



## METHODOLOGICAL APPROACH IN AIR POLLUTION HEALTH EFFECTS STUDIES

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### ABSTRACT:

Number of scientific studies linking possible effects of air pollution on health are increasing. However, the disparity in the effect estimated from different studies and recognizing important determinants of these diversity are essential. We have explained the types and sources of air pollution, and the common terms in epidemiological studies of air pollution. Then we reviewed the study design and critically evaluated methodological approach to estimate association between air pollution and health with deep insight into dispersion model. The quality of exposure measurement is critical determinant in an environmental epidemiology study. However, the available exposure data and feasible methods for its collection are often the determinant of the design to be used. Beside vast development in this field, epidemiological approaches to find out the risks of exposure to air pollutants is still challenging.

## REVIEW

### *Ambient air pollution, common term*

#### *Air pollution*

Air pollution is the presence of substances in the atmosphere in concentrations high enough to cause adverse effects on man, animal, vegetation or materials. The substances may be a mixture of solid and liquid particles (Particulate Matter), gases (such as O<sub>3</sub>, NO<sub>x</sub>, NO<sub>2</sub>, SO<sub>2</sub>) and biological aerosols or agents in atmosphere that can disperse, transport, and may transform from time to time in the other forms [1].

### *Emission inventory*

An emissions inventory is assessment of the quantity of pollutants discharged into the atmosphere in a certain geographical area and within a specified time span. Characterizing the emissions inventory usually depends on the activities that cause emissions, the chemical or physical identity of pollutants, topographic area covered, time and methodology are used to estimate the emission. Usually environmental policy makers use emissions inventories to track progress towards emission reduction targets, development control

strategies, and as the inputs in air quality models. The inventory uses two classes of data, point sources (source-specific data) and area sources or category-specific data in the most refined spatial level (for non-point and mobile sources) [2]. Emission inventory needs information on type and location for each emission point, as well as several release features (for example mass emissions, height and diameter of stack, temperature, vertical emission speed) in annual or hourly periods [3]. Mobile sources such as traffic emissions are a subcategory of the area source. Traffic emissions are usually estimated by traffic counts using standard emissions factors for different types of vehicles, speeds, and gradients of the road network [4].

### **Human exposure**

Any contact (that is internal or external) to a particular environmental agent is called total exposure. Exposure is defined as the concentration or sum of a particular environmental agent that reaches the target population, organism, organ tissue or cell overtime and space [5]. The quality of exposure measurement is critical in the validity of environmental epidemiology study.

### **Dose**

The term is defined as amount of pollution that reaches the target tissue [6]. Most epidemiological studies currently employ exposure methods to find the linkages between adverse health effects and air pollutants. However, this method cannot reflect the mass or concentration of a pollutant that is inhaled by an individual. Dose can also be stated as the total amount of pollutants that was taken, or absorbed by an organism.

### **Exposure modeling**

According to the World Health Organization (WHO), exposure modeling is a logical or empirical set up which allows estimation of individual or population exposure parameters from available input data [7].

## **Methodological approach in air pollution health effect studies**

### **Study design in air pollution health effect studies**

Researches on air pollution and health related issues using all the standard study designs comprise both experimental and nonexperimental studies. When epidemiological experiments do not meet minimal standards of feasibility or is unethical, epidemiologists design observational studies. Here we explain the five main types of nonexperimental epidemiologic studies:

1) Cross-sectional studies are used to study the association between long-term exposure to air pollution and prevalence of chronic symptoms and disease. In a cross-sectional study, exposure to air pollution and health status of population are determined at the same time. However, such studies cannot find out the time-based relationship between exposure and disease.

2) In the case-control study, a particular health issue is recognized in a group of people, then people are classified depending on the exposure of air pollution. A match sample of same population who were free of the disease at the time event is also selected as control. An estimate of the relative risk of event that is associated with exposure to air pollution, odds ratio, can then be calculated.

3) Case-crossover studies, are types of cases-control studies and were introduced in the early 1990s [8] to estimate the association between short-term exposure to a particular pollutant and change in a rare acute-onset disease. This design has been commonly applied to air pollution health effect studies. For each person, exposure to air pollution is a period just preceding the time of events (the case period) and other periods during which health event did not occur (control periods). Thus for matched case-control data relative risk can be estimated.

4) Cohort studies used to estimate long-term health effects of exposure of air pollution on mortality and morbidity because of chronic disease. In a cohort study, people who are free of

disease are followed over an extended period of time. Individual are classified according to their exposure of air pollution, often determined based on place of residence. The rates of health events that occur among the exposed and unexposed are compared and, normally presented as a ratio of rates, or relative risk.

5) Ecological studies also called the aggregate level study. Often the exposure are measured in population level and is not collected on individual. This design may be the best or only way to find out the relationship between average rates of disease or death and average exposure of air pollution in the population. Common ecological approaches include investigation of regional disparity through mapping, time-trend change and either variance in time trends across regions over the time. Since relative risk of disease obtained through ecological studies is based on data about population, there is more difficult to interpret in comparison with those from case-control or cohort studies.

There are four research approaches in air pollution studies [9]:

- 1) Episodes study like 1930 Meuse Valley episode in Belgium [10], Donora 1948 [11] and the London fog of December 1952 [12], and other growing number of studies [13]. This before and after design comparing within community is ideal for examining short time (a few hours to a few weeks or months) affect of air pollution, where migration is not wide-ranging, and when a clear line isolate unexposed from exposed time period.
- 2) Some studies compare health-related problems in populations with low and high-level exposure to pollutants.
- 3) Community time series analysis that explores how changes in air pollution levels influence the morbidity. This approach reduces the affect of individual levels confounding since these remain constant over short period of time. Also this approach is useful when the population in the study area is unclear. For example for hospital-based studies in densely populated areas where not all hospitals can be included, counts of admission

might be comparative for high versus low- population days.

- 4) Studies in which individual-level data are integrated with community or individual level exposure. Such studies provide further understanding about mechanism of effect, susceptibility, and more specific indication of the harmful pollution. For example in Wellcome Trust Genetic (Well-Gen) study of extensive phenotypic database on type 2 diabetic patients allowed us to examine the effect of exposure to ambient air pollutants which are related to chronic respiratory problem [14], glycemic levels [15] and C-reactive protein [16].

#### *Air pollution exposure assessment methods in epidemiological studies*

Exposure is the contact of pollutants and targets who are either individuals or a population [17]. Human exposure assessments can be considered as a science to define how an individual or a population (who) exposes to a contaminant (what), including quantification of the amount (how much) of exposure across space (where) and time (how long). It is an interdisciplinary science that involves environmental sciences, toxicology, and environmental epidemiology. Exposure assessment links the pollution source and health outcome (see Fig.1).

*Adopted from [18, 19]*

Individual or population exposures of air pollutants, can be estimated either qualitatively (for example questionnaires) or quantitatively (e.g. air pollutants concentration), depending on the purpose of exposure assessment and the availability of relevant data. In exposure studies, measurements of pollutant concentrations are often come with questionnaire surveys. Qualitative exposure assessment is perhaps the simplest method but it is useful only in studies involving many subjects to avoid bias in design (e.g. questionnaire design).

To quantify the individual exposure, we need to know the concentration of a pollutant in the contact boundary of the body [20]. Therefore, we could take personal exposure measurements di-

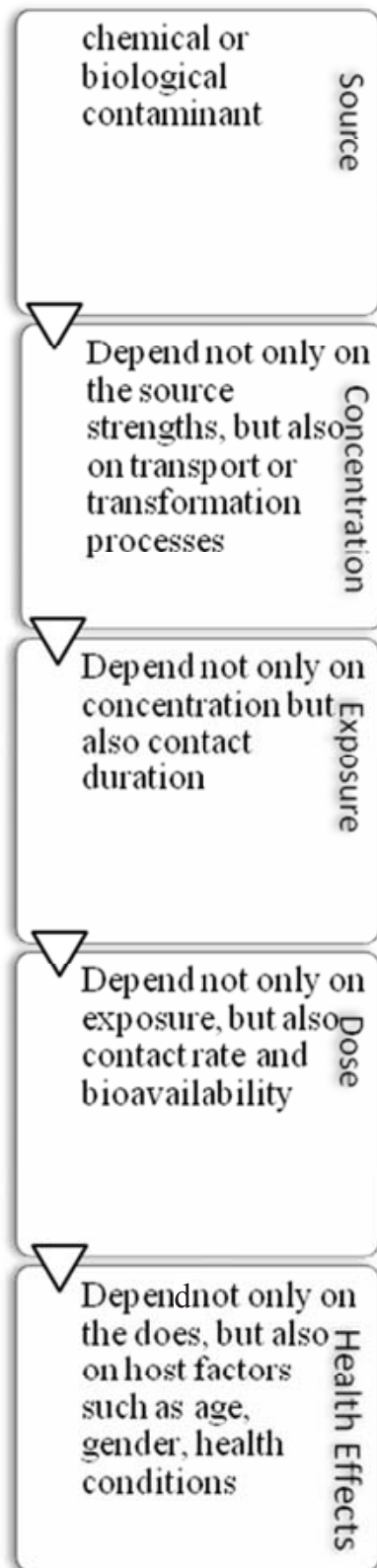


Fig.1. Human health effect of air pollution

rectly in the point of contact while it is occurring [21] or we could estimate exposure retrospectively as sum of all exposures in a microenvironment (e.g. home address) and over a time period (e.g. few hours to lifetime). Personal monitoring and added data such as biological markers in human tissue (e.g. adipose tissue, blood, breath, hair, and urine) can be used as a tool for exposure assessment. Such direct measurements of exposure are often too costly and time-consuming to do on many subjects. We can also access pollutant concentrations indirectly through mathematical modeling of pollutant fate and transport from emission sources in specific microenvironments. By using historical air pollution data and time-activity data, we can estimate the exposure retrospectively for epidemiological studies.

Several models such as proximity, and dispersion have been developed to assess personal exposures for individuals. Despite the fact that such models are useful, in epidemiological studies, it can be obtained just population or community level exposure information. So it is also important and necessary to develop proper surrogates to determine a community's exposure to ambient pollutants.

Measuring or estimating the exposure is essential in environmental epidemiological studies. Such studies use a number of methods to examine associations between exposures of outdoor air pollution and various health outcomes (e.g., mortality, cardio-pulmonary events). Nevertheless a number of exposure assessment are introduced, exposure misclassification is still recognized as an important source of confusion in studying the health effects of air pollution. Table 1 shows advantages and disadvantages of different exposure assessment models used in air pollution studies [22-24]. In this section, we have explained dispersion models and their application in greater detail.

#### *Dispersion model*

Pollutants discharged into the air are transported over long distances and scattered. This dispersion

Table 1. Critical evaluation of important air pollution exposure assessment methods

Method	Advantage	Disadvantage
Direct		
Personal monitoring	- Direct measurement of exposure during the surveying period	- Expensive and time-consuming for large study populations
Biological	- Measure internal dose of a pollutant in human body - High reliability to confirm result produced from other exposure assessment methods	- Hard to differentiate between exposure pathway and chemicals - The role of biomarker was limited by confounding - High cost and time-consuming
Indirect		
Qualitative	- Useful in study large number of human subject - Can improve the quality of epidemiological analysis	- Accuracy can be biased design and subjective responses
Urban monitoring network	- Useful for both cross-sectional and cohort study showing community exposure	- Need proper surrogates for exposure - Biased by time activity and other source of exposure such as indoor
Proximity	- Simple and proper for exposure research for unclear etiology of health outcome	- Exposure misclassification and biased risk estimates
Interpolation (e.g. Kriging, splines, Inverse Distance Weighting (IDW) and Thiessen triangulation): produce estimates of the concentration of pollutant at sites other than locating monitoring stations	- Use of real pollution measurements in their calculation of exposure estimates	- Do not take terrain or localized patterns into account - Requires a reasonably dense network of sampling sites - Proper application usually needs experience with geostatistical models
Land Use Regression (LUR): predict pollution concentrations at a given site based on surrounding land use and traffic characteristics	- Provide within city variability in pollution concentration	- Care must be taken to correctly select the independent variables and buffer radii for the pollutant (e.g. wider for NO <sub>2</sub> and narrower for estimates of diesel)
Dispersion: use of data on emissions, meteorological conditions, and topography in estimating spatial exposure estimates of air pollution concentrations	- Provide more complete spatial and temporal variation of air pollutant concentration - Provide high resolution analysis of patterns in health outcomes and environmental factors	- Costly input data - Need cross approval with monitoring data - Provide environmental exposure concentration but not internal dose inhaled by individual



Table 1. Critical evaluation of important air pollution exposure assessment methods

Method	Advantage	Disadvantage
Hybrid: personal or regional exposure plus one of models above	<ul style="list-style-type: none"> <li>-Provide more accurate exposure</li> <li>-Can use existing methods and do not have to struggle on new methods</li> <li>-Measurement validation</li> </ul>	-Assessment cost and results are partly influenced by pollution under study (that is passive NO <sub>2</sub> inexpensive vs. real time particle monitor expensive) and scale affect respectively

through the wind is a complex process. An atmospheric dispersion model is used to mathematically simulate how air pollutants transport, disperse and transform in the atmosphere [25].

The process of air pollution modeling contains four stages (data input, processing, drawing concentrations, and analysis). Models can be set to estimate concentrations of pollutants for either a short-term (3 min) period or for a longer term (years). The most common and easiest mathematical estimate of plume behavior is the Gaussian plume equations [26]. They allow us to combine GIS in dispersion models to analyze a mix of information and form more reasonable scenarios.

There are several competing needs for designing an air pollution model. The model must capture the essential physics of the dispersion and provide sound and repeatable estimates of downwind concentrations. This needs detailed knowledge of source features, topography and meteorology, but it is also desirable to keep these requirements to a minimum. Simplicity is an important asset in any model. To test the robustness of a model, we need to evaluate the accuracy of each stage. In other words, the quality of input data will directly affect the quality of the output. Standard statistical techniques have been settled for expressing the doubt and variability of the predicted results when comparing them to measured concentrations [27].

In choosing an air dispersion model, several types of models are available, with gradually increasing levels of mathematical complexity, input data requirements and user ability.

## CONCLUSIONS

Air pollution exposure assessment and exposure misclassification remain as the most important source of bias in health effect studies. In addition diversity of findings may be related to individual and environmental differences. The evidence for long-term air pollution health effects is mostly based on cross-sectional comparisons.

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## COMPETING INTERESTS

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## ETHICAL CONSIDERATIONS

“Ethical issues (including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission,

redundancy, etc) have been observed by the authors.”

## REFERENCES

- [1] Gifford F. Atmospheric Chemistry and Physics of Air Pollution. Eos, Transactions American Geophysical Union. 1987;68(46):1595.
- [2] EPA. Procedures For Emission Inventory Preparation: Emission inventory fundamentals. U.S. Environmental Protection Agency, Monitoring and Data Analysis Division: 1981 EPA-450/4-81-026a
- [3] EPA. Procedures for Emission Inventory Preparation: Area sources. U.S. Environmental Protection Agency, Office of Air Quality Planning and Standards: 1981 EPA-450/4-81-026c.
- [4] Dobie N. Procedures for emission-inventory preparation. Volume 4: Mobile sources. Environmental Protection Agency, Ann Arbor, MI (United States). Office of Mobile Sources, 1992.
- [5] WHO I. Environmental Health Criteria 155, Biomarkers and Risk Assessment: Concept and Principles. World Health Organization, Geneva. 1993.
- [6] Watson AY, Bates RR, Kennedy D. Air pollution, the automobile, and public health: National Academies; 1988.
- [7] Organization WH. Estimating human exposure to air pollutants. 1982.
- [8] Maclure M. The case-crossover design: a method for studying transient effects on the risk of acute events. American journal of epidemiology. 1991;133(2):144-53.
- [9] Khafaie MA, Yajnik CS, Salvi S, Ojha A. CRITICAL REVIEW OF AIR POLLUTION HEALTH EFFECTS WITH SPECIAL CONCERN ON RESPIRATORY HEALTH. Journal of Air Pollution and Health. 2016;1(2):123-36-86.
- [10] Logan W. Mortality in the London fog incident, 1952. The Lancet. 1953;261(6755):336-8.
- [11] Helfand WH, Lazarus J, Theerman P. Donora, Pennsylvania: an environmental disaster of the 20th century. American journal of public health. 2001;91(4):553.
- [12] Bell ML, Davis DL. Reassessment of the lethal London fog of 1952: novel indicators of acute and chronic consequences of acute exposure to air pollution. Environmental health perspectives 2001;109(Suppl 3):389.
- [13] Anderson JO, Thundiyil JG, Stolbach A. Clearing the Air: A Review of the Effects of Particulate Matter Air Pollution on Human Health. Journal of Medical Toxicology. 2012;8(2):166-75
- [14] Khafaie MA, Salvi SS, Khafaie B, Ojha A, Yajnik CS. The impact of air pollution on respiratory health among diabetes and non-diabetes subject in Pune, India. Environment and Health—Bridging South, North, East and West; Basel: Research Triangle Park, NC:Environmental Health Perspectives: Environmental Health Perspective; 2013. p. 1-25-16.
- [15] Khafaie MA, Salvi SS, Khafaie B, Ojha A, Yajnik CS. Long-Term Exposure to Air Pollution Associated with Glycemic Levels in Type 2 Diabetic Patients: Result from Wellcome Trust Genetic (Wellgen) Study. From Local to Global: Advancing Science for Policy in Environmental Health; Seattle, Washington: Research Triangle Park, NC:Environmental Health Perspectives: Environmental Health Perspective; 2014. p. 3-730.
- [16] Khafaie MA, Salvi SS, Ojha A, Khafaie B, Gore SS, Yajnik CS. Systemic inflammation (C-reactive protein) in type 2 diabetic patients is associated with ambient air pollution in Pune City, India. Diabetes Care 2013;36(3):625-30.
- [17] The R. A quantitative definition of exposure and related concepts. Journal of Exposure Analysis and Environmental Epidemiology. 1997;7(4):411.
- [18] Smith KR. Fuel Combustion, Air Pollution Exposure, and Health: The Situation in Developing Countries. Annual Review of Energy and the Environment. 1993;18(1):529-566.
- [19] Liroy PJ. Assessing total human exposure to contaminants. A multidisciplinary approach. Environmental science & technology 1990;24(7):938-945.
- [20] Assessment E. Guidelines for exposure assessment. Federal Register. 1992;57(104):22888-938.
- [21] Liroy PJ. Measurement methods for human exposure analysis. Environmental health perspectives. 1995;103(Suppl 3):35.
- [22] Zou B, Wilson JG, Zhan FB, Zeng Y. Air pollution exposure assessment methods utilized in epidemiological studies. Journal of Environmental Monitoring : JEM. 2009;11(3):475-90.
- [23] Zhang JJ, Liroy PJ. Human exposure assessment in air pollution systems. The Scientific World Journal. 2002;2:497-513.
- [24] Jerrett M, Arain A, Kanaroglou P, Beckerman B, Potoglou D, Sahuvaroglu T, et al. A review and evaluation of intraurban air pollution exposure models. Journal of Exposure Science and Environmental Epidemiology. 2005;15(2):185-204.
- [25] Bluett J, Gimson N, Fisher G, Heydenrych C, Freeman T, Godfrey J. Good practice guide for atmospheric dispersion modelling. Ministry for the Environment, Wellington, New Zealand. 2004.
- [26] Bellander T, Berglund N, Gustavsson P, Jonson T, Ny-

- berg F, Pershagen G, et al. Using geographic information systems to assess individual historical exposure to air pollution from traffic and house heating in Stockholm. *Environmental Health Perspectives*. 2001;109(6):633.
- [27] Hanna SR. Confidence limits for air quality model evaluations, as estimated by bootstrap and jackknife resampling methods. *Atmospheric Environment* (1967).1989;23(6):1385-98.