, but the results do reflect our intuitive understanding: the Brominated Flame Retardants were evaluated in a framework very similar to risk assessment, familiar to the participating experts. For Cancer, such an evaluation and the use of the DPSEEA framework have never been reported before: the result may thus reflect both the large differences in knowledge in the different elements of the framework, and the uncertainty from the relative novelty of the approach. Based on the results, we feel that this quantitative procedure provides a good basis for expert discussions leading in the next step to identification of possible actions.

Practical tools to use research in decisions

Decision support tools (DSTs) are a special kind of research-based instruments that support the translation of research results to decision-making. We have developed a DST database [17], with descriptors derived from the DPSEEA framework.

In order to help potential users to decide whether or not a given tool is useful for their purpose, we have suggested a scheme to evaluate the tool's applicability and ease of use. The evaluation results are included in the database. Often, users ask how a DST was validated. A formal validation lies with the DST's author or provider, but the user

needs to be informed whether or not the tool was validated, and should be able to find the validation results.

The process to create the database took almost two years. A number of issues were thoroughly discussed, such as how to translate the DPSEEA framework into descriptors that would be both general and specific enough, how to define categories of information to be included, and what descriptors are essential. Feasibility of information gathering, access rights to the database and technical implementation were other important considerations. The database is in operation, open to public and can be further built upon.

Means to communicate: social networks

At about the midpoint of the project, we asked the project advisory board to review our activities up to that date. We received serious criticisms along the lines "more of the same": the reviewers could see the scientific value, but did not recognize any activities that would promote the networking and communication aspects, and thus were in doubt whether the project would reach its goal. The consortium responded by brainstorming and arrived at the idea of creating a social networking tool. We have identified the essential functionalities and content, and built and promoted the tool. The process and its results are described in [21] and [22]. The tool provides also access to all the products from the project.

Addressing future issues

It takes time to formulate scientific information in a form ready to be used for policy advice. We have provided an initial scientific assessment on selected issues that arose as knowledge gaps during the work on knowledge evaluation, but did not pursue the full HENVINET chain leading to a policy brief. In one case, we have organized a workshop to explore how a group of major stakeholders, city administration representatives, perceive scientific advice in health and environment.

Environmental risk factors for xenoestrogens and estrogen-related cancers were reviewed by Fucic et al [16]. Leijts et al. [23] reviewed thyroid hormone metabolism and the impact of environmental chemicals, and generated new data. Letasiova et al. [24] reviewed knowledge on bladder cancer, and Volkovova et al. [25] reviewed available studies on cutaneous melanoma. Cumulative risks of mixtures of chemicals were reviewed from the point of view of policy making by Sarigiannis and Hansen [26].

Keune et al [27] report on the workshop that addressed the future concerns in environmental health in urban areas. They asked what may be the consequences of climate change, and how best to address them. Cities are often charged with implementation of various legislative instruments and mitigating measures, but do not always

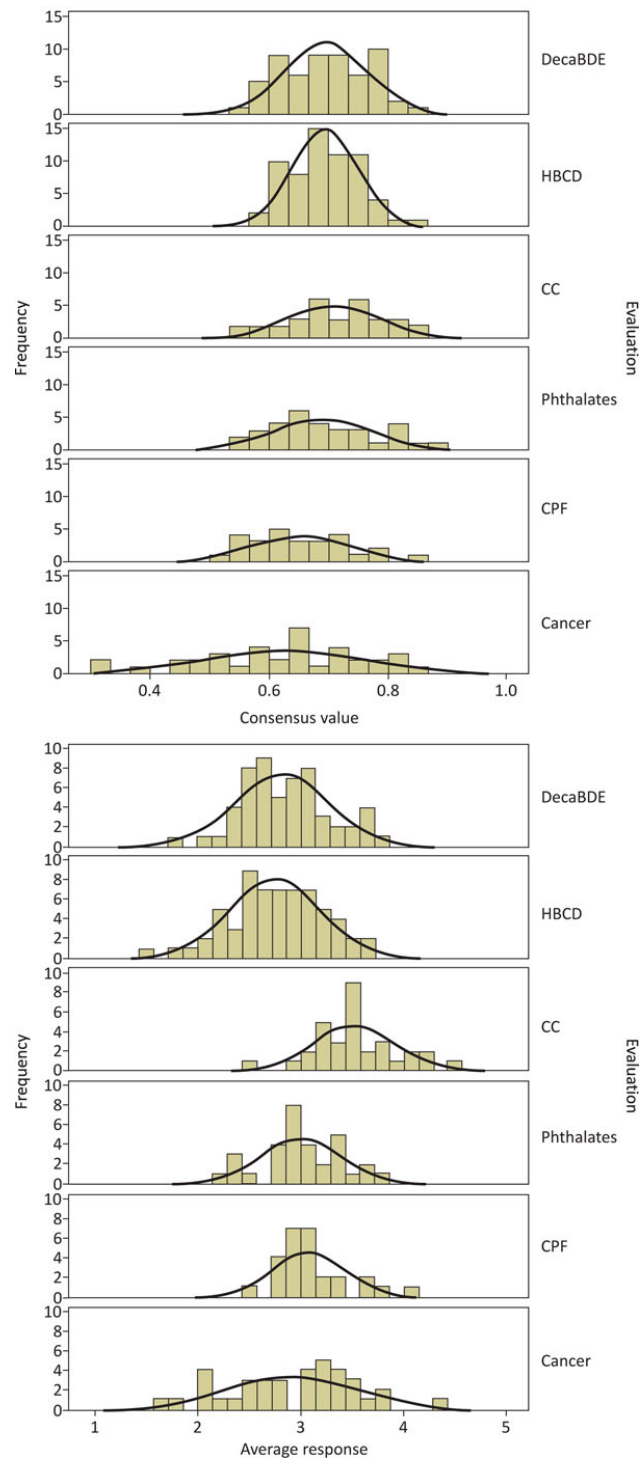


Figure 2 Consensus and agreement values across the evaluations. Frequency distribution of (1) consensus values (upper panel, values range from 0=disagreement to 1=consensus) and (2) average responses (lower panel, categories from very low=1 to very high = 5), for five HENVINET case studies – online questionnaire evaluations of (from top) DecaBromoDiphenylEther DecaBDE and HexaBromoCycloDodecane HBCD [13], Climate change CC [10], Phthalates [12], Chlorpyrifos CPF [11] and Cancer [14]. The curves represent a theoretical normal distribution, and serve as a visual aide. Number of questions in the 5 online questionnaires ranged from 27 (CPF) to 63 (HBCD).

have enough information upon which to act. The workshop provided an example where a shared future vision to maintain or improve on the quality of environmental health by 2030 allows issue framing and identifying of knowledge gaps, as well as defining actions to take.

Context of inter-disciplinarity

HENVINET allowed the participants to develop an understanding of work in an inter-disciplinary consortium. This statement, however obvious it may seem, hides many difficulties encountered along the way. Despite the ubiquity of “inter-disciplinarity”, not many definitions are available. Aboelela et al [28] have reviewed existing literature, interviewed experts and tested a draft definition, and finally suggest the following: *“Inter-disciplinary research is any study or group of studies undertaken by scholars from two or more distinct scientific disciplines. The research is based upon a conceptual model that links or integrates theoretical frameworks from those disciplines, uses study design and methodology that is not limited to any one field, and requires the use of perspectives and skills of the involved disciplines throughout multiple phases of the research process”*. To begin with, we approached “inter-disciplinarity” intuitively, using a parallel disciplinary approach and providing an arena for information exchange (the semi-annual consortium meetings). With time, we have moved to inter-disciplinary research, and possibly beyond, towards engagement with society.

Inter-disciplinarity promotes perspectives that enable us to arrive at solutions to problems arising in “real life”, often significantly supplementing mono-disciplinary approaches. Yet this desirable state is difficult to achieve. Insights are offered by Hall et al [29] who give a systematic attention to inter-disciplinarity in health research in Canada. They note that institutions (and educational systems) are usually not set up for inter-disciplinarity. They summarize the main challenges, and suggest potential measures to promote inter-disciplinarity in health research, which seem to have general appeal. These measures fall into four categories: (1) provision of resources, (2) recognition and reward, (3) training, and (4) professional organizations. Looking at these categories one by one, we can state that (1) HENVINET obtained funding to do inter-disciplinary research. The issue (2) of recognition and reward in academic terms was a challenge for the team: to publish an inter-disciplinary review is difficult; mono-disciplinary journals may not recognize such texts as deep enough or in scope to be accepted, and when contrasted with mono-disciplinary excellence, “inter-disciplinarity” can be perceived as shallow, possibly also because not much room is available for the mono-disciplinary deliberations. Regarding (3) training, research scientists do not usually receive training in inter-disciplinarity; however, a risk assessment perspective is a good starting point.

Learning about concepts in integrated assessment, or integrated environmental health impact assessment, also provides for excellent training. Addressing (4), to create a platform for a professional community was a key aim for HENVINET. Thus, moving from the intuitive, HENVINET has been implementing measures to address the four challenges. Often, this was difficult, but unlike Laberge et al. who found that the majority of scientists participating in their study [30] were sceptical to the added value of inter-disciplinarity, the HENVINET consortium has grown more and more enthusiastic with time, confirming perhaps the view of Whitfield and Reid [31] that an inter-disciplinary approach brings more insight to environmental health problems.

Moving beyond inter-disciplinarity, i.e. engaging with society and societal issues has been a goal of HENVINET. Guimarães and Funtowicz [32] give an overview of the different terms related to “trans-disciplinarity” and provide a comprehensive example of a process in governance of groundwater resources. They describe the example as follows: “... GOUVERNe process was strongly based on trans-disciplinary principles, combining hybrid methodologies, integrating social research methods with evaluation tools”. The HENVINET effort stemmed from natural and medical sciences and only at a late stage incorporated a professional in social sciences. Our approach to the trans-disciplinarity challenge was not systematic to begin with, but has moved in a similar direction to that described by these authors. The process was helped greatly by a critical complexity perspective [18] that allowed us to look at inter-disciplinarity from another angle, and provided further incentives for inter-disciplinary engagement. Another perspective, a framework that allows placing health sciences in the “Knowledge Universe”, is offered by Choi and Pak [33] who promote the appreciation of links between disciplines, the “vastness of the knowledge universe”, and identification of issues suitable to foster “multiple disciplinary efforts”.

A pertinent aspect of inter-disciplinarity in environmental health is the integration of social sciences for solving environmental health issues. In HENVINET, we have experienced a different level of understanding and ability to approach problems with the arrival of a social scientist in our midst. As Lewis [34] points out, the social scientist’s perspective provides insights that are essential to the interfacing of the scientific results with policies. Yet, Albert et al [35] report that many biomedical scientists have a negative attitude towards social sciences, claiming that the research methods do not generate valid experimental results. In HENVINET, we believe that we have generated experimental results (in the on—line evaluations), and they were essential to arrive at a valid product – the policy briefs generated in the case studies [10-15].

Networking and the science-policy link

In HENVINET, we found it difficult to establish an inter-disciplinary network and a link between science and policy. One could argue that this was due to the lack of social sciences involvement early in the project: their perspective on processes of knowledge development and problem solving would undoubtedly have enabled us to adopt systematic approaches earlier. Several authors have offered a wider perspective, resonating well with our experiences.

Choi et al [36] looked into how to promote collaboration between scientists and policy makers. They point out that goals of scientists (in-depth disciplinary understanding) and of policy makers (to obtain public support) are divergent, that each community has their own distinct language, and that their time perspectives for finding solutions are different (policy makers work in the “now” while scientists need time to test their findings). Barriers that they identify bear similarities to those reported in the results of the HENVINET survey [22]. Some of the solutions that Choi et al [36] suggest – the role of “facilitators” to use of research in policy making – were identified also in HENVINET through a more organic development process, and were implemented in the form of a the social network portal. Promoting contact through social media network will not supersede own personal physical network. Social media may however provide access to experts and to timely and relevant information about research that confirms current policy, or point out areas of possible community pressure or client demand for research.

Traceability of information is an issue that has been mentioned as a requirement for accepting results for policy or decision making [12]. Our somewhat limited experience is that traceability of information, or the information pedigree, is one important factor in the acceptance of a “policy brief” created by scientists. This is also discussed by Eden [37], who gives an example of work of the Forest Stewardship Council’s network for environmental governance. This complex network seeks to establish a standard for forest management, acceptable to environmental, social and economic member organizations, and as in any standardization or certification process, also here the “chain of custody” or information pedigree is central. HENVINET can be seen as an attempt to establish a complex network that can employ the knowledge evaluation process to arrive at standardized policy-relevant information – the policy briefs. Being able to access information about every step of the process that led to the brief will increase the acceptance of such aggregated knowledge presentations.

For research results to be accepted by non-researchers, traceability is one consideration, but the situation is more complex. Owens [38] has been studying science-policy link for many years, using examples of different

environmentally related decision making processes in the UK. In a 2005 commentary, she reflects on the potential of “research to make a difference”, and to exert influence on public policy and practice. She notes that there is a tendency to attribute the problem of “never using knowledge for the benefit of policy” to shortcomings in communication, and analyzes this premise, concluding that the linear relationship, the “technical rationality” model in which results from research/science become raw material for the policy, is inadequate. She discusses the “strategic knowledge” model and its aspects including the choice of knowledge and the delay between results generation and their use in the policy process (when the results are used, the science may have moved forward). Owens argues that a way forward may involve a move from strategic knowledge to cognitive perspectives, acknowledging that questions may be trans-scientific and unstructured, and require different kinds of knowledge to be considered. Finally, Owens suggests employing intermediaries to seek and interpret the results of relevant academic research, since “hero researchers” who manage both an academic career and active dissemination of their research to policy communities are an unrealistic concept. She also argues for more research into the “boundary” between science and policy, and analyses the process deeper in [39] and [40]. It is easy to relate these concepts to our own experience: not least, most consortium members are familiar with some examples of a failure of the linear model, and many have served on committees that were created to take upon themselves the role of “hero researcher” moving towards the “strategic knowledge” model. The HENVINET expert elicitation process is an attempt to deal in practice with some of the potential shortcomings of the “strategic knowledge” model. To achieve fairness in terms of representativeness of scientific opinions, we needed to define criteria for eligibility of experts to be invited to the evaluation: these criteria are also a part of the final result, and an aspect of the information traceability.

Overall, the HENVINET as it has developed, has tried to become the intermediary between research results and their use for decision and policy making: some members of the consortium are the “hero scientists”, but the development of the knowledge evaluation process has changed us all towards being more perceptive to the difficulties of the “mediation” or “facilitation” process.

The role of social media

Using social media to facilitate collaboration between science and policy is a novel approach: we were not able to find prior examples that could guide our own work. Facebook-like solutions are used only sporadically by

the scientific community, and then mostly by professional societies, with much lower need for “inter-disciplinarity” of the participants, and usually with up to a few hundred of members.

A number of information and communication solutions promote scientific collaboration, as reviewed by Schleyer et al [41]. It seems quite likely that social networking will be more and more common, but to be used, it needs to bring to the participants a clear added value. The HENVINET portal provides access to tools for communication between science and policy, as far as they were developed in the project. The potential added value to the users, beyond the tools, seems unclear. As Choi et al [36] point out, the agendas of different actors vary, and there are numerous other barriers. How can these barriers be overcome for the common goal of improving environmental health? In the absence of pressing problems or agendas, there is limited interest (as an example, we have seen on an example of brominated flame retardants, that when an issue was taken on a political agenda, the portal activities have increased). We have identified and implemented core functionalities, but the resources necessary to gain a critical mass of users, and to maintain the content, are beyond our current reach. The chances that electronic social networks will supersede traditional personal networks for professional purposes seem at the moment not overwhelming. But web-based social media offer a way to carry out a dialogue also between scientific communities and between science and the society, and are thus likely to diminish the communication barriers.

Conclusions

HENVINET addressed key issues that arise in inter-disciplinary research on health and environment and in communicating research results to policy makers. It did so by accepting that to communicate between science and society we need to go beyond traditional scientific tools and methods. The resulting dialogue between participants from complementary scientific disciplines has increased their knowledge of and respect for multiple perspectives and complexity; it also enhanced appreciation of the significance of these complexities for decision making.

The HENVINET project provides insights that may lead to lowering the existing barriers. Based in the common framework, HENVINET has developed a variety of methods and tools for collaboration and communication, and implemented them as concrete novel products. Through the web portal <http://www.henvinet.eu>, serving both as the repository of the methods and as a social networking tool, we hope to extend this awareness to scientists and decision makers outside the consortium.

The project has demonstrated the process of producing scientifically based politically relevant advice based on an open participation of experts. Our experience

provides concrete examples of difficulties inherent in such process, but also of the added value that this process provides. To carry this work further, scientists in health and environment need to liaise with disciplines in “soft” sciences including social sciences and liberal arts. There is much more to be done in this field; we hope that our experiences will be useful to our successors.

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Competing interests

There are no competing interests.

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