Chapter 8

Practical Issues in Study Implementation

Learning objectives

- Be able to describe the elements of the organization and conduct of a study.
- Be able to prepare a study protocol.
- Be able to describe approaches for ensuring the ethical clearance and conduct of a study.
- Understand the necessity for incorporating multidisciplinary expertise in a study team.
- Understand the importance of quality assurance procedures (e.g. standardization, validation).
- Recognize the typical problems encountered when undertaking a study under special circumstances, such as dealing with a highly concerned community or having very limited resources, and be able to identify possible solutions.
- Appreciate the benefits and special needs of conducting multicentre investigations.

8.1 Steps in study implementation

Before undertaking an environmental epidemiology study, the investigator must have a clear understanding of the nature of the problem to be addressed and the motivation for resolving it. The investigator should therefore inform him- or herself about the circumstances of concern by reviewing available scientific literature and documents, and discussing the problem with community representatives and government officials. A literature review should not be limited to published epidemiological research. Environmental, clinical, or toxicological research can often provide useful information for an epidemiological study. Similarly, many useful studies conducted by governmental agencies may be more analogous to the proposed study than research published in the scientific literature. These are often reported only in official publications.

After reviewing existing data and the state of knowledge regarding potential exposures and health outcomes, the investigator should formulate hypotheses to be addressed by the study. The final preliminary step is to choose the study design that appears to be most feasible and efficient in terms of addressing these hypotheses.

After choosing a study design, the first step in study implementation is to develop a protocol describing the study's purpose and methods. The protocol identifies the personnel and resources needed to conduct the study and serves as a guide for its implementation. With some modification, the study protocol can also be used for justifying the study's use of funds or to seek additional funding.

Before initiating a study, it is worthwhile checking whether the requirements for conducting the study can be met. For instance, if mortality data or hospital admission data for a certain disease for the years in which the investigators are interested in are unavailable or incomplete, the proposed study will not be possible. The same applies if approval from relevant authorities or cooperation from communities is likely to be withheld, or if basic examination facilities are lacking. Financial resources and/or funding must also be assured.

A preparatory stage should be carried out during which study methods are finalized. This generally includes training of staff, pretesting of study instruments, and planning of field survey logistics. A "pilot" study may be undertaken in order to gain insight about potential problems in implementing the proposed study. A pilot study may involve collecting data on a small number of subjects to evaluate the feasibility of accessing the population and collecting the desired information. Sponsoring agencies sometimes require that a pilot study is undertaken before they will provide funding for a full study.

The main study consists of collecting data on the exposures and health outcomes, followed by laboratory analysis of environmental or biological specimens, data management and statistical analysis. A study cannot be considered to have been completed until the findings have been reported to the individual subjects, the involved community, study sponsors, and if relevant, the general scientific community. Table 8.1 shows the steps in study implementation.

8.2 Study protocol

A protocol should be prepared for every epidemiological study. The details of a protocol will depend on the precise nature of the study. For example, the protocol for a straightforward descriptive analysis of existing data by the staff of a governmental agency may require only a few pages of explanation and justification. However, the protocol for an expensive, multicentre research study, of several years duration, could run to several hundred pages, containing detailed descriptions of all aspects of the study methods and organization. But whatever its length, the protocol should provide sufficient information to serve as complete documentation for the study, without being verbose or too complex. That said, however, many governmental agencies and foundations establish guidelines limiting the page length of protocols submitted for funding requests, and these should be adhered to.

Box 8.1. Purposes of a study protocol

- helps the investigators focus on the critical issues to be addressed by the study;
- delineates objectives, hypotheses, study design, study populations, methods of measurement, ethical and legal issues, methods for data analysis, and anticipated results:
- helps to remind the researchers of the details of the study plan during the study;
- helps to maintain continuity should key investigators leave the study;
- documents the procedures of the project for future reference;
- provides material that can be used for external or peer review of the study;
- can be used as a source of information about the study.

Source: adapted from Miettinen (1985) and Hernberg (1992).

Table 8.1. Steps in study implementation

- 1. Conduct background research
 - Nature of problem
 - Relevant prior studies
 - Study approaches and data collection methods
- 2. Develop study design and methods
 - Objectives and hypotheses
 - Study protocol
 - Statement concerning ethical use of human subjects
 - Feasibility assessment
- 3. Assemble study team
- 4. Prepare for study
 - Contact with community and government officials
 - Plan logistics and make arrangements for field studies
 - Study material and instruments
 - Staff training
 - Pilot study, if necessary
- 5. Conduct main study
- 6. Complete data management and analysis
- 7. Report study findings
 - Individuals
 - Community and funding agency
 - Scientific community

The study protocol should include a detailed description of all activities to be performed during the preparatory phase and the main study. The recommended components of a study protocol are shown in Table 8.2.

Objectives and hypothesis formulation

The protocol should begin by clearly stating the study's objectives. These will vary according to the nature of the study. For example, the objective of a descriptive study may be to determine the distribution of blood lead levels among children living in densely-populated cities. The objective of an analytical study of lead in children, however, might be to determine whether living within a 0.5 km radius of a lead smelting facility is associated with an increase in blood lead level among children between one and five years of age. The specific aims or tasks of this

study may be to use a household survey to randomly select an age-stratified sample of 100 children in the identified study area, in order to administer a questionnaire, perform a physical examination, and obtain a blood specimen for analysis of blood lead concentration.

If possible, investigators should state study objectives in specific and quantitative terms. Likewise, the anticipated study findings should be presented as explicit and quantitative hypotheses. For example, the hypothesis of the aforementioned example of a blood lead study may be that mean blood lead concentration among children living within a 0.05 km radius of the lead smelting facility is twice as high as that of children of similar age living in communities beyond this radius. Of course, epidemiological studies do not have to be oriented toward confirming or rejecting specific hypotheses using tests of statistical significance. Nevertheless, a statement of specific hypotheses is useful in guiding the development of the study design and interpretation of findings.

Table 8.2. Components of a study protocol

- Summary (usually not to exceed a few hundred words)
- Study objectives and hypotheses
- Statement of the problem, background, and significance
- Previous research and qualifications of investigators
- Study design and methods
 - description of study base and statement of study design
 - characteristics and size of study population(s)
 - · methods for selecting study samples, including inclusion/exclusion criteria
 - data sources and data to be collected
 - methods for measuring exposure and effects including specifications of measurements to be performed and instruments to be used
 - list of anticipated activities and specifications of members of the study team;
 recruitment plan and training of field workers
 - quality assurance plan for monitoring staff, instruments and procedures
 - analytical strategy and methods, including plans for data entry and data management, control of confounding, evaluation of bias, and estimation of statistical power or precision
 - plan for archiving data and procedures for future review
- Timetable of the study including time schedules of each phase of the study
- Required resources including premises, equipment, materials, administrative services
- Ethical considerations, especially procedures for studying human subjects
- Reference list of all cited material
- Appendices, containing letters of agreement from participating colleagues and agencies.

Background and significance

A protocol should provide sufficient information for a reader to understand the objectives and proposed study methods. The background section should describe the problem to be examined, review previous studies of the problem, and describe any previous relevant work carried out by the investigators. In addition, the background section should explain the purpose of the proposed

study. The study may aim to answer a specific question about environmental exposures or health effects in a particular community. If so, the protocol should indicate how possible study findings will be used to make decisions regarding management of the problem. Alternatively, if the study is intended to address broader scientific issues, the protocol should explain the significance of the possible findings. It should be clear how the study relates to or differs from prior research identified in the literature review. The protocol should include a summary of a thorough review of the relevant literature and of an examination of related studies either completed or in progress.

The background section should also provide information on the possible environmental exposures and disease association, and address issues such as the nature of the study base, potential confounding factors, and effect modifiers. The options for exposure and disease measurement should also be reviewed. It will thus be clear why the selected study methods are appropriate to the problem and hypotheses to be addressed.

Description of study design and methods

The methods section of a study protocol should describe the variables that are to be assessed. It should also provide an overview of the study design, methods and procedures for population selection, measurement of exposure and outcome variables (including reference to sources of instruments and quality assurance), and preparation of data and data management. Inclusion of a description of the analytical strategy and statistical methods to be followed is also advisable.

The type and size of study samples, including reference to the sampling scheme and questionnaires and instruments to be used, and methods for the laboratory analysis of specimens should be described in detail. Procedures to monitor the quality of the study activities and data should also be mentioned. For planning purposes, the length of time required to collect each data set should be indicated.

The specific nature of the data may not be known until the initial data management, data exploration, and data reduction steps have been undertaken (Miettinen, 1985), but it is important, nevertheless, for the protocol to present an overall strategy for the analysis, including identification of the key variables and proposed causal relationships to be examined. A useful procedure is to discuss how the findings will be presented, including perhaps the structure of anticipated tables of the findings.

Box 8.2. Reasons for considering data analysis at the design stage

- Specific consideration of the data analysis plan will indicate whether the core objectives have been clearly identified.
- The data analysis plan may identify essential variables determinants, confounders, or effect modifiers that are not addressed adequately in the data collection plan.
 Conversely, it may be possible to identify data collection efforts that, as currently designed, would not contribute to meeting the study's objectives.
- The study team's data analysts are encouraged to participate at the planning stage, and to examine critically the entire study from a statistical point of view.
- Consideration of the data analysis plan and the nature of the variables to be evaluated is essential for determining whether the planned study size is adequate.
 Source: adapted from Miettinen (1985).

The format and manner in which the study results will be reported to individual participants, and how they will be published, should be described. Reference should be made to the clearances that must be sought before data can be released. If any of the participants are discovered to be suffering adverse health effects, they should be referred to their physicians for further clinical observation, examination or treatment. Agreements concerning these arrangements should be described in the protocol.

Timetable for study

Once the study activities have been described, a detailed timetable should be drawn up. This timetable can:

- help the team leader to organize and assign the study tasks;
- serve as a combined calendar and checklist enabling the team-leader to see at a glance whether or not the various activities are proceeding as planned;
- enable the team-leader to identify the optimal sequence of events i.e. the sequence in which all tasks will be performed at maximum efficiency which will determine the overall timing of the study;
- help the team leader identify points of obstruction in advance, so that schedules can be modified or assignments redistributed.

The execution of a study can be divided into four parts: preparatory phase including pilot study, main study, data management and statistical analysis, and report preparation. A timetable for each of the essential activities is helpful. The timetable usually consists of a table listing the specific beginning times and duration for each major study activity or a figure showing the activities according to a time line. Particular attention should be paid to the time required to:

- order equipment and supplies;
- develop and test instruments;
- hire and train study staff;
- manage and clean data before undertaking the statistical analysis;
- prepare reports and scientific publications.

These activities can be quite time-consuming, yet investigators often do not take them sufficiently into account when planning a study. For studies involving examinations of subjects in community locations, attention should be paid to the times when study subjects are available (such as evenings on work days) and the seasons when field studies are possible.

Human subjects and ethical considerations

The human subjects section of the protocol describes the participation of subjects in the study, making clear the potential benefits and harm — from the participants' point of view — that will or could arise from this participation. The protocol should describe the methods for identifying and recruiting the study populations, the medical procedures to be applied, and the procedures for ensuring the confidentiality of the study subjects. It should also indicate how informed consent will be obtained and describe how the subjects will be notified of study findings.

A separate human subjects protocol is usually prepared for review by the investigators' institution or an ethics committee. The human subjects protocol describes the study methods and gives detailed information about the involvement and protection of the subjects. It includes copies of consent forms to be used when asking persons to participate as human subjects. Ethics committees often require that a copy of the full study protocol be attached to the human subjects application. Preparation of an application for approval by a human subjects or ethics committee is described in Section 8.3.

Resources required

Detailed estimates of the personnel, equipment and financial resources required should be presented in the protocol. Such information is necessary for internal planning and for presentation to funding agencies. Preparation of a detailed budget for a large-scale study demands considerable skill and experience. Poor planning may result in underestimation of the funds and time required.

A budget typically includes the following components:

- salary support (including indirect salary costs such as medical insurance) for personnel (investigators, technicians, administrative and staff), with an indication of who will work part-time and who will work full-time;
- support for consultants and advisors;
- travel costs, including meals and lodging, for personnel and consultants;
- purchase or hiring of equipment; if equipment is to be shared among investigators or studies, it is appropriate to indicate what proportion of the equipment and costs are to be allocated to this particular study;
- supplies, e.g. office supplies, and consumable supplies such as blood test tubes;
- office and/or laboratory space, and clinical testing facilities;
- dissemination of study findings (e.g. via printed report or in the scientific literature);
- charges for access to computers, maintenance of equipment, telephone calls.

Besides listing specific budget items, the protocol should provide a statement explaining and justifying the costs listed. Such a statement is usually necessary if the protocol is to be submitted to authorities for approval or funding. If not, it will still be useful as an internal document and assist the investigators with adjusting the budget if the total anticipated funds do not materialize.

Personnel and resources

The study protocol should list the key personnel and staff (see Section 8.4). The qualifications of the key study personnel should be documented if the protocol has to be submitted for the approval of a funding agency or external institution. However, even if this is not so, such documentation may be useful, helping to familiarize new collaborators with the formal qualifications of study team members, and serving as a source of documentation about the investigators' expertise should the study be evaluated at a later stage.

Existing institutional resources and equipment that are available and to be used for the study should be described, particularly if external funding is being sought. Funding agencies generally want evidence that the investigators have the necessary facilities to undertake the proposed research. Obtaining written approval for proposed use of resources may not be necessary if the protocol is for internal use only. Nevertheless, it is advisable. This written approval should indicate precisely for how long the equipment will be available and who will be responsible for expenses such as supplies and repair. In the event of collaboration, the protocol should also include statements of collaboration from key collaborating personnel and institutions.

8.3 Ethics review and informed consent

Commonly, an application for epidemiological research must be accompanied by proof that approval of the proposed study has been received from an appropriate ethics committee. Indeed, committees and boards, such as Ethics Committees, Institutional Review Boards, Human Subjects Committees, Research Ethics Boards, or Ethics Review Committees are established in most medical institutions and public health agencies to ensure that the public interest is protected whenever any medical investigation is proposed. These committees generally comprise a lay person and members from a variety of disciplines such as medicine, science, law and philosophy. Broader ethical considerations in conducting epidemiological research are discussed in Chapter 3, while this section describes the completion of a human subjects application.

Procedures for obtaining ethics approval

Completing an ethics application form requires the applicant to describe clearly the aims of the proposed research and consider its potential consequences. The emphasis is on respecting the rights of study participants. Thus, not only must the scientific intent of the proposal be described, but also why the participation of human subjects is needed. If participating in the study could harm a subject (for example, through venipuncture or by providing personal information that is recorded onto a questionnaire which could be misused), the proposed information sheets and informed consent documents should be included for review by the ethics committee. Because the committees generally have some members with a non-technical background, all procedures to be performed should be describe in language understandable by non-physicians/scientists.

Environmental epidemiology studies are sometimes based exclusively on existing archived data. Nevertheless, obtaining the approval of an Ethics Committee for such studies may still be necessary. In this instance, ensuring confidentiality would be the most important ethical issue.

Ethics reviewers will also wish to be assured that a proposed study can produce useful results. Otherwise, public funds and participants' time could be wasted.

Completing application forms for ethics review

Each institution has its own application form for ethics review, but the required elements are similar in most institutions. Issues to be addressed in a typical application are listed in Table 8.3

Table 8.3. Issues to be addressed in an ethics review application form

- Title
- Summary of study in lay terms
- Study objective(s) and specific hypotheses
- Statement of the problem
- Significance of the proposed study, not only not only in terms of the agency's mandate, but also in terms of public health
- Credentials of the investigators, to enable reviewers to judge the competence of those proposing the study in relation to its objectives
 - explain any potential for conflict of interest
 - original signature of investigator(s) and supervisor
- Study methods including:
 - summary of study design
 - sample size considerations (how many subjects are necessary)
 - explanation of sampling and recruitment procedures
 - subject inclusion and exclusion criteria
 - control selection procedures and justification for inclusion of controls
 - data sources and data to be collected on individual subjects
 - outcome assessment and methods for follow-up of subjects
 - archival of data and procedures for review/audit
- Results: dissemination to study subjects, public, peers
- Financial/budgetary considerations with justification for use of equipment and services
 - describe any plans to compensate subjects for participation
 - information about sponsoring agency, including potential conflict of interest
- Ethical considerations (informed consent, confidentiality safequards, etc.).
 - provide copy of consent form with all required elements
 - adverse event reporting and treatment (if any) is addressed

Questions about the investigator and sponsorship

The ethics application form for most institutions requires the applicant to specify the names of the study investigators, the institution(s) where the research will be carried out, the title of the study, and the scientific hypothesis of the proposed study. The signatures of the person proposing the study and also that of his or her supervisor are also required. The name of the funding agency that is to be approached for financial support must also be provided. The form highlights the potential for conflicts of interest concerning funding and accordingly poses certain questions concerning remuneration.

Questions about the proposed procedures

Subsequent questions on the form concern the type of study design to be used and any proposed intervention(s). Background information on the study helps ethics reviewers to understand why participants are required. Inclusion and exclusion criteria, as well as recruitment procedures, are also generally described at this stage, and a description given of the proposed methodology, focusing on the manipulations, if any, of the participants. If the proposed study is based solely on existing records and no direct human participation will be needed, this must be clearly stated.

At some institutions an expedited review process can be followed if the proposed study:

- requires only the collection of blood or urine samples;
- and/or the examination of medical records;
- and/or the examination of redundant recorded data;
- and/or use of a questionnaire;
- and/or the use of specimens collected non-invasively or of materials normally discarded such as hair;
- and/or if the project is a previously approved routine clinical protocol.

Questions about potential harms and benefits

Assurance must be given by the applicant that the participants' privacy will be protected and that participants will not be exposed to hazardous substances such as radiation, if these form part of any of the investigative procedures. The applicant must also explain clearly what will be gained by the study.

Informed consent

A written consent form, though not an absolute requirement, is commonly used to convey information about the study to each participant. It should be written in language that can be readily understood by any person who may be eligible to participate in the study. It will thereby contribute to full comprehension and to truly informed consent. In the case of an illiterate participant, the information on the form should be read aloud. If the study population comprises several ethnic groups, it may be necessary to print the consent form in several languages.

Informed consent requires that each potential participant:

- is fully informed about the nature of the study and each of its component procedures;
- is not pressured in any way to participate;
- is given every opportunity to ask questions about the study;
- is provided with answers to those questions;
- is given the opportunity to withdraw his/her participation, at any point, without prejudice.

The consent form should include an indication of the length of time for which participation is requested. A copy of the document should be retained by the subject after signature. As an example, Table 8.4 shows the elements of a human subject informed consent form required for research sponsored by the US federal government.

A deviation from the truth, which may initially appear unethical, but which the informed consent procedure permits, concerns the title and objectives of the study. This is particularly relevant to environmental epidemiology studies since disclosing precise titles or objectives could predispose subjects to providing biassed responses to questions thereby rendering the study findings uninterpretable. For example, if the putative agent of an etiological study is tobacco smoke, it would be legitimate to broaden the study title and objectives to "environmental pollution". Specific questions about tobacco smoke could of course be included in the questionnaire.

Table 8.4. Required elements in an informed consent form

- A statement that the study involves research.
- An explanation of the purposes of the research.
- An explanation of the expected frequency, type of activities or procedures and duration involved in the subject's participation. A description of the procedures to be followed.
- Identification of any procedures which are experimental.
- A description of any foreseeable risks or discomforts to the subject. A description of any benefits to the subject or to others which may reasonably be expected.
- A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained
- For research involving more than minimal risk, an explanation as to whether any compensation and/or medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained.
- An explanation of whom to contact for answers to questions about the research and subjects' rights, and whom to contact in the event of a research-related injury.
- A statement that participation is voluntary, refusal to participate will involve no penalty and the subject may discontinue participation at any time.
- Consent form is written in uncomplicated language appropriate to the subject population.
- A statement regarding any financial interests the researchers may have in the particular study or research program.
- Note: Additional consent requirements may apply for research involving certain populations (i.e., assent forms may be required for minor subjects, translated consent forms are required for subjects who speak a different language).

8.4 Composition of the study team

The composition of an environmental epidemiology study team will depend on the design, objectives and scope of the study. For some preliminary studies, the aim of which is simply to generate a hypothesis, a principal investigator only may be sufficient. A small study team would include between 3 and 5 persons. But for more complex studies, requiring collection of extensive field and laboratory data, a core team of several specialists may be necessary. In some public health institutions, such a study team may already exist. If not, it must be formed expressly for carrying out the proposed study.

Team leadership and epidemiology

Generally, the epidemiologist of an environmental epidemiology study team acts as the team leader. This is because he or she will have the best overall perspective of the project and should also be familiar with other relevant disciplines. The team leader is responsible for the overall planning and conduct of the study, for standardization of study procedures and maintenance of quality assurance, and for the accurate analysis, interpretation and reporting of data.

Principal collaborators and specialists

Clinical specialists

Studies incorporating medical examinations or clinical measurements may require the services of a clinical specialist, even if the epidemiologist on the study team is a medical doctor. Including a clinical doctor on the study team will also ensure that diagnosis and classification of the health effects or disease experienced by cases will accord with current diagnostic thinking and practice. Study subjects may have to be brought to the clinician, although the development of portable equipment for clinical tests now makes field examinations easier to undertake.

Clinical specialists participate in environmental epidemiology studies as study co-investigators or as expert clinical evaluators. If a clinical specialist is being considered as a study co-investigator, the team leader should carefully evaluate his or her qualifications and reputation. This is important since, as study co-investigator, the clinical specialist selected may be assigned responsibility for all the clinical aspects of the study.

The role of expert clinical evaluator on a study team is different from that of a co-investigation in that the clinical evaluator's role is primarily to measure clinical outcome variables. For example, he or she may serve as a member of a clinical review panel that is responsible for independently evaluating medical records, X-ray films and other clinical materials. The clinical evaluator need not be highly trained in research techniques, but he or she must have strong clinical qualifications and must understand the importance of adhering to the study protocol.

Exposure assessment specialists

In environmental epidemiology studies, assessment of exposure to environmental pollutants is as important as assessment of the health outcomes. Thus the role of environmental scientists in ambient air monitoring, for example, is crucial to establishing exposure—response relationships for air pollution. An exposure assessment specialist should help the team leader to establish an exposure assessment protocol, including reference to environmental sampling and monitoring, transport and handling of samples, laboratory analysis and interpretation of results. Such a specialist should also be assigned responsibility for calibrating equipment and implementing quality assurance procedures.

If a study requires use of sophisticated equipment, employing a repair and maintenance specialist may be worthwhile. Even if a study relies on simple equipment, such as air samplers, a specialist may be necessary during fieldwork so that environmental monitoring is not disrupted unduly in the event of breakdown of equipment. Alternatively, if a specialist is not available full-time, field workers should be trained in basic repair and troubleshooting techniques. This training is especially important for studies in developing countries where there may be no local facilities for equipment repair.

Laboratory scientists

Most environmental epidemiology studies involve collection of environmental samples or biological specimens so laboratory scientists are needed to analyze these specimens. Indeed, considerations of the quality of laboratory analysis and of cost and feasibility, may be major determinants of the overall study design. Consequently, the relevant laboratory scientists should be included at the earliest stages in planning a study.

In many instances, environmental samples and biological specimens can be collected in the field and then transported to the laboratory for analysis even if this requires special handling procedures. For example, in a study of organochlorine pesticide exposure in the US State of Hawaii, the investigators obtained specimens of human milk and serum from subjects throughout the islands (Baker et al., 1991). The specimens were processed in local medical laboratories and immediately frozen in specially prepared containers. Subsequently, the containers were packed in dry ice and shipped by express mail to research laboratories on the mainland US for analysis. The laboratory scientists in this study were selected on account of their expertise, even though they were not located in the vicinity where the specimens were collected.

Computer data processing and statistical specialists

A statistician's advice is generally sought even for small-scale studies. Such a specialist should be proficient in using computers or microcomputers for data management and familiar with the different software and hardware available for working with different volumes and quality of data.

The statistician's tasks include helping the team leader to select and finalize the study design, to decide upon procedures for selecting study subjects, and to develop questionnaires and other survey material for standardized collection of data. The statistician should help the team leader to formulate the study hypotheses quantitatively to ensure that the statistical analysis addresses the hypotheses.

During the study, the statistician should review the original data and computer files, indicating any omissions, inconsistencies, or errors. The statistician should also assess the quality of the data by comparing the data collected by different observers and coders, and assist the team leader with data analysis and interpretation.

Interviewers and technicians

Interviewers and technicians often play as important a role in a study as the key staff. The task of interviewers is to obtain questionnaire data and that of technicians to carry out environmental sampling and perform clinical examinations. If adequately trained personnel are not available, less experienced personnel must be trained in the specific tasks.

If administering the questionnaire requires in—depth medical knowledge, the interviewers should be recruited from among nurses or others who have received medical training and possess appropriate experience. This will help ensure the accuracy of interview results and thus increase cost—effectiveness. This applies particularly if information is sought on many closely-related symptoms. Nurses and medical technologists are also commonly recruited as interviewers because of their experience in dealing with people or patients. Likewise, sociologists and mass communication professionals are often recruited to work on a study because of their communication skills. Specially trained interviewers must be hired if any of the study subjects are disabled (e.g. blind or deaf) or illiterate.

Medical or public health students can also be valuable as interviewers because of their training. They will also be aware of the need to avoid bias and to exercise professional responsibility. However, they are generally only available during vacation times, and thus may be unable to participate in studies for extended periods.

Technicians who are to be responsible for carrying out personal monitoring or examination of study subjects must also possess good communication skills. For example, they must be able to motivate study subjects to actively participate and cooperate in the performance of their tasks. The number of interviewers and technicians required will depend on the study design, and the study's objectives and scope. However, the optimal number must be maintained to minimize observer bias and inter-observer differences. Random allocation of interviewers and technicians to study subjects will make assessment and further reduction of interviewer bias possible.

Senior interviewers and technicians may be necessary for a large-scale field study, to supervise the work of other interviewers and technicians. One of their principal tasks is to ensure that questionnaires and other interview forms are completed properly, returned and edited, and that tests or environmental sampling are carried out correctly.

Other team members

Other professionals may be helpful in developing questionnaires and interview schedules (e.g. sociologists, psychologists), tests (e.g. physiologists, toxicologists), and environmental sampling procedures (e.g. industrial hygienists, chemists). Their participation may be part-time only but crucial to the development of an appropriate sampling frame and strategies.

Vital community information for the planning the study can often be obtained from local health staff nurses, medical technologists, nursing aides, social workers and community volunteers, all of whom will be familiar with the study area and its social customs, and with the health status and other important characteristics of the community being investigated. They might also be very effective recruiters of potential study subjects, although care would have to be taken to ensure that selection bias did not occur.

For large-scale studies, clerks, secretaries or receptionists may be needed to provide administrative support for field workers, technicians, interviewers and project staff. For smaller studies, clerks and laboratory aides may be the only support staff required.

8.5 Study implementation

The quality of the study findings depends greatly on how carefully the investigators plan and prepare for the data collection. Therefore, prior to collecting the data — referred to as the "Main Study" — a preparatory phrase must be undertaken during which details of the study plans are finalized, the study instruments pretested, the study team members trained, and the logistics of any field or community-based data collection planned.

Preparatory phase

There are two basic types of data collection: data collection based on existing data pertaining to mortality, morbidity, disability, hospital or emergency room admissions, absence from school or work, and environmental monitoring data; and data collection that requires contact with study subjects or collecting environmental samples.

If a study is to be based on existing data, permission to access and make full use of it must be obtained from local authorities or relevant institutions. Enquiries should also be made concerning the completeness of the data, the time period covered and the frequency with which the data were recorded (e.g. daily, weekly, monthly, annually). Information should also be sought on the coverage of the data (e.g. the geographical areas covered by a population census), and whether the data can be subdivided into smaller study areas which differ from municipal administrative areas. It should also be determined if the existing data have been collected in such a way that they can be used directly for study objectives.

If the study necessitates contact with study subjects, the preparatory phase should include the following steps:

- negotiations with local authorities, community leaders, professional associations, etc.;
- purchase or rental of equipment and other materials;
- preparation of instructions for field workers, including specifications for completing forms (including coding instructions);
- recruitment and training of members of the field study team;
- pretesting of questionnaires;
- pretesting of instruments and observers;
- pretesting of examination procedures and content on a few of the study subjects;
- rental of space and facilities for field study and equipment
- setting up of computer programmes or software for analysing data.

Arrangements with local authorities, study population and other interest groups

The cooperation and approval of local authorities should always be sought. Indeed, in some countries, an environmental epidemiology investigation cannot proceed unless the approval of the relevant local authorities has been obtained. The local authorities should be informed of the study's objectives and its organizational aspects. This information should convince them that the proposed study is in the community's interest. The investigators must be able to assure the local authorities that the study methods that are to be used are safe. Once the consent or approval of local authorities has been obtained, it is generally possible to secure their help in gaining access to the environmental monitoring data routinely collected in the study area, or in acquiring premises for the field study, such as an office for the study personnel or clinical examination facilities.

Before embarking on a study, meetings should also be held with community leaders and representatives of interest groups or professional societies. They too should be provided with information about the study and their cooperation sought. The value of the study should be described, but the anticipated outcomes should not be exaggerated; otherwise disappointment may ensue if findings are not as substantial as expected.

The way in which the study subjects are informed about the nature and purpose of the study will depend on the study design. If a high proportion of the population is to be asked to participate, community meetings or communication via mass media (radio, newspapers, or TV if available) would be the most efficient. But if the sampling fraction is small, individual contact, by telephone, letter, or home visits, would be more appropriate.

Identification of sampling frame and selection of sampling methods

Identification of the sampling frame should be oriented around the study hypotheses and objectives. (The concepts of a sampling frame and sampling methods are described in Chapters 3 and 6.) Preliminary evaluation of a sampling frame should be performed by an the investigator during the study's preparatory phase to confirm that the sampling frame is representative of the characteristics of the study population as required by the study, that adequate coverage can be achieved, and that a sufficient number of participants can be drawn from the sampling frame to achieve the statistical precision required. A final evaluation of the sampling frame can be carried out during the pilot study, and any necessary adjustments or modifications made.

Training staff

Training of the study team staff should be undertaken by professional training experts or experienced senior staff, according to a well-prepared programme. At the beginning of the training, all staff should be given complete sets of instructions and forms to be used in the study. The objectives and organization of the study, and the proposed investigative methods, should then be described. Group training is usually more efficient and economical than individual training. Ideally, study staff should be trained and recruited at the start of a research project. If study staff remain with a project until its completion, observer variation will be minimized and training costs kept to a minimum.

Training interviewers should enable them to gain a good understanding of the study, so that they can explain the study's objectives to participants in an unbiased manner. Additionally, study questionnaires should be explained to interviewers in depth and detailed written instructions provided concerning how to administer them. Instruction how to avoid bias during interviews will also be crucial. (See, for example, the instructions for interviewers of the Epidemiology Standardization Project, of the American Thoracic Society (Ferris et al., 1978)). Administering of questionnaires should be practiced several times under simulated conditions so that potential interviewer bias can be identified and interview techniques modified as necessary.

Training should also enable interviewers to develop the necessary interpersonal skills, including how to motivate and win the trust of respondents, and how to convince them of their important contribution to the study. "Role playing", in which the interviewers alternately play the role of study subject and interviewer, using the study questionnaire, is a particularly useful method for training interviewers. Interviewers must also be instructed about the significant effects that their behaviour, language and attire can have on participants, and of the need to be aware of participants' social customs.

Plans should be established in advance for training of new staff in the case of turnover in personnel during the study. It is a common error to provide less or more informal training to new staff brought into a study after the initial training has been completed. One approach toward this problem is to keep records and use the identical agenda, schedule, and materials for all training. In some larger studies, investigators have made video recordings of training sessions so that now staff can observe these tapes later on.

Designing and pretesting recording forms and questionnaires

The preparatory phase is used to design and pretest all recording and questionnaire forms to ensure that they facilitate accurate and efficient collection and recording of the data required.

The ease with which data can be extracted from the form, for tabulation, coding, or direct entry into a computer, should be pretested before finalizing the form's format. The need for extracting or copying information from forms completed in the field or in the laboratory should be minimized. Such copying may be inevitable, however, if data is to be extracted from existing vital statistics files, or if a number of clinical or subclinical examinations are to be performed by a number of departments of a hospital. In the latter case, the study subject's ID number should be placed in a conspicuous position on each form and used consistently. In some instances, investigators may have the resources to use portable computers for the interviewers to administer the study questionnaire. This approach can be efficient and reduce the potential for error by allowing direct entry of subject's responses and other data. The basic steps of developing forms should still be followed before transferring the forms to the computer format.

The preparation of forms should include the following procedures:

- listing all items of information required on the form; if the data are to be copied from existing files such as vital statistics files, the contents of the form should be based on the data available; unfilled space is both wasteful and frustrating;
- deleting superfluous or redundant items;
- arranging the items sequentially, according to the anticipated flow of information;
- preparation of a first draft layout of the form;
- obtaining comments and suggestions for improvement from team members, particularly those who will be responsible for completing the forms and processing the data;
- amending the form as needed;
- deciding on the size, material, and format of the form and producing a prototype;
- testing the prototype in a pilot-study situation;
- testing the ease with which the data entered on the form can be processed;
- finalizing the form and arranging for it to be printed or photocopied.

Questionnaires are perhaps the most important of all the forms used in environmental epidemiology fieldwork. Questionnaires should be as precise and easy to complete as possible, and leave little room for ambiguity. They should be designed so as to facilitate checking (of completeness and accuracy) and data processing. Standardized questionnaires such as the ATS-DLD (American Thoracic Society and the Division of Lung Diseases of the United States National Heart and Lung Institute) questionnaire for respiratory symptoms (Ferris et al., 1978) provide useful starting points when designing a questionnaire since they have been field-tested successfully in a number of countries. Use of standardized questionnaires also facilitates comparison of data generated by different studies. However, minor modifications can be made to adapt standardized questionnaires to local conditions. Thus the ATS-DLD questionnaire has been translated into a number of languages. Translation of questionnaires can be problematic though. Some terms do not have direct equivalents in other languages. For example, "wheezing" cannot be easily translated into French (Osterman et al., 1990). In such cases, a video tape may be of help (Shaw et al., 1992).

Pretesting the questionnaire and forms before the main study is undertaken is especially important if the study team has not used them before, or if the questionnaire has been translated from another language, or was previously used in a different social-cultural setting. Questionnaires should be standardized to ensure accuracy and comparability, but they should also be relevant and specific to local situations.

Establishing laboratory analysis and data management procedures

If laboratory tests are to form part of a study, laboratory procedures should be established in advance of the study. All measurement methods should be evaluated during the preparatory phase to verify that valid results will be obtained from all instruments and all observers when the main study is carried out. This is usually done by measuring the reliability (reproducibility) of the measurements. If specific reference measurement methods (e.g. a biological specimen with a known concentration of lead) are available, the accuracy of measurements should be evaluated by performing analyses on the reference material. The accuracy, precision, sensitivity and specificity of instruments should be evaluated too.

Errors in laboratory measurements can arise following power cuts or voltage fluctuations, in which case, remedial counter measures should be considered. For instance, using simpler instruments or analytical procedures for field use may be possible. Comparisons should be made between alternative testing methods and any necessary adjustments made.

During the course of a study, data may be generated from a variety of source points (e.g. interviewers, laboratories, hospitals, vital statistics departments) and over various periods of time. The flow of the data from the source to the location where they are to be stored and analyzed should therefore be planned and controlled. The methods for storing and computing the data should be determined during the preparatory phase. Plans should be made as to how the data are to be entered, edited and checked, and how data reports are to be generated. It is worthwhile preparing computer programmes for file creation and manipulation, for checking errors, and for checking the consistency of information "within" each subject in the study, before the field study starts. New programmes can be written or suitable programmes selected from existing software packages such as EpiInfo (available from WHO, or CDC in the United States), or SAS or SPSS for (statistical analysis). The suitability and validity of the prepared programmes can be checked against a set of specially-prepared dummy documents. It is advisable to prepare dummy data that include a number of deliberate errors. A check can then be made to ascertain whether programmes will perform as anticipated.

Feasibility assessment

Feasibility assessment of the proposed study should be undertaken before or at the same time as the pilot study. Table 8.5 lists the principal items that should be evaluated to assess feasibility. A decision can then be made either to proceed with the study design as it is, or to modify it. Further clarification of feasibility issues will be possible after the pilot study.

Pilot study

A pilot study is undertaken to evaluate the overall adequacy, feasibility and appropriateness of the proposed study. It also enables the accuracy of cost and time estimates to be checked. Usually limited to two or three days work in a single location, the pilot study should nevertheless be a "full-dress" operation and designed so that the adequacy of each study component (including the study protocol, questionnaires, instruction for field workers, arrangements for the transportation and analysis of biological specimens, methods for statistical analysis of data, and computer programmes) can be assessed. An effort should be made to produce the tempo and spirit of the actual study. At the conclusion of the pilot study, the team leader should be able to decide whether to abandon the main study, if it appears to be irremediably impractical, or to modify it, or to proceed as originally planned.

A sufficient period of time must be allowed between the pilot study and the main study, so that adjustments can be made. The pilot study should also provide an opportunity for testing the adequacy of training under field conditions.

The data analysis methods may be tested in a pilot study. However, a pilot study is not intended to address study hypotheses. The purpose of a pilot study is to obtain information on how the study methods could be refined to improve their application in the main study. Thus measurement instruments are often revised on the basis of the pilot study results. Therefore data from the pilot study generally should not be merged with data from the main study.

Table 8.5. Checklist for feasibility assessment

- Obtain the approval of the relevant authorities
- Seek the cooperation of relevant communities, interest groups and collaborative institutions
- Assess the availability, completeness, applicability or usefulness of environmental exposure data
- Assess the availability and completeness of existing health effects data contained in existing vital statistics or hospital data files
- Ensure that an adequate population size exists, from which a suitable sample size can be drawn
- Secure sufficient resources, including funding, qualified personnel, time and equipment
- Check the availability of examination premises, equipment, power supply and facilities for storing biological specimens
- Check availability of facilities for the transportation of personnel and specimens
- Check the availability of laboratory facilities
- Check the availability of computing facilities and software for data storage, data analysis, and reporting

Main study

Two concepts are central to the planning and conduct of the main study:

- everything and every person involved must be on site at the time specified;
- interviews and examinations should be conducted strictly according to the study protocol, or as modified after the pilot study.

Advance contact

Issuing a letter in advance to the study subjects is strongly recommended for population studies. The letter should inform subjects of the objectives of the study, the procedures, time schedules, and other details, as appropriate. An advance letter should motivate the study subjects and encourage them to cooperate with the interviewer, to attend the medical examinations, or to complete the questionnaires. It should be signed by the team leader, the director of a medical institution, or by a person who is trusted by the study subjects. If the study population is illiterate or semi-illiterate, a community meeting, personal contact, or message sent via a primary health-

care worker can serve the same function as a letter. If students of a school are to be requested to participate in a study, contact with parents can be made via a teacher, the principal of the school, or the school's parent-teacher association.

Interview studies

Studies based exclusively on interviews may be done by staff in a project office, by staff in the participant's home, or through the mail. If an interviewer-administered questionnaire is to be used, interviewers should be allocated randomly among the study subjects or dwellings selected, as specified by the study protocol, and a schedule of visits drawn up for each interviewer. This random allocation will minimize the possibility of any bias due to systematic differences among the interviewers in how they interview. A letter requesting participation in the study (following the advance contact letter) should be delivered before the interviewer's visit, giving the time of the visit and the name of the interviewer.

If the questionnaires are to be self-administered, a check should be made to verify that all the study participants in the community to be studied are literate. The questionnaires can be sent with the advance contact letter, or separately, depending on the local situation. Records should be kept of questionnaires sent out and returned, and the accuracy of responses should be checked. Appropriate procedures for dealing with non-responses should be worked out in advance. These may consist of sending one or more reminders, or making home visits or telephone calls. Decisions must also be taken regarding how to deal with incomplete answers. Making a home visit, writing to the respondent again, or telephoning, are all possibilities.

Medical and laboratory examinations

If medical and other examinations are to be undertaken, special premises should be arranged in advance. Appropriate premises for studies can often be found in clinics, hospitals or schools. A school is often a reasonable choice during school vacation time, particularly if large numbers of children are to be examined.

To encourage study subjects to participate in the examinations, the premises should preferably be within walking distance of homes or places of work, or easily reached by public transport. Participants can be provided with bus tickets or reimbursed for their travel costs to and from the examination site. Adequate parking space should be available and transportation to and from the examination premises provided for people with special needs such as the disabled and the elderly.

Reception areas, waiting rooms, interviewing or examination rooms, and toilets are usually required. A snack-bar may also be needed if study subjects are requested not to eat before the examination — as with liver function tests or gastrointestinal radiography — so that they can obtain refreshments after the examination has been carried out.

Study subjects can be invited to participate in an examination through one of several channels. If medical or other laboratory examinations follow an interview, the interviewers themselves or attendant primary health-care workers can make the request. They should explain the objective of the examination and how the examination will be performed and provide assurance that participants or their physicians will be informed of all clinically irregular findings. This approach is generally successful. Alternatively, potential study subjects can be contacted by letter. The response rate is likely to be low, however. Procedures for dealing with refusals or with difficult subjects should be determined before initial contact is made. Personal visits by

interviewers and primary health-care workers serving the area, recall letters, and telephoning, are generally considered the most appropriate. If portable instruments are available, taking certain measurements in the home of the subjects may be possible, thereby increasing the response rate.

Following study subjects over time

Follow-up studies often depend on regular contact with study subjects over an extended period. Such studies are easier to undertake in communities where populations are relatively stable, or residents legally required to register with the local authorities, or where a household registration system is in force. Most local authorities maintain records of the residents who live or lived in the area under their jurisdiction, including data on where residents came from and where they moved to. Conversely, communities with highly mobile populations, or without a household registration system, or in which registration with local authorities is not required, may be unsuitable, particularly if a prospective cohort study is planned. The duration of the proposed study and possible means of tracing subjects if they move to another new area (such as names and addresses of next of kin or close friends) are also important considerations when deciding whether to undertake a cohort study in a particular community.

If follow-up relies on the extraction of information from vital statistics records, registries, hospital admission or discharge records, a check should be made to identify any changes that might occur during the follow-up period, and to determine whether these could influence the consistency of the data. For example, hospital admission policies could change over time so that data based on these records would not be consistent. Consequently, the investigators should be prepared to monitor whether these type of policies do change during the follow-up period.

Reporting of results to subjects

The extent to which study results are reported to individual subjects will depend on what was agreed before the study was initiated and the nature of the findings. Informed consent is solicited before a study is started, so subjects have the right to be informed of the study results.

If the number of study subjects is large, and medical or other examinations show that most of the subjects are in good physical condition, it may not be necessary to report detailed results to each individual participant; however, the investigator still should inform individual participants that the findings are normal. In addition, the investigator should provide an assurance that clinically irregular findings will be reported to the individual, and/or his or her physician as soon after detection as possible. Individual findings can be communicated to the participant in a letter or via the primary health-care worker serving the area. Alternatively, a letter can be sent to the participant's physician who can then contact the participant regarding treatment. The study team should stress from the beginning of the study that it cannot be held responsible for treatment of disorders detected during examinations.

Once the study has been completed and reviews carried out, the study team should report its findings to all relevant parties, including local authorities, institutions, and all participants. The study findings can be reported to the community residents at a meeting, presented in a summary report of the technical report using language and a writing style that is appropriate to the community, or disseminated through the mass media.

Quality assurance

Quality assurance is the process of ensuring the accuracy and precision of the study measurements by systematically following a number of procedures when designing the measurement instruments, preparing for data collection, applying the measurement instruments, and processing the resultant data. For an environmental epidemiology study, this means that all possible efforts have been made to reduce any potential errors or uncertainty in the findings to an absolute minimum. The basic elements of quality assurance planning include procedures for staff training, data collection, instrument calibration, instrument maintenance and inspection, laboratory practices, data management, and auditing of study activities. Principles of quality assurance are discussed in Chapter 3. Armstrong et al. (1992) compiled a list of such procedures relevant to measuring exposures, which is adapted as Table 8.6. The table makes clear that data collection consists of many steps and that error could be introduced at any of these.

Collaboration is recommended only with those laboratories that operate internal and external proficiency tests to demonstrate repeatability and reproducibility of performance. Such tests also enable comparison between laboratories so that systematic errors made by individual laboratories can be detected. A laboratory must adhere strictly to the quality assurance/quality control rules defined by recognized certifying agencies to obtain accreditation (legal recognition of the results of its research). Even if formal accreditation is not necessary for their activities, responsible laboratories use standard operating procedures that guarantee a high degree of quality control.

A separate quality assurance procedure should be established for each set of data measurements that are to be collected. This should define:

- Calibration of study instruments: which is performed in order to avoid systematic "drift" in instrument readings and variability in measurement when more than one instrument is used. An external calibration device can be used for some instruments; e.g. a calibrating syringe can be used with spirometers when assessing lung function. If no external standard exists, a calibration curve has to be constructed on the basis of controlled conditions (e.g. using reference samples).
- Assessment of repeatability: which refers to agreement between results of successive measurements carried out under the same conditions. Some procedures, such as pulmonary function tests, should be repeated 3–5 times and the results of these fall within a predefined range of variation if they are to be considered valid (see, for example, ATS, 1995). Environmental measurements can be validated by random collection and analysis of duplicate samples.
- Measurement reproducibility: which refers to agreement between results of successive measurements taken under varying conditions (e.g. different operator, weather, place and time). If the measuring takes the form of an interview, reproducibility may depend on the thoroughness of interviewer training.
- Sensitivity, specificity and limits of detection: which refers to measures of performance on the test relative to known true values. These measures are often determined by analysing reference specimens with known values of the environmental or biological variable (e.g. serum specimens with known pesticide concentration).

Table 8.6. Quality control procedures for data collection in epidemiological studies

Design of the instrument

Design of forms

- Include all items needed to compute dose, timing of exposure, etc.
- Include adequate subject identifiers at least an identification number and a check digit or alphabetic code on all forms.
- Make instructions clear and data collection items unambiguous.
- Use different typefaces for instructions, data collection items, and responses.
- Provide mutually exclusive and exhaustive response categories for closed-ended items.
- Make forms self-coding for simple items e.g. data collector circles a number corresponding to the appropriate response category.
- Make response codes consistent within and across forms e.g. 1 = no, 2 = yes.
- Provide for coding without loss of information i.e. do not design forms so that continuous data are categorized at the coding stage.
- Do not require computation by data collectors.
- Design forms for direct entry of data into the computer.

Study procedures manual

- Always have a study procedures manual.
- Include at least the following in the study procedures manual:
 - · description of the study in general terms
 - sample selection, recruitment and tracking procedures
 - · informed consent and confidentiality procedures
 - · data forms
 - · general methods of data collection
 - item-by-item clarification of questions and responses, including special cases
 - · editing procedures
 - · coding instructions for items not self-coded on form
 - codebooks
- Update manual and distribute updated pages whenever procedural changes are made.

Preparing for data collection

Pre-testing instruments

- Have instruments reviewed by other researchers.
- Pre-test instruments on samples of convenience.
- Train data collectors and pre-test instruments on samples similar to study subjects.
- Identify problems through feedback from pilot-test subjects and data collectors and by monitoring data collection and make appropriate changes as early as possible.
- Review frequencies of responses to identify items with little variation in responses.

Training of data collectors

- Discuss importance of complete and accurate data.
- Review study manual.
- Practise data collection.
- Monitor initial data collection by each data collector.

Table 8.6. Quality control procedures for data collection in epidemiological studies (continued)

Quality control during data collection

Supervision of data collectors

- Assign cases and controls in a case-control study (or exposed and unexposed subjects, in a cohort study) in the same proportions to each data collector.
- Maintain ignorance of data collectors to status of subjects, as far as possible.
- Replicate some proportion of data collection (e.g. 10 per cent of subjects) to identify fictitious data, items with poor reliability, data collectors with errors on certain items, etc.
- Compare the distribution of study variables among data collectors.
- Compare distributions of study variables over time.
- Address problems identified through monitoring immediately with the relevant data collector(s).
- Conduct staff meetings for retraining, discussion of problems, and motivation.

Editing and coding

- Have data collectors edit data forms immediately to clarify responses and check for missing items.
- Have editor perform a second edit soon after data collection to check for missing items, inadmissible codes, inconsistencies among responses, illegible responses, etc.
- Have editor code open-ended questions and query those inadequately answered.
- Correct errors by call back to subjects (or check-back to records).
- Have one staff member maintain an editor's log to ensure consistency of recording and coding of unanticipated responses, and to record comments and responses coded as 'other'.

Quality control during data processing

Key entry

- Create a codebook with format and codes of 'raw' data items.
- Enter data contemporaneously with data collection.
- Double-enter (verify) all data.
- Edit data by computer by performance of range and logic checks contemporaneously with data entry.
- Correct errors and feed back findings of relevance to data collection.

Creation of new variables

- Check and recheck the programming code used to create new variables.
- Check the correctness of new variables by manual computation from a sample of original records, whenever reasonably possible.
- Review distributions of original and created variables.
- Create a codebook with detailed descriptions of new variables created, including the original variables and programming code used to create them.

Source: adapted from Armstrong et al., 1992.

Particular attention should be paid to the following activities which could affect study quality:

- collection of primary study materials (e.g. collection of biological material from study subjects or air sample collection for air pollution studies);
- transportation of samples (i.e. procedures to avoid sample contamination or degradation, or chemical reactions between samples and containers, should be established);
- storage of samples (for immediate analysis and for future analysis and reference);
- analytical operations.

Quality assurance procedures for dealing with these issues can be based to some extent on existing methodologies or guidelines. For example if a collaborating analytical laboratory follows well recognized standard operation procedures, it may be possible to use the standard procedures in the study. Additionally, standard rules regarding the taking of measurements — for example methods for spirometry testing recommended by the American Thoracic Society (ATS, 1995) — can be included in the study protocol.

Besides instituting a quality assurance procedure for each measurement activity, a quality assessment of the entire study should be carried out on a regular basis throughout the study to detect any weak points. Follow-up action to remedy these weak points might include redirecting the study resources to where they are most needed (e.g. changing to a more expensive but more accurate measurement procedure), additional training, or modifying use made of equipment.

8.6 Tools for data management and analysis

Most of a study's activities involve defining the exposure and health outcome variables that are to be assessed and selecting the appropriate methods for measuring them. However, effort expended on these tasks may be wasted if the data collected are not correctly recorded and processed, or edited. Additionally, even after the data have been evaluated, and the results of the study presented, the data should not be discarded, since an opportunity for re-analysis may emerge after the main investigation has been concluded. For example, a new hypothesis may be generated but must be tested by further analysis of the data. An attempt might also be made to expand the study by undertaking a follow-up investigation of the study group. Long-term secure storage, and/or archiving of the data must therefore be assured.

Computing software

Most epidemiology studies involve a considerable amount of data collection and data processing, and therefore use computers to store data. This text assumes that each team conducting an epidemiology study has access to a computer.

Recent advances in computer technology now make it possible to analyse almost any epidemiological study on a personal computer (PC). In addition, a wide variety of software is available for data entry, data analysis and graphical presentation of data on PCs. One particularly useful package is EpiInfo, which is available from WHO and the US Centers for Disease Control and Prevention (Atlanta). This package is especially useful for data entry and editing, and can be used on portable computers in the field as well as on desktop computers. There are many

other comparable packages but some of them are costly or less widely available. Programs for data entry and data management include dBase, FoxPro, and Access. Statistical analysis programs include SAS, SPSS, BMDP, and Systat, for example. Various packages for regression analyses also exist, including EGRET, EPICURE, and STATA. But unlike EpiInfo, these latter programs are not free of charge.

Linkage of data

In most environmental epidemiology studies, study subjects undergo several procedures, such as interviewing, medical examinations and laboratory tests. The data collected may be stored in different database files. All the information relating to each study subject must then be linked. Consistent use of each subject's identification number (ID) on all forms and questionnaires will facilitate this. If serial numbers are used, as in medical examinations or laboratory tests in clinics or hospitals, these should be recorded in a data entry book for cross reference with the subjects' ID numbers. Follow-up studies may require that the same subjects are re-examined one or more times. If so, each form used for a subject should be marked with that subject's ID number.

Data recording and storage

For the sake of simplicity, two principal methods of data entry can be distinguished: the information is collected by study participants or staff and recorded manually on prepared forms; or the information is directly recorded in a computer, as when computerized questionnaires or measuring devices equipped with an electronic digital recorder are used. In principle, the latter alternative involves fewer steps which means that fewer opportunities for human error are created. It is also generally faster. However, it is not always practicable due to higher equipment costs. Nevertheless, whichever method is favoured, the data processing software should be defined and selected at the study planning stage.

Effective data entry depends on well-designed study forms and questionnaires (see section above on designing and pretesting recording forms and questionnaires). In addition, the following steps should also be carried out using the data management and statistical software:

- 1. **Data entry and formal checks.** These include verification of the type (text, logical, date or numerical), field length and range of values allowed for each variable. The software used for the data entry should detect inconsistencies and prompt the operator for correct data. Most databases or statistical packages, including EpiInfo, do this. For the EpiInfo package the entry format of each variable is defined at the time the EPED editor designs the questionnaire.
- Double data entry. It is recommended that two operators enter the data independently.
 Inconsistencies detected due to misreading of unclear hard copy, for example should be corrected to ensure that the computer record is compatible with the hard copy forms.
- 3. **Logic checks.** The logical links between the variables should be verified. For example, an error must have occurred if pregnancy complications have been entered on a record as the reason for the hospital admission of a male subject. (In this instance, the gender of the subject or the diagnosis would have been entered incorrectly.) If the error is not

due to a typing mistake (as is the most often the case), the data should be verified at the data source. For the above example this would mean consulting the hospital records. If data on one individual are collected on several occasions, the different data sets should be compared. However, changes in the values of the controlled variables do not necessarily indicate an error in recording and/or in data entry. They may be related to real changes in the studied parameters or to interview reporting errors. The latter are difficult to correct if the check is not conducted simultaneously with the interview. In extreme situations, the inconsistency of a record may indicate a mistake in the subject's identifier. A longitudinal study of lung function changes in an adult population provides a clear example of this. For a 55-year old smoking man, the record had shown a 1200 ml increase (over 30%) in lung function for the eight-year period following the previous survey. Such a result is very unlikely; based on an average rate of lung function decline with aging, a decrease of at least 300 ml in the lung function level of the subject could have been expected. For a record of another subject, a 28-year old non-smoking male, a rapid decline of 1500 ml was found. This was also unlikely, unless a severe deterioration of respiratory health had occurred. After close investigation of the study forms, it was found that the records of father and son, who bore the same first name, and who were tested on the same day, had been interchanged.

4. **Analysis of univariate distribution of each factor.** If the factors being investigated are continuous variables, outliers may be due to mistakes in data measurement or recording.

Only after the above checks have been completed and any errors corrected in the data file, and also on the forms (if the error occurred before data entry), can a data file be regarded as "clean". Running all the procedures again to verify that all corrections have been entered and were sufficient is often worthwhile. At each stage of data processing, backup copies of the data files should be made and stored independently of the "working file". The copies should be updated regularly.

Data editing

Often, the raw data collected at the beginning of a study must be transformed to create variables for additional analysis. Such transformations, or data editing, may consist of combining several variables to create a single, new, well-defined variable. The creation of a diagnostic category, "chronic bronchitis", from a series of questions relating to the occurrence of cough and phlegm symptoms, and their frequency and duration in recent years, would be an example. Other examples would be calculation of a "body mass index" from data on body height and weight, or calculation of mean exposure values from a series of measurements performed over a period of time. For example, this could consist of calculation of the maximum daily 1-hour average concentration of an air pollutant such as ozone, based on measurements recorded by an automatic monitor every 2 minutes. This initial step of data analysis is also described in Chapter 7.

A general rule for data editing is that the original variables should be stored and remain accessible as the source of all newly-created variables. If the definitions of transformed variables change, access to the original data may be crucial so that the revised transformed variable can be calculated. An example of inappropriate "data reduction" would be recording only the mean

value of a series of measurements relating to air pollution; reconstruction of the measurements distribution, or a frequency of exceedance of a certain level would not be possible. Sometimes, the results of a measurement (producing a continuous value) are converted to a variable indicating an "exceedance of a (standard) level". Although this information may be sufficient for regulatory purposes, lack of any indication of how much the level is exceeded could restrict analysis significantly if an attempt is being made to estimate quantitative relationships.

The precision of computations to create a transformed variable (generally indicated by the number of significant digits used in the calculations) may be important, especially if arithmetical or logical calculations are performed using a computer. The necessary steps include proper definition of the variables (e.g. appropriate type, sufficient field length, sufficient number of decimal places) and consideration of possible hardware restrictions.

When selecting software, the desired format of the final data set must be considered. Most of the available statistical packages provide quite flexible data processing procedures and create data files suitable for easy input into their analysis programmes. However, some analysis methods may not be available in the package used, or the intention may be to combine the data set with other data sets, for processing elsewhere. In either case, it must be ensured that the data can be recorded in a format that is compatible with other software or hardware (i.e. so that files can be exported). The size of the data file to be processed and analyzed is also an important factor when selecting software. Some packages may restrict the number of variables, the number of records or the record length.

Archiving and documentation

Several copies of the clean, edited data files should be stored. Currently, copying files from a hard disk to large capacity removal disks or a tape back-up drive is the most common means of storing data. However, temperature changes, magnetic fields and mechanical damage can render the back-up disks or tapes unuseable. Files should therefore be rewritten periodically and multiple copies should be stored in different locations.

Archived data should be documented so that even someone who did not work on the study can interpret the data correctly. This is crucial for the study review (audit) and for any reanalysis of the data. The study activities should also be thoroughly documented. Study documentation should include:

- the study protocol;
- a description of the data collection methods (or measurements) used;
- a description and the results of the quality assessment/quality control procedures;
- copies of the study documents (forms, questionnaires, instructions, letters to subjects requesting participation, etc.);
- a description of the data processing and editing procedures, including definitions of all transformations performed;
- detailed description of each field in the data file;
- detailed description of the codes used for each field of the data file;
- an indication of the units used.

Some items relating to the data characteristics (e.g. definitions of code values) can be stored in the data analysis computer program file. However, a printed copy of the documentation should also be available. The documentation accumulated during the study should be prepared on the assumption that no decision is "obvious".

In addition to a description of the basic methodology of the study, extensive documentation describing all of the study data management and analytical procedures and accounting for its results, may also be required; for example, if various members of the study team conducted the data analysis, and the results were published in several different publications.

Confidentiality of information may be an issue if data on individuals is to be processed and stored. Identification of the subjects may be crucial for study purposes (e.g. to link exposure and health data, or to link health data derived from different sources), but open access to personal information may violate ethical rules of research. The identifiers used in a study should therefore be coded so that unauthorized identification of the study subjects is prevented. The simplest means of doing this is by separating personal information (names, exact address, date of birth, etc.) from the other information collected for the study, and storing it and the corresponding identifiers (usually numerical) in a separate file to which access is restricted.

8.7 Study contexts

Community epidemiology studies

Epidemiological investigations are often conducted in response to community fears that exposure to certain environmental conditions — caused by dumping or discharge of toxic substances, or following natural or man-made disasters, for example — are resulting in adverse health outcomes. If adverse health outcomes are indeed found, the next step is to determine whether environmental exposures are the cause of the health outcomes. However, using an epidemiological study to make this determination may not be feasible due to unavoidable factors (e.g. very small population or unmeasured past exposures), or due to limited resources (funds, time and manpower).

Three basic issues must be considered before conducting epidemiological research in a community that believes significant health risks are associated with an environmental exposure:

- the level of scientific information available in the community;
- the quantity and quality of existing health and environmental statistics;
- the resources available for conducting an epidemiological investigation.

Community perceptions of risk are often based on inadequate information concerning the biological plausibility of disease causation or occurrence. For instance, many people assume that a rare disease such as cancer must have an environmental etiology. However, responding immediately to community concern about the occurrence of a specific disease or health effects can do much to allay fears. Provision of basic scientific information about the natural history of the disease of concern, and the importance of measuring exposure when investigating cause—effect relationships, may be all that is required. In fact, experience has shown that in many of these situations an epidemiological study is unnecessary.

Epidemiologists should inform themselves about existing health and environmental statistics that could have contributed to or been responsible for perceptions of risk, and assess their reliability and validity. If the community's perceptions of risk turn out to be solidly based, an epidemiological investigation could be considered. If the converse is true, the community should be informed accordingly. Describing the difficulties involved in identifying the population at risk, and explaining that the observed spatial occurrences of deaths and disease do not differ from those in other places may be necessary. Alternatively, it might have to be pointed out that although temporal variations have been observed in disease or death occurrence, but in this case there is no cause for concern.

Epidemiological investigations should be undertaken if health and environmental data suggest that increased disease incidence in a particular community is biologically plausible. Time and other resources should then be focussed on exposure assessment and determining the specific mechanism of disease causation (rather than on determining the general patterns of disease occurrence). The feasibility of the proposed study should be examined.

Community participation should be sought at an early stage of the study design process, i.e. when setting the study objectives and developing the research methods. However, the study team must be alert to sources of bias that could be introduced if the study subjects' perceptions are allowed to "direct" the study. Meetings can be held with community representatives to explain the significance and limitations of the study, the need for sustained community participation, and to establish mechanisms for informing the community of the study's progress. The study findings must be communicated clearly to the community

Conducting studies in communities with limited resources

Even if resources are limited, an epidemiological study should follow standard procedures for problem identification, preparation of the study protocol, organization of the study team, data collection, and analysis and reporting of results. However, if funding, trained personnel, and appropriately equipped laboratory or data processing facilities are lacking, the scope of a study may have to be restricted. Studies dependent upon extensive laboratory pilot studies, such as toxicological assessment of environmental pollutants, may even have to be discouraged.

When developing a study protocol, the relevant literature should be reviewed carefully. Many libraries are not well equipped with information retrieval systems and communication facilities, and scientific periodicals and journals are generally held in government institutions or agencies located in capital cities and urban centres. Obtaining the literature may therefore be difficult in less developed regions. Even so, obtaining assistance from governmental sources and organizations such as the WHO is often possible, although the pace of research may be slower.

Lack of trained personnel can sometimes be resolved or alleviated by seeking the participation of community volunteers (e.g. primary health workers). They can help to identify study subjects, facilitate communication between local government officials and the study team, and act as interviewers if the study includes a survey. They must be thoroughly briefed by the study team regarding the study's objectives and methodologies so that they adhere to the correct procedures. Some form of incentive should be offered in recognition of their contribution to the study.

Technical persons who work for government implementing agencies, particularly those operating in the health and environment sector, are sometimes willing to act as resource persons for a study. Their participation can be particularly useful during the data collection phase, when exposure assessment or health examinations are required, and if the study results have a bearing on the guidelines, policies, rules and regulations implemented by their agencies.

Laboratory facilities and instrumentation are as crucial as trained personnel. Countries with good laboratory facilities and instrumentation technology sometimes offer use of these free of charge or at nominal cost to local communities with limited resources. Inter-laboratory calibration is vital, however, if quality assurance of results is to be maintained. Laboratories in other countries may also provide assistance for specific tasks such as analysis of split samples, calibration of instruments, and sharing of control specimens or reagents.

Good epidemiological investigation can require substantial resources. It is not necessarily the case, though, that epidemiology studies can be conducted only if sophisticated computers are available. The compilation of cancer prevalence maps in China, for example, was undertaken "by hand", using abacuses and mechanical calculating machines (Atlas, 1987).

Table 8.7 shows a checklist of issues to be considered when undertaking an environmental epidemiology study with limited resources.

Table 8.7 Checklist for conducting epidemiology study with limited resources

- Design the study to match the resources and analytical tools that are available.
 Multivariate analysis should not be attempted in such studies, and the sample size should be the minimum size required to attain the necessary statistical precision.
- Keep the questionnaire as simple as possible, preferably adapting a standardized questionnaire which has been field-tested repeatedly in the past in a number of countries. Only data which is strictly relevant should be collected.
- Transcribe the data from questionnaires onto cards made of durable paper which is able
 to withstand repeated sorting and shuffling. Make sure that these cards can be sorted
 either by hand or by some kind of simple mechanical device.
- Sort the cards by sex, age-group, exposure level, educational level, socioeconomic status, personal habits (such as smoking) and so on, according to the study design.
- Count the number of cards sorted for a specific purpose (e.g. number of females who smoke) and compile the tables necessary for further calculation. Repeated shuffling and sorting should be carried out until all the counts needed for the study have been made.
- Make the necessary calculations by hand or with the aid of an electronic calculator, a
 mechanical calculator, or even an abacus. A programmable calculator can facilitate the
 calculations for performing Mantel-Haenszel chi tests.
- Do not be over-zealous. Be content to limit the data analysis to univariate analysis and bivariate analysis of the principal variables.

Box 8.3. Philippine environmental epidemiology study with limited resources

In 1992, an epidemiological investigation of child "scavengers" exposed to environmental pollutants and hazardous working conditions at a large refuse dump in Metro Manila, the Philippines, was successfully carried out with limited resources. The 20-hectare open dump receives about 200 tons of municipal, industrial and hospital wastes daily and some 1000 child "scavengers" (7 to 15 years of age) work there for at least 6 hours a day. Smoke is emitted continually by the dump-site because of the spontaneous combustion of the materials it contains. The study sought to assess the children's exposure to air pollutants and to construct their health profile. The study methodology consisted of interviewing the children's mothers or guardians, environmental air and water sampling, pulmonary function tests, physical and medical examinations of study subjects, and blood tests for lead.

In Manila, personnel costs generally amount to about 50% of the budget of an environmental epidemiology study. Since the budget for this study was very limited, the study team first made a preliminary inventory of potentially available human resources, including volunteer health workers (community members and members of local nongovernmental organizations (NGOs)), youth leaders, church leaders, midwives of the Rural Health Unit, and community ("barangay") leaders. Individuals were screened based on their willingness to work, willingness to undergo training, and availability for interviewing people. Character references were also obtained from community leaders or NGO supervisors. Those selected underwent two weeks of training including orientation sessions, workshops, field simulations, and field tests. The only costs incurred were for transportation and meals. The participants' principal responsibilities were to persuade the child scavengers and their parents or guardians to participate in the study, to administer the questionnaires, and to help technical staff with environmental sampling, pulmonary function tests and medical examinations.

Physical and medical examinations were performed by volunteer physicians of NGOs involved in programmes to improve the living conditions of the urban poor. Graduate public health students. They used the research findings in their theses or special studies, and assisted with the literature search and review in particular.

An inventory of laboratory equipment and facilities available for the collection and analyses of environmental and biological samples was drawn up. This inventory referred specifically to governmental departments of environmental, science and technology, public health and academic institutions. The laboratory costs were generally nominal since the government subsidizes the operational costs of these departments.

Collaborative and multicentre studies

Multicentre epidemiology studies may involve several populations and research centres within one country. For example, the French PAARC study was conducted in 24 areas of seven French cities (PAARC, 1982). Alternatively, a multicentre study might be based on populations from several countries, as in the case of the World Health Organization/Commission of the European Communities multicentre study on lead neurotoxicity in children (Winneke et al., 1990). Multicentre studies have several advantages:

- increased potential to generalize the study results since the power of a study to assess causality is greater if it examines several populations, rather than a single population;
- an increased range of exposure levels;

- diversification of unknown or uncontrolled confounders (e.g. genetic background);
- increased sample size;
- efficient distribution of resources, workload and expenses;
- effective use of expensive or complex equipment;
- transfer of expertise from more experienced to less experienced groups.

Multicentre studies rely on the same principles as any other epidemiology study, but are more difficult to organize than a basic environmental epidemiology study. Effective and consistent standardization of methods of data collection, processing and analysis are particularly important. Efficient communication between participating centres is also essential. Planning must take into account the possibly unequal opportunity for research (such as availability of specialists and measurement instruments), and differences in communication facilities and administrative capacity. Feasibility of the study with respect to social and cultural constraints must also be assessed for each participating centre.

Study protocol and timetable

The draft study protocol should be prepared by the coordinator of the multicentre study and sent to each participating study group before a consultative meeting is held to discuss it. Any necessary revisions can be made at this meeting, which should also be the occasion for obtaining approval of the study protocol from each of the participating groups. Although the protocol should be similar for each group, socio-cultural or political conditions may dictate a slightly different approach for a particular group. Nevertheless, the results obtained must be comparable.

The timetable for each group should be coordinated centrally. However, it is not usually necessary that each group performs its respective tasks at the same time as the other groups. Indeed, seasonal differences in climate may mean that the field studies have to be carried out in different months in different countries to ensure that the results are obtained under similar climatic conditions.

The study protocol should specify study methods and how the study results are to be published and disseminated. In particular, it should be decided if and when individual participating centres can publish their individual results, how the contribution of the entire multicentre team is to be acknowledged in published results, and how the revision process is to be undertaken.

Organizational and sampling procedures

Even if the staff of each participating centre is highly qualified, training aimed at methods standardization will probably be necessary. Ideally, the key study personnel of each centre are trained centrally. The training of any additional local staff should use standardized methodology and materials. Detailed instructions should be prepared for each group of field workers and, if necessary, translated.

In principle, the centres should follow the same study methods so that study results can be compared. Admittedly, local conditions may be such that different procedures in study organization must be followed in different participating countries. But the number and extent of "local solutions" should be kept to a minimum. Each modification of the generally accepted protocol should be evaluated by the study coordinator to anticipate the influence that the modification(s) could have on the study results. All modifications should be described clearly in the study protocol.

A standard sampling frame should be developed and agreed upon by the participating teams in order to minimize sampling errors. This applies particularly to collaborative studies based on general population surveys. A decision must be taken as to whether separate analysis is required for each of the centres and whether any differences between centres in the results must be investigated. If additional separate analysis of results is planned, a sufficiently large sample must be selected by each centre.

Standardization of study instruments and methods

The questionnaires, field and laboratory instruments and equipment used in multicentre studies must be standardized if comparable results are to be obtained. The questionnaires used in international studies must be translated so that semantic equivalence of the questionnaire contents is assured. When translating questionnaires, linguistic differences, levels of literacy, educational background, and cultural differences must be taken into account. The "correctness" of a translation can be tested by translating the translation back into the original language. Exact translation of a term is not always possible (Osterman et al., 1990). In which case, agreement must be sought between specialists (e.g. physicians) and lay representatives of the population to be interviewed. To overcome translation difficulties, a video-tape can be used to demonstrate symptoms or situations that people may have difficulty in understanding (e.g. in the International Study on Asthma, wheezing was demonstrated by a child). A translated questionnaire should be pre-tested before it is finalized and reproduced.

The same measuring equipment and methods should be used by each participating country or centre. If this is not practical, the comparability, reliability and validity of the equipment and methods that are to be used should be assessed. A cross-validation or inter-calibration exercise may be planned as part of the pilot study.

A standard quality assurance programme should be developed and approved by all participating countries. The programme should cover procedures for standardization of sampling and analysis, the development of criteria for acceptance of analytical results, and quality assurance auditing of the analyses of study samples.

Data management and analysis

To facilitate common analysis of the collected data, the computer files created by each of the participating centres should be easy to link and exchange. This requires coordination of computer hardware and software, and of input/output formats. Data analysis methods should also be agreed upon. Types of statistical procedures to be followed and the definition of units or categories of qualitative variables are just two of the issues that must be considered.

Chapter 9

Critical Assessment of Environmental Epidemiology Literature

Learning objectives

- Appreciate the rationale for assessing environmental epidemiology literature carefully and systematically.
- Be able to critically assess the introduction, methodology, results; and discussion and conclusion of a report on scientific paper of an epidemiology study
- Understand the role, methods and limitations of meta-analysis as a tool for summarizing research.

9.1 Rationale for assessing literature

There are many reasons to develop a means of scientifically assessing the literature in environmental epidemiology. First, such assessment is the best approach to independently determining the state-of-the-art with respect to an environmental health issue. Second, it helps to evaluate whether, and what kind of, epidemiological investigations may be needed. Third, it affords the opportunity to distinguish between valid research and research which is too flawed or limited to be used as a basis for causal inference or for public health management.

Recent rapid advances in information technology have resulted in vastly increased access to large amounts of information of relevance to the environmental epidemiologist. Computerized bibliographic retrieval services, and development of the Internet, have made available a considerable range of environmental and medical publications that were previously obtainable only in print form, often at high cost. These include scientific journals, newsletters of various organizations, and the less formal communications of interested groups of environmental and health professionals, such as GEENET (see Chapter 12). Moreover, this access is becoming truly global, with professionals in developing countries approaching a level of access comparable to that of professionals in more economically developed countries. These advances, and their potential benefits, are discussed further in Chapter 12. A downside to the rapid proliferation of accessible information is the increased difficulty of discriminating between information of good scientific quality and information of poor scientific quality. It may be a great temptation to accept information which is "published" on the Internet, for example, even though no meaningful peerreview is usually afforded to material placed on-line.

This chapter presents a systematic method for critically assessing a report or publication of an epidemiological study. Having applied this method, and depending on the study's validity and the characteristics of the population studied, the reader should then be able to assess whether the study's findings are relevant to a local situation. The specific attributes recommended for critical

review have been discussed elsewhere in this book and the reader should therefore be familiar with them. For example, this chapter offers guidance on how to examine "adequacy of the study's sampling method", but sampling methods *per se* are discussed in Chapters 3 and 6. The reader may thus need to refer to earlier chapters (principally Chapters 3 to 7), when working through this chapter. Gehlbach (1988) can be consulted as a handy companion for assessing the general medical literature in a systematic manner.

9.2 Proposed scale for assessing a paper's adequacy

Evaluating the validity of every scientific paper according to an arbitrary numerical system is unnecessary; forming an overall assessment through a less structured format is often sufficient. Nevertheless, some readers may find a checklist or a numerical system a convenient means of keeping track of their evaluations and summarizing their opinions. A numerical approach can also help readers to crystallize their opinions and to communicate them to those — government officials and citizen groups, for example — who require an interpretation of a study.

Persons employing a numerical system should be aware that they will be required to rank various methodological attributes of a study even though they may be somewhat ambivalent about making a specific determination.

Box 9.1. Numerical system for rating the attributes of a scientific paper

- "1" The study attribute was **satisfactory** for its intended purpose. Generally acceptable scientific standards were employed. There is no reason to suspect that the observed results differed from the underlying "truth" because of this particular study attribute.
- "2" The study attribute was of **limited or uncertain adequacy**. Nevertheless, the authors' approach or presentation was not erroneous, neither did it violate scientific standards. With respect to this attribute, it is reasonably likely that the observed results reflect the truth. However, bias or error cannot be ruled out.
- "3" The study attribute was not addressed at all or the attempt was poor relative to its intended purpose. This has resulted in **significant doubt** that the observed results reflect the underlying "truth".

Box 9.1 presents an ordinal, three-point scale as an example of a numerical system for rating a scientific paper's characteristics or "attributes" (e.g. presentation of the study methods, the results, or a discussion section). Modifications may be made to the system, if deemed suitable. After completing the rating of individual attributes, a summary score can be determined by averaging the scores of the attributes (a quantitative "score") or by a more qualitative appraisal of the number of attributes that were regarded favourably, or otherwise.

No two evaluations of the same paper, carried out by different individuals, are likely to produce exactly the same results. Assessments will differ due to differences in professional training, experience and opinions. Nevertheless, competent evaluations performed systematically should be in general agreement. Imperfect agreement is not necessarily problematic, especially if

assessments are supported with examples of why specific study attributes were considered adequate or not.

9.3 Critical assessment of a study report (paper)

Introduction

In the introduction to their paper, authors should present a concise background statement concerning the problem being investigated. Brief mention of the important characteristics of an environmental hazard, the disease being studied, and the perceived impact on a local population would be appropriate, for example. The reader should be given sufficient information to enable him or her to understand what motivated the study, and how the present study was expected to increase specific understanding of an environmental health problem.

Literature review

In their review of the literature, the authors should provide an up-to-date and comprehensive picture of what is known about their chosen research topic, including all the key issues of relevance to their study. If they are reporting the results of an epidemiological study, the authors should summarize and cite the preceding epidemiological literature. The summary should be balanced; for example by referring both to reports which agree with and reports which disagree with the current report. Certain related studies from other domains such as toxicology, engineering, biochemistry, immunology and genetics might also be mentioned; authors frequently review related areas if they consider that these provided additional reasons for conducting the study. The reader should determine whether the literature review presented by the authors helps to explain why they undertook the study.

Review of the study's rationale

The reader should ask whether the reasoning that underlies the study objectives or hypotheses has been described clearly. In short, given the background information and literature review, have the authors provided a convincing argument that the study was a logical step in elucidating this environmental health problem? Many epidemiological studies of environmental health issues involve secondary analyses of databases that were collected for reasons unrelated to the current research question. While it is not wrong to exploit available data for new or provocative purposes, authors should clearly inform the readership whether it was the case that the study rationale led to collection of new data, or that existing data led to the development of an auxiliary hypothesis.

Hypotheses and objectives

Every environmental epidemiology study should incorporate general goals relating to the promotion of public health and specific objectives. (The latter are much more narrowly defined.) The section of a paper that deals with these should be evaluated according to whether the main hypotheses, or otherwise stated central objectives, are clear and precise. This section usually consists of only a few sentences. Yet these sentences are among the most important in the paper since they should enable the reader to understand why the authors chose a particular study methodology and, if applicable, why data were collected in the way they were, as well as providing a context within which to interpret the study. Studies with ill-conceived or poorly-supported objectives usually fail to provide enlightening results.

Methodology

Study design

A critical assessment of the study methodology should address any of the following study design characteristics that are relevant:

- **General approach:** was this study designed to be descriptive or analytic (i.e. did it evaluate an etiological hypothesis)? By virtue of its design and methods did it have the capacity to be conclusive with respect to the questions it addressed?
- Level of measurement: were the data collected at an individual or ecological level?
- **Specific design**: was the study design clearly identified (i.e. cohort, historical cohort, case—control, cross sectional, experimental, etc.)?

Population at risk

The reader should be given a full description of the target population and the source population. This will help the reader to decide whether other groups exist to which the results can be applied. This "generalizability" is called "external validity". The premise is that if a research question is important enough, studies will be repeated in numerous local populations to determine whether a comparable local effect is occurring. However, in environmental epidemiology, repeating studies in numerous locations is often expensive, impractical or impossible. Ascertaining whether the underlying association reported by a study is valid, and that the study results are applicable to another situation, can therefore have important public health consequences, since they may constitute the sole research upon which public health measures are based.

Sampling method and sample size

The reader should assess whether the study population was selected adequately from the source population. This can be done by asking:

- Was the sampling method clearly identified?
- Was the resulting sample size adequate for investigating the stated hypotheses?

Selection and exclusion criteria for study population

The reader should assess the criteria used to select the sample from the source population. Were any criteria used to exclude any study subjects from the final database that was used for the statistical analysis? Authors sometimes fail to present such decisions in sufficient detail. This can result in tables with totals that do not "add up" when examined in relation to data presented in previous tables or in the text. This can be a source of confusion for the reader and may imply carelessness in other methodological areas.

Selection and exclusion criteria for control or comparison groups

A control or comparison group is required in nearly every epidemiological study. The source of this group and the manner in which it is selected can influence the overall validity of a study considerably. The reader should assess these attributes and any restriction criteria applied by the authors. This assessment, and assessment of the method used to select study subjects, will indicate whether the study was susceptible to selection bias.

Measurement of exposures and health outcomes

The reader should evaluate whether the principal exposures and health outcomes were adequately defined and measured by the authors. A check should also be made to ensure that any significant

opportunities for misclassification, and the likely directionality (away or toward the null) and type (random or systematic) of potential misclassification, have been specified. The reader should also evaluate whether the definitions and specifications of the exposures and disease outcomes are sufficient given the specific hypotheses being addressed.

Treatment of potentially confounding or effect-modifying variables

Readers may find it useful to make a list of the confounding and effect-modifying variables, comprising those the authors have noted, and others they themselves consider important. Potential confounders can be grouped into three categories, as follows:

- controlled by the study design (e.g. matching, randomization, restriction);
- controlled by analysis;
- not controlled.

Evidence of information bias

The reader should judge whether the investigators were successful at preventing or reducing information bias. For example, did the same interviewers collect information from both exposed and non-exposed study participants? Were interviewers aware of the exposure status of individual respondents? Were those responsible for assessments of health status "blinded"? If information bias is suspected the reader should attempt to estimate the directionality of the bias (e.g., is the true effect likely to be closer to or further from the null value, relative to the observed effect?) Estimating the magnitude of the bias (i.e., what is the true point estimate likely to be?), given the observed estimate, is more difficult.

Statistical analysis

The reader should evaluate whether the methods of statistical analysis were appropriate and clearly described. A very important consideration is whether the authors presented confidence intervals for all the major variables, thereby providing an estimate of the precision of the results. Taking into account these intervals, the reader should also consider whether the study had sufficient power to detect important associations of relevance to the central objectives.

Study results

Major findings

The reader should determine whether the authors summarized the study's major results objectively in terms of the magnitude and directionality of the hypothesized effects. He or she should question whether the study produced any potentially important results that are not discussed fully in the paper. Additional questions to be asked concern whether negative findings were presented alongside positive results, and whether the authors compared their findings to other published findings and tried to explain divergent results.

It is important to look carefully at the tables and figures to understand the presented data. The text presents the authors' summary or interpretation of the data. Readers should independently assess whether they agree with the authors' interpretation of the data.

Missing data

The results should be evaluated carefully in relation to subject response rates, drop-outs, compliance, or other types of missing data. Attention should be paid to how the authors

addressed these issues and a check made to establish if there are any other data gaps or problems, but which the authors did not take into account.

Control for confounding

A number of issues should be examined regarding control for confounding. For example, were the confounding variables postulated in the earlier phase of the assessment accounted for properly? What is the likelihood that residual confounding is present as a result of incomplete adjustment procedures? If the threat of confounding remains, how likely is it that the reported effect estimates would be meaningfully affected?

Discussions and conclusions

Internal validity

Assessing the internal validity of a study demands that the reader synthesize the evaluations of individual study attributes into an overall assessment. If a high degree of confidence can be assigned to the attributes reviewed, the reader will be likely to draw the same conclusions as the authors. Nevertheless, the reader should consider whether the authors sufficiently examined alternative explanations (for example, relating to other biological mechanisms, or systematic or sampling error) that could account for the results obtained, and what other interpretations of the findings could be addressed now or in future studies. The reader must decide whether these alternative interpretations are sufficiently credible to jeopardize the internal validity of the study.

External validity

Determining whether a study's results have external validity (i.e. can they be generalized or extrapolated, and if so, to what population?) is appropriate only if the reader believes that the study is internally valid. In environmental epidemiology, the extrapolation of research findings performed in one setting to other settings is a major issue. Government policy makers are often reluctant to change public health management unless it has been shown that a health problem exists in the relevant region or country. This seemingly necessitates repeat studies. However, if the external validity of a study is deemed to be high, and this can be communicated effectively, repeat studies can be avoided.

Consistency with other studies

The paper should be evaluated according to whether the authors attempted to integrate their results with those of previous studies. For example, were findings consistent or inconsistent and can the present results be explained with a cogent and plausible biological rationale? If not, the reader may wish to determine whether this is because the result is too new and has therefore not yet received enough attention from other scientific disciplines, or because it is unlikely to be true.

Practical importance of results

The practical importance of study results can be evaluated by asking questions such as the following. Do the results add to existing knowledge about the problem under study? How might these results affect public health? As a result of this study, should individuals or agencies modify any of their activities?

Further study

Generally, authors suggest directions for further research. Additionally, readers can ask themselves if their local environment, or the social and political context in which they work, has

any special characteristics that should be accounted for in future investigation. For example, a study suggesting that ingestion of volatile organic compounds via consumption of drinking water can cause fetal developmental abnormalities may require follow-up studies to determine the specific water supply networks within a local population that are implicated, as well as a full characterization of the levels and types of compounds found in the local water supply.

9.4 Alternative system for evaluating the literature

The system for evaluating the report of an epidemiological study that is described in this chapter consists of two activities. The first involves determining the quantitative or qualitative scale to be used when assessing the sections of a paper; the second involves categorizing the specific attributes of a paper that must be assessed. Readers should feel free to modify the methods proposed in this chapter to suit their individual preferences. The major requirement is that the method followed be systematic. An example of another evaluation scheme is provided in Table 9.1, adapted from a paper that reviewed the published epidemiological literature concerning the health effects of polychlorinated biphenyls (PCBs) (Swanson et al., 1995).

The rating system is on a two-point scale (+ for satisfactory; - for unsatisfactory). The attributes evaluated were fewer and more general than those presented in this chapter. It should be noted that this system, or one like it, should not assign favourable quality scores based on the specific findings of the study. A negative study is, inherently, of the same value as a positive study of comparable merit. It is essential to remain neutral and objective with respect to the outcomes of an environmental epidemiology study.

A major conclusion of this evaluation of the PCB/health effects literature is that the methodology used in PCB/health effects studies and the reporting of the methodology used therein contain gross deficiencies. Seventy percent of the studies reviewed were classified as "inconclusive", based on one or more serious deficiencies. Moreover, authors' conclusions were assessed as compatible with study results in only 56% of the environmental studies and 69% of the occupational studies.

Table 9.1: Health effects of PCB — analytic literature review

Key study criteria and evaluation measures							
(D)	Design	(SR)	Evaluation of study results				
+	Cohort study; case control study	+	Presented clearly, accounting for				
-	Case study; exposure only study;	-	strengths and limitations Lacks coherent organization or				
	descriptive study	0	presentation Unclear or ambiguous				
(S)	Subject selection	(C)	Author's conclusions are compatible with results				
+	Unbiased	+	Yes				
-	Biased	-	No				
0	Not reported						
(R)	Response rate	(O)	Overall assessment in terms of human health effects				
+	75% or higher						
-	74% or lower	+	Clear conclusions; no important methodological flaws				
(E)	Exposure	-	Limited results having some value in spite of flaws.				
+	Measured	0	Inconclusive: study was				
-	Not measured		methodologically flawed; authors				
			failed to report significant details				
(SA)	Statistical analysis						
+	Appropriate						
-	Not appropriate, not done						
0	Not reported						
(OCRF) Analysis includes other critical risk factors							
+	Yes						
-	No Notara and a						
0	Not reported						

Source: adapted from Swanson et al., 1995.

9.5 Summarizing the literature through meta-analysis

Meta-analysis is quantitative analysis of the combined results of several individual studies on a related topic and is undertaken in order to reach a summary interpretation. Regarding environmental epidemiology literature, it has two major advantages over non-quantitative summaries (i.e., reviews). First, it establishes a single estimate that is an average of the results of the individual studies. This eliminates confusion caused by having to interpret multiple studies with divergent results in terms of the observed size, and even the directionality, of the observed effect estimate. Second, it results in an increase in statistical power because the individual study sizes are pooled.

Meta-analysis has its roots in clinical trials research in which experiments to determine the efficacy of drugs or medical procedures have generally used almost identical, standard methodologies (e.g. standard diagnostic criteria, randomization, blind assessment of outcome). If published information suggests that a new drug may be effective, ethical considerations would probably dictate that investigators do not undertake any additional randomized studies; this is because some of the patients would be randomized to receive a placebo or some other, possibly less effective treatment. In this context, meta-analysis can provide a useful summarization and interpretation of the available results; these, in turn, can help guide clinical decision-making. Numerous texts review the application of meta-analysis to clinical studies (see, for example, Chalmers et al., 1981; DerSimonian & Laird, 1986; Simes, 1986).

Meta-analyses of observational epidemiological studies, such as case—control and cohort studies, are more problematic than those of clinical trials since these studies do not adopt uniform approaches for data collection, case definitions, subject restriction criteria, confounder specification, and so on. Nevertheless, meta-analysis is often used to pool results from observational studies of environmental health research questions.

In environmental epidemiology, a meta-analysis can serve as a state-of-the-art literature review (Dickersin & Berlin, 1992). The quantitative approach should lead to a more objective integration of results than an "expert review" undertaken by one person because the subjective interpretation is removed. Meta-analysis may also serve as a logical first step when proposing a new research study, especially if external funding will be required. This is because demonstrating the combined weight of existing knowledge may be necessary before agreement can be reached about planning a new study. The outcome of a meta-analysis may also help identify specific topics or questions that require further research and clarification.

However, meta-analysis also has some limitations. Some epidemiologists view the widespread acceptance and promulgation of meta-analysis with scepticism (Goldman & Feinstein, 1979; Feinstein, 1989). A major concern is that in seeking to arrive at a central risk estimate, meta-analysis could overlook the methodological advantages and disadvantages of individual studies. Put simply, merging several inconclusive studies into a single analysis to produce an average estimate, may not advance our understanding of an environmental health problem, even if the resulting confidence limits become very narrow.

The perception that journal editors are more likely to accept positive studies rather than negative studies for publication, even if the latter are of comparable quality, also creates a problem (Chalmers et al., 1990; Dickersin, 1990). If the perception is well-founded, and if meta-analysts

include only published papers in their analyses, a publication bias towards positive conclusions will arise. While some have attempted to prove that publication bias exists (Easterbrook et al., 1991; Dickersin et al., 1992), in practice its presence depends on the specific journal, the time-period in question, and the topic being reported. The methods proposed for evaluating and adjusting for publication bias in meta-analysis may represent only a makeshift solution to what could be a serious and incorrectable bias (Rosenthal, 1979; Hetherington et al., 1989).

Meta-analysis methods

Several statistical methods exist for carrying out a meta-analysis of the combined results of research studies. A detailed discussion of how to undertake meta-analysis is beyond the scope of this presentation, but the initial steps of a meta-analysis are outlined below. More specific details can be found in several publications (see, for example, Greenland, 1987b; Laird & Mosteller, 1990; Fleiss & Gross, 1991).

1. Locate all the studies pertaining to the research question of interest

A MEDLINE (see Chapter 12) or an equivalent search, using key words, is typically undertaken when trying to locate published studies on a specific topic. The reference lists of the identified articles are also usually examined. If it is decided to include unpublished reports in the analysis, these must also be identified and obtained. Meeting abstracts and directories of ongoing research can also be examined and personal communication with researchers who have been active in a certain area may be worthwhile. Unpublished studies that have not been peer-reviewed present a major dilemma regarding assessment of their study's scientific merit, however. (Publication at least suggests that a paper has undergone external quality assessment and been judged satisfactory.)

2. Resolve issues of study quality and conflicting results

Since variations between studies with respect to study population and methodology can account for divergence between these attributes should be examined to decide whether they account sufficiently for divergent results. Any study deemed unsatisfactory in its execution should not be included in the meta-analysis. The basis for determining that a study is unsatisfactory must be documented. Establishing minimum quality standards such as the quality scoring system of Chalmers et al. (1981) before starting a meta-analysis is generally helpful. Unfortunately, no uniform criteria exist as to what to use as standards. Assigning a study weight based on quality may be commendable in principle, but difficult in practice if consensus must be reached about the value of each study.

If studies with divergent results seem to be of satisfactory quality, meta-analysis will tend to provide a "middle" position between the divergent studies, but will weight the larger studies more heavily. Several have suggested that studies that are sufficiently heterogeneous should not be combined and have proposed statistical approaches for quantitatively assessing study heterogeneity (see, for example, Simon, 1987; Naylor, 1988).

3. Calculate study weights and summary risk estimate

Generally, the weights that are assigned to an individual study are determined by the study size. This is analogous to a Mantel-Haenzel analysis where weight is proportional to the inverse variance estimate of each study (Greenland & Salvan, 1990).

Three methods are available for calculating the summary effect estimate: the Mantel-Haenzel method; the Peto method; and the General-Variance-Based method. The first two require data from the published paper to be available in contingency table format (e.g. 2 x 2 table). An advantage of the third method is that only the effect estimate and associated confidence limits are required (Petitti, 1997).

Meta-analysis for environmental health policy development

Its limitations notwithstanding, meta-analysis is bound to remain a popular technique for summarizing environmental epidemiology studies, for combining individual studies that are limited by low statistical power, and for helping investigators to arrive at a consensus when the results of several studies conflict with one another. It can therefore be a useful tool for communicating to policy-makers, financial donors, and others, that specific environmental health risks are real and require preventive or remedial action.

Finally, limited budgets for supporting new research in environmental epidemiology is a worldwide problem. By contributing to a fair and valid summary of the state of epidemiological knowledge of a specific topic, meta-analysis can help avoid the initiation of expensive new research where it is not needed. Hopefully instead, these research funds will be applied to supporting other worthwhile environmental health research initiatives or interventions.

Concluding comments

Environmental epidemiology research is proliferating rapidly. New journals in print and electronic format are emerging to keep pace with the need to disseminate results. While keeping abreast of all new developments by thoroughly reading all new research papers is an overwhelming and unnecessary task, passive acceptance of summarized results as found in the abstract of a paper may result in only a superficial understanding of the complex associations between environment and health. Researchers in environmental epidemiology should therefore try to remain current with respect to the topics that most concern them, and review new research findings with a critical eye. This is not to say that minor deficiencies should be allowed to invalidate studies that are of generally good quality; adopting a hyper-critical posture is counter-productive since useful research observations will be discarded along with the truly deficient. Indeed, experienced researchers recognize that minor flaws in data and even in methodology do not usually negate research findings in epidemiological studies. Moreover, since environmental epidemiology is likely to remain a discipline fraught with inherent limitations, we must learn how to efficiently and accurately distinguish between valid studies and Fortunately, consideration of this literature is usually a pleasurable responsibility, and if carried out carefully and systematically, leads to a deeper understanding of environmental epidemiology.



Chapter 10

Environmental Epidemiology in Public Health Practice

Learning objectives

- Understand how epidemiology is used in public health programs to evaluate environmental hazards and plan public health responses.
- Describe the major purpose and components of public health surveillance and environmental monitoring programs.
- Describe the steps in conducting a disease outbreak investigation.
- Be aware of the "public health assessment" process to evaluate data and information for communities potentially exposed to environmental hazards.
- Understand the importance of effective communication with the public and community members.

The previous chapters in this book have presented the principles and methods of conducting environmental epidemiological studies. The remaining chapters of the book examine the use of environmental epidemiology in public health practice (in relation to monitoring, surveillance, outbreak investigations and disease clusters) and its role in the public policy or regulatory arena (in relation to risk assessment, standard setting, environmental impact assessment and decision-making).

10.1 Exposure monitoring and health surveillance

Basic principles

The United States Centers for Disease Control (CDC) defines "public health surveillance" as the ongoing, systematic collection, analysis and interpretation of health data essential to the planning, implementation, and evaluation of public health practice, closely integrated with the timely dissemination of these data to the appropriate individuals or institutions. More simply, a surveillance system collects, analyses and disseminates data (CDC, 1988).

The concept of public health surveillance has evolved over time and may be confused with other uses of the term surveillance. Thus the current concept of surveillance as the monitoring of disease or associated risk factors in **populations** is somewhat different from the close observation of **individuals** who have been exposed to an infectious or toxic agent, and which is carried out in order to detect early symptoms and institute prompt control measures. The latter is now referred to as "medical surveillance", while the term "surveillance" is generally taken to mean public health surveillance. Many surveillance systems are initially established to monitor the occurrence of communicable diseases and then, following industrial development, extended

to include monitoring of the occurrence of other diseases, environmental monitoring, and surveillance for known risk factors such as smoking and drug usage.

The goals of public health surveillance are to:

- identify or confirm the existence of a public health problem;
- define the scope of the problem;
- identify and target populations for prevention and intervention;
- evaluate the effectiveness of the intervention or prevention programme.

Surveillance may also identify areas for further epidemiological research and, more importantly, act as a "sentinels" for emerging problems. A "sentinel" event is the occurrence of a disease case or disease pattern that identifies the need for public health investigation and follow-up.

Environmental health surveillance encompasses both health surveillance and environmental monitoring. Environmental health surveillance is used to generate epidemiological data on the magnitude and trend of environmental pollution, exposure, and related adverse health effects. Identifying and quantifying the occurrence of risk factors, that are theoretically already known, are also elements of Environmental Health Surveillance. But surveillance does not include etiological research, identification of interventions or experimental testing of potential interventions (Halperin, 1992).

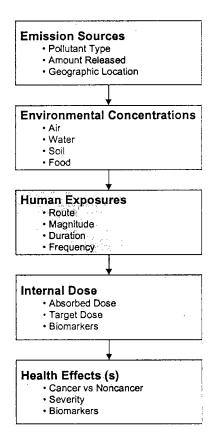
Surveillance may provide further evidence of exposure and effect associations that epidemiological research has already detected, but for which the mechanism of causation remains unknown. Information obtained by surveillance and monitoring activities may provide support for causal criteria such as that the distribution of the effect relates to the environmental agent's spatial distribution; or that elimination or significant reduction of the environmental agent results in the disappearance or decline of the effect (see discussion of causation in Section 3.6).

Surveillance and monitoring should form operational components of environmental health control and management programmes, and should be directed at assessing the impact of such programmes. Environmental health surveillance obtains and analyses various environmental monitoring and health data. In general, information obtained through surveillance of a particular contaminant and its related health effects, can be categorized as follows:

- Information on sources of the pollutant, including frequency and amounts of releases, and major media affected (food, air, soil and water).
- Characteristics of the agent's behaviour in the environment, e.g. transport, chemical changes, interaction with biota and fate.
- Concentration levels of the contaminant in media, that might represent a harmful human exposure.
- Characteristics and modes of exposure to the environmental agent of population at risk.
- Information on occurrence of adverse effects (type, frequency and severity) in
 populations at risk of exposure. Data on adverse effects can be generated at the preclinical level (biological monitoring, screening or health survey), at the clinic level
 (health monitoring, reporting system or specialized registries) and from death certificates.

Fig. 10.1 describes the principal information sources that may be required to interpret the exposure to a specified hazardous environmental agent of a given population. The sources of information to be considered reflect each step of the environmental hazard pathway described in Chapter 4 and illustrated in Figure 4.1 on page 67.

Figure 10.1 Principal sources of information to assess an environmental hazard



Data obtained under this scheme come from a number of sources. This diversity of information requires that strict quality control and quality assurance procedures be followed during data collection; otherwise, the quality of the data and subsequent analysis will be questionable (see Chapter 4). Data from environmental monitoring activities can be used:

- to compare current environmental or biological levels of contaminants, for which environmental or biological regulatory values exist;
- to estimate quantitatively the risk level of a population through risk characterization procedures;
- to assess the effectiveness of preventive and control measures by analysing contaminant concentration trends, for the environment and inside the human body;
- to identify and assess factors concerning pollution sources such as increase/decrease of releases, early detection of new pollutants, compliance with emission standards, emphasis on primary preventive measures, and time and space variation of pollutants.

Data from health surveillance activities can be used to:

- conduct health care resource planning;
- set health care priorities;
- provide early warning system of emerging public health problems;
- identify appropriate intervention and control procedures;
- evaluate health policy or management strategies; and
- provide guidance areas regarding research priorities.

The information obtained from **linked health surveillance activities** (that is, linking exposure monitoring and health surveillance data) can be used:

- to establish dose—response relationships by linking frequency and/or severity of adverse effects with data on levels of environmental or biological pollutants;
- to verify the effectiveness of environmental standards;
- to assist on-going epidemiological research into specified pollutants;
- to assess the impact of a prevention and control programme by analysing occurrence of and trends in specified adverse health effects.

A number of documents and publications on surveillance and monitoring can be obtained from WHO. Section 12.3 describes additional references for water, air, food, the work environment and others. WHO and UNEP have been collaborating on monitoring activities, and the Global Environmental Monitoring System (GEMS) collects monitoring information on air, water and food, and also biological monitoring information on lead, cadmium, organochlorine pesticides and polychlorinated biphenyls.

Environmental monitoring programmes

Environmental monitoring is defined as a systematic programme to measure environmental concentrations of agent(s) of concern as well as related parameters, such as temperature or weather which may influence exposures. The goal of environmental monitoring programmes is to observe a population's exposures to environmental agents, and, if possible, to quantify those exposure. Environmental monitoring is fundamental to any environmental health surveillance programme. Typical analyses of environmental monitoring data include status and trend data for various environmental agents, correlation of exposure data with the occurrence of related health effects, and linkage of health data sets with environmental monitoring data.

An environmental monitoring programme should include:

- identification and selection of sampling sites that are representative of exposure conditions within populations;
- establishment of the sampling frequency;
- standardized methods for the collection, transport, and laboratory analysis of samples;
- standardized recording of results and their subsequent analysis.

With respect to generating information of epidemiological interest, environmental monitoring has several advantages. It:

- is relatively easy to implement;
- can include a large number of parameters for study;
- can be carried out for long periods;
- is independent of community acceptance;
- can be modified easily according to the varying conditions of the environment;
- is a simple means of following the concentration, distribution, variation and trends of a contaminant in the environment.

Environmental monitoring programmes should be structured in such a way that the actual pollutant concentration measured is recorded and reported. Programmes that use single-action levels (i.e. only reporting whether a pollutant concentration is above or below a specified criterion) limit the utilization and interpretation of the data. Measuring actual concentration levels allow for dose-response relationships to be estimated for the populations surveyed. Additionally, special surveillance approaches must often be adopted in order to assess exposure according to the population's patterns of activity and so that variables such as smoking, drinking and diet are taken into account. Information pertaining to these variables is best obtained through specific cross-sectional surveys rather than from systematically and routinely collected data.

Health surveillance

The goal of health (disease) surveillance is to understand the ongoing pattern of disease occurrence and the potential for disease in a population so that public health officials can be effective in investigating, controlling, and preventing disease in that population (CDC, 1992). The majority of disease surveillance programmes collect mortality and morbidity information for selected diseases. The use of morbidity and mortality information for health surveillance associated with environmental exposures has been limited. Disease surveillance requires clear case definitions including descriptions of symptoms, clinical findings and diagnostic tests. This information should be disseminated widely among the clinical and laboratory staff whose responsibility it is to detect occurrences of the disease(s).

If chronic effects or diseases with long latency periods are being investigated, the identification of early indicators of the disease will be of particular interest. Information on long latency effects can be obtained by using surveillance screening techniques to identify biomarkers of early preclinical damage, or to at least confirm that a biological exposure has occurred.

Exposure registries

Information about the effects on general populations of low-level exposures of long duration (as in the case of a community living in the vicinity of a hazardous waste site), or the effects of a short-term, high-level exposure may be of interest for environmental health management. However, this information requires a mechanism to collect and maintain exposure information over time to link to health outcome surveillance.

An exposure registry is a system for longitudinally collecting and maintaining information (in a structured record). Exposure registries document environmental exposure to specific hazardous substances for defined populations. The National Exposure Registry in the US, for instance, comprises chemical-specific subregistries that list persons for whom environmental exposure to the specific chemical(s) of concern has been documented. Information concerning an individual is entered into the registry if the following criteria are met:

- validated evidence exists that a media is contaminated;
- there is a route of transmission from the media to the person;
- evidence exists that transmission actually occurred or that the individual was actually exposed (ATSDR, 1994).

The purpose of an exposure registry is to aid assessment of the long-term health consequences of environmental exposures to hazardous substances. More specifically, an exposure registry aims to facilitate epidemiological studies by creating data files that are large and complete enough to enable the verification, at a predetermined level of statistical probability, of what are thought to be known adverse health outcomes (hypothesis testing), or the identification of previously unknown adverse health outcomes, should they exist (hypothesis generating).

Exposure registries are especially useful for assembling the information needed to generate hypotheses. In fact, for most hazardous substances and mixtures of hazardous substances, health outcomes, are not known or else are not well defined. With few exceptions, chemical-specific health information is based either on occupational exposures or on toxicological studies of short-term, high-level exposures. Yet many chemical exposures occur by a route other than inhalation and affect vulnerable subgroups such as the elderly, children, pregnant women, and those in ill health. If the specific health outcomes are not known, exposure registries collect information on all health outcomes.

Since the end-points or health outcomes are unknown or ill-defined in most cases, the latency period to disease, should it apply, is also likely to be unknown. This is why exposure registries are longitudinal (i.e. ongoing) and the same basic demographic, environmental exposure, occupational and health information collected for each registrant at baseline and at each follow-up (every year or two years) for each subregistry. Biomonitoring data (see Chapters 2 and 5) or biological specimens are also collected if the capability exists and resources are available.

An exposure registry can also provide the information required to carry out health surveillance and to estimate the economic or social burden of the effects of the exposures on a population as a whole. Perhaps even more importantly, an exposure registry can be used to respond to three of the needs that are commonly expressed by communities that consider themselves to be at risk due to environmental exposure. That is, they can be used to help secure recognition that exposure has occurred; they can form the basis of an ongoing effort to resolve the problem; and they can contribute to efforts to ensure that all information relevant to the exposure is made publicly available.

By facilitating the comparison of rates of reporting of health outcomes with existing national norms, potential health problems can be identified or confirmed. This phase should be followed by more in-depth health studies to explore the validity or the extent of the health concern. By comparing longitudinal information within a subregistry, possible health changes or trends can

also be identified and appropriate actions taken. Exposure registries can also be used in conjunction with environmental monitoring data or health surveillance data to evaluate the effectiveness of previous preventive actions, whether these were health- or environment-related..

The Trichloroethylene (TCE) Subregistry of the United States National Exposure Registry is an example of an exposure registry that has proved to be a useful tool for environmental epidemiology (ASTDR, 1993). Data was collected on 4 880 persons at 13 waste sites for which exposure to TCE had been documented. Individuals affected had consumed water contaminated with TCE. The rate of reporting of health conditions was compared to rates in a national health survey (National Health Interview Survey (NCHS, 1989)). After controlling for several factors, including sex, age and highest level of education, the reporting rates among the TCE exposed population were found to be significantly elevated for several health outcomes for selected sex-specific and age-specific subpopulations. Of particular concern were the increased reporting rates for speech impairment, hearing impairment, anaemia, and heart conditions, for children under 10 years of age. The Agency for Toxic Substances and Disease Registry (ATSDR) is carrying out epidemiology studies of the registrants to test the hypothesis that the reporting rates are higher than would normally be expected because the reporting is more efficient at these sites than elsewhere. In addition, ATSDR is carrying out studies of the statistically increased reporting for the total TCE registrant population for stroke, heart conditions, and hypertension.

10.2 Investigations of disease outbreaks

"Whoever wishes to investigate medicine properly should proceed thus......When he comes into a strange city, he ought to consider its situation, how it lies to the wind and the sun, and consider the waters the people use. For if he knows these things well he cannot miss knowing the diseases peculiar to the place". (Hippocrates)

Public health officials must deal with the traditional health problems of infectious disease and chronic disease by measuring the prevalence of known risk factors (lifestyle, environment and demographics) that might impact the occurrence of disease. If a disease is easily identified and relationships between it and the relevant exposure or risk factors well understood, established procedures for epidemiological evaluation and population protection can be followed. But the situation may be very different if there is no apparent agent of infectious, toxic or other origin, or if the relationship between the suspected agent and the health effect is unclear. Environmental health problems include not only disease outbreaks, however, but also concern about potential or existing exposure to environmental contaminants that could lead to disease.

Exposures to environmental contaminants are often seen by the public and government officials as linked to illness patterns, although the links may be very tenuous at best. These "outbreaks" or alleged relationships between environmental conditions and illness patterns should therefore be investigated in order to respond to or allay public concern. Such investigations also can help to ensure compliance with legal requirements (such as public health laws to contain infectious disease outbreaks), serve as a response to political concerns, and provide an opportunity for epidemiological research and training (CDC, 1992).

An outbreak investigation should incorporate basic epidemiological principles. Several manuals describe these and the procedure that an outbreak investigation should follow (WHO, 1991b; CDC, 1992). An administrative protocol is crucial since it will ensure that the investigation

proceeds systematically and that important steps are not missed along the way. Table 10.1 presents an example of such a protocol; in practice, several steps may be carried out at the same time and a different order may be followed depending on the circumstances.

Table 10.1. Outbreak investigation protocol

- 1. Prepare for field work
- 2. Establish the existence of an outbreak
- 3. Verify the diagnosis
- 4. Define, identify and count cases
- 5. Perform descriptive epidemiology
- 6. Develop hypotheses
- 7. Evaluate hypotheses and consider additional studies
- Reconsider/refine hypotheses and execute additional studies
- 9. Implement control and prevention measures
- 10. Communicate findings.

Source: adapted from Fiore et al., 1990.

Field work preparation

It is often imperative that an outbreak investigation proceeds quickly. By establishing a standard protocol, to be used in all outbreak investigations, and ensuring that public health officers are fully prepared for outbreaks, unnecessary delay can be avoided. To prepare for any likely investigations a library or a set of reference books on a variety of common environmental diseases is essential. This will enable the investigator(s) to develop an understanding of the basic science of the disease (if known) or the environmental contaminant (if known). There are two reasons why such an information source is necessary. Firstly, given the expanded development and manufacturing of chemicals, it is virtually impossible for an investigator to be fully and currently informed about the toxicological properties and uses of all chemicals on the market. Secondly, new emergent microbial pathogens that could be the etiological agents of an outbreak are identified regularly, so that an investigator is unlikely to be aware of all such pathogens.

A basic field kit should also be available including, for example: clinical specimen collection material; environmental sampling kits; reporting or outbreak data collection forms; camera; tape recorder, and calculator or portable computer (IAMFES, 1979; IAMFES, 1983; and IAMFES, 1988; CDC, 1992). In the event of an outbreak, further items can be added, once more precise needs become known.

Outbreaks are generally investigated by a team of people, including an epidemiologist, relevant medical specialists and environmental scientists (microbiologist, chemist, etc.) as appropriate. Once the investigation team has been formed, the role and responsibility of each member can be established. This can be done during the development of the study plan. It is recommended that one of the team members be assigned the task of providing information for other public health or elected officials, and the general public. The same member should also serve as a clearing

house of information for the other team members. The larger the outbreak, the larger the team and the greater the need to facilitate communication.

Establish the existence of an outbreak

The possibility that an outbreak has occurred usually becomes apparent in one of two ways: either through the analysis of surveillance data, or following the report of an increase in the number of "disease cases" or of a contaminant in the environment (e.g. chemical spill, air inversion). In either instance, the previous medical or environmental monitoring history of the affected community should be examined to ascertain whether the purported increase is real. This may include analysing the results of surveillance and monitoring programmes, and consulting hospital or clinical records. Conducting an informal survey of health officials, or comparing the health status of the community of interest with that of a neighbouring community, may also be worthwhile.

Many factors can contribute to the belief that an outbreak of disease has occurred. These include:

- changes in local reporting procedures (new personnel may be more consistent in reporting disease);
- improvements in diagnosis;
- increased local or national awareness of the specific disease;
- changes in local health care services that encourage more cases to seek care;
- sudden increases in the population (as occur in resort towns, college towns or convention centres) which reflect increases in the denominator.

Verify the diagnosis

A fundamental step in establishing the existence of an outbreak is to verify the identification of the disease or health condition. The diagnosis must be verified so as to ensure that the problem has been accurately diagnosed and to rule out laboratory error — if diagnosis requires laboratory analysis of samples —as the reason for the increase in the number of diagnosed cases. If an increase in environmental exposure is being investigated, laboratory records, procedures and quality control programmes must be reviewed in order to confirm that laboratory error is not the cause of the apparent increase in exposure.

As well as verifying the diagnosis, the specific symptoms and signs of the disease must be recorded. Many of the guidelines and procedures discussed in Chapters 4 and 5 can be applied at this stage. It is recommended that the investigator or members of the investigating team interview individuals who have contracted the disease, to help generate hypotheses about the cause of the outbreak.

Establish a case definition and count cases

A case definition is a standard set of criteria for deciding whether an individual can be classified as at risk from the exposure of interest, or as having contracted the disease of interest (See Section 5.1, page 115). If an outbreak is being investigated following a reported increase in the

incidence of a specific disease, the case definition may be very simple. Conversely, if the investigation is being conducted because of a sudden increase in exposure to an environmental contaminant, the reverse may apply. Many environmental contaminants can cause several health effects, for example. Alternatively, health effects may be subjective; that is, they cannot be easily verified or quantified. They might therefore include fatigue, headache, myalgia, loss of sleep or eye irritation. Time is an essential component of a case definition. For example, people who have a long history of the disease should not be considered cases if the exposure and related health effect are recent.

The case definition may need to be modified as the investigation proceeds. Early in the investigation, the information on cases may be incomplete (e.g. clinical specimens are not available for each case) or in the process of being obtained (e.g. clinical specimens are being examined). This is particularly likely in the case of mortality. If an investigation is initiated as soon as an outbreak occurs, information on deceased cases may be lacking. Categorizing cases as definite, probable or possible, can therefore be useful. As the investigation proceeds and more information becomes available, the criteria for inclusion in a specific category may change, enabling the case definition to be refined.

Once the case definition has been finalized, the number of cases must be ascertained. This can be done in a variety of ways; the type of outbreak and the particular community will serve to define which is the most appropriate. If the outbreak is a disease for which hospitalization is probable, the logical place to begin is the local hospital or the nearest specialized referral hospital. Some outbreaks may require that the public is alerted through the local media. If so, public health officials can request that individuals with certain symptoms or other characteristics either telephone or report to the investigation centre. If the disease does not require hospitalization, door-to-door surveys in targeted neighbourhoods, although very labour-intensive, are likely to be the surest means of obtaining an accurate case count.

Five types of information must be collected for each case.

- 1. Name, address, and telephone number (if available), are useful for verifying laboratory results, checking for duplicate records, mapping the geographic extent of the problem, and seeking additional information.
- 2. **Demographic information** enables standard descriptive epidemiology to be carried out; i.e. the outbreak can be characterized by age and gender.
- 3. **Clinical information** permits the verification or categorization of each individual as a definite, probable or possible case.
- 4. **Risk factor information** includes information on possible risk factors associated with the exposure or disease of concern.
- 5. Identification of the individual(s) who provided initial information about the case is important if an outbreak has resulted in death, severe disease, or affects the very young or the elderly.

Perform descriptive epidemiology

Descriptive epidemiology characterizes a disease outbreak primarily in terms of person, place and time — this is basic epidemiological practice (Beaglehole et al, 1993). (See Section 6.2, pp.

145, for a discussion of descriptive epidemiology.) In addition to providing a preliminary description, it should suggest or generate hypotheses as to the cause of the outbreak and identify clues or possible errors in the data pertaining to it. Descriptive epidemiology should be carried out as early as possible in the course of an investigation. Descriptions or definitions can be modified or updated later if additional data becomes available.

The "person" is defined using the standard demographic characteristics of age, gender, race (ethnic group), occupation (current and past) and any other individual characteristics of relevance to the disease (e.g. dietary habits).

Description of the outbreak by "place" provides information on the geographic location of the problem and may demonstrate clusters or patterns that support hypotheses. The most common technique for describing place is through use of a "spot map".

The time course of an outbreak is usually depicted by drawing a histogram of the number of cases according to date of onset. This graph is called an epidemic curve. The construction of this curve and its interpretation is discussed in *Basic Epidemiology* (Beaglehole et al, 1993). A classic example is the 1854 outbreak of cholera in London investigated by John Snow, shown in Figure 10.2.

160 140 120 80 60 40 20 19 20 21 22 23 24 25 26 27 28 29 30 31 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 August September

Figure 10.2 Outbreak of cholera, London, August-September 1854

Source: Beaglehole et al., 1993; adapted from Snow, 1855.

Develop hypotheses

Following notification of a possible outbreak of disease, investigators generally start to develop hypotheses as to its cause. As additional information is analysed, hypotheses are revised or refined. The hypotheses should address the source of the agent, the mode of transmission, and the exposures believed to have caused the disease, or the diseases that could be caused by the relevant exposures.

Evaluate hypotheses and consider additional studies

The hypotheses as to the cause of an outbreak are initially tested by examining them in the light of established facts. This testing relies on clinical, laboratory, environmental or epidemiological evidence. Laboratory techniques for hypothesis testing include the identification or serotyping of microorganisms found in clinical specimens and the matching of these with organisms found in environmental specimens. Either method can be used to produce conclusive evidence for the support (or refutation) of proposed hypotheses.

If the descriptive data do not support the initial hypotheses, additional studies must be undertaken. The study designs for these are usually analytic (etiological) (see Chapter 6).

Deciding whether to conduct additional studies can be difficult. It is always possible that they will not provide information that confirms (or refutes) the hypothesis. A common axiom in epidemiology is that if you cannot generate a "good" primary hypothesis (by talking to cases and examining the descriptive epidemiology), proceeding to analytic epidemiology will not be worthwhile. Sometimes an analytic study will provide some support for a hypothesis, but the hypothesis may need to be refined or additional information obtained. However, it should be borne in mind that one reason for investigating an outbreak is to expand our knowledge base. In other words, an outbreak is an "experiment of nature" which provides an opportunity to study all possible exposures and their effects on humans. Similarly, the circumstances of the outbreak may provide an opportunity to learn more about an environmental hazard. In refining hypotheses, it is also helpful to consider unanswered questions about a particular disease or environmental exposure.

Implement control and prevention measures

The goal of any outbreak investigation is to identify control and prevention measures. The measures required often become evident before the investigation has been completed and should be implemented without delay. For environmental outbreaks this may mean controlling the source (e.g. pipestack emissions), interrupting the mode of transmission (e.g. by disinfection of drinking-water) or removing the populations at risk (e.g. by evacuating populations from contaminated sites). Outbreak investigations sometimes also indicate long-term policy measures for prevention (e.g. drinking-water treatment) or suggest priorities for public health (e.g. screening of blood for lead) or preventive measures (e.g. prohibition of smoking in public places).

Communicate findings

Once an investigation has been completed, two types of communication should be prepared. The first should be an oral briefing for government officials that presents the findings of the investigation in plain clear language. The second communication should be a written report or reports, possibly directed to different audiences - the public, government officials - and the scientific community. Written reports should follow the usual scientific format of introduction, background, methods, results, discussion and recommendations. A written report serves as a reference for future outbreak investigations. It can also serve as the basis of plans for redirecting or modifying existing environmental health policies. The importance of communication is discussed further on in Section 10.7.

Box 10.1 Case study: Waterborne Disease Outbreak

Establish existence of outbreak

On 9 July 1990, the infectious diseases department at Cook County Hospital in Chicago was notified that several staff physicians had experienced the onset of diarrhoea on 7 and 8 July. At approximately 01:00 hr on 5 July, the main water pump had stopped and the roof storage tanks accordingly emptied in a physicians' residence building. At about 07:00 hr on the same day, the pump was repaired and restarted. Numerous complaints about low water-pressure and lack of water were received during this time. Later the same day, at around 09:00 hr, another short pump failure occurred. Several more complaints about lack of water were made by the hall residents.

Verify diagnosis

From 10 July until 7 August stool specimens were collected from 20 sick persons (17 house staff physicians and three other employees). Cultures were negative for *Salmonella, Shigella, Campylobacter, Yersinia*, and *Vibrio*, and ova parasites were not detected. However, direct and acid-fast stain microscopic examination of stool specimens from 9 of the house staff physicians and one of the other employees revealed the presence of cyanobacteria-like-bodies (CLB).

Define and identify cases

Clinical symptoms included a 1-day prodrome of malaise and low-grade fever, followed by explosive watery diarrhoea, anorexia, severe abdominal cramping, nausea, and occasional vomiting. Remission of diarrhoea usually occurred after 3–4 days but was followed by a cycle of relapses and remissions lasting up to 4 weeks. During remissions, patients noted continued malaise and anorexia, sometimes accompanied by constipation. Between 18 and 21 cases of illnesses were confirmed.

Perform descriptive epidemiology

The incubation period for this illness was estimated to be 48 hours. This estimate was based on the length of time that occurred between the initial failure of the pump (5 July) and the reporting of the first case (7 July). A descriptive analysis of the data indicated that the outbreak was limited to residents of the building.

Box 10.1 (continued)

Develop hypothesis

The presence of CLB in stool specimens and the epidemiological investigation implicated exposure to a contaminated water supply as the source of infection. The timing of the pump failure (just prior to the onset of the outbreak) also implicated the water supply.

Evaluate hypothesis

Cook County Hospital staff sampled water from several taps throughout the building on 10 July and all the samples proved negative. On 20 July, water samples and scrapings were taken from the bottom of the two storage tanks on the roof. Blue-green algae was not found but alga diatoms were present and considered to be viable.

A random survey of 25% of the Hall's residents and workers identified an additional 18 people who had been symptomatic during the time interval of concern.

The drinking-water supply for the residential hall is connected to the public water supply for Chicago. The water entering the hall passes through three pressure filter units. The filters are plumbed in parallel and each one is between 1.5 and 2 m in diameter and about 2.3 m tall. Or investigation it was found that when water is flowing through the filter, some pressure loss occurred across each filter, indicating that media was present in each filter. The hall's service personnel indicated that the filters had not been backwashed for at least 10 years (the length of time for which the personnel had been employed at the hall).

After the water passes through the filters, it flows into a surge tank that feeds the main pump The main pump then transfers the water to two roof storage tanks that feed the Hall's distribution system by gravity. The two roof storage tanks (each approximately 20,000 I in capacity) are housed in a penthouse area and basically uncovered. A tarpaulin was available for covering the tanks, but did not appear to be in constant use. The waterline from the basement pump is splir into two lines and each line serves one of the storage tanks. The influent enters at the top of each storage tank and then free falls into it. The effluent lines from the tanks are located approximately 25-30 cm above the bottom of the tanks. The effluent from the two tanks is recombined before it enters the hall's distribution system. The water depth in each storage tank normally varies from a low of 1.5 m to a high of 2.7 m.

The penthouse area was not sealed from the outside. Several windows were broken and screens were unavailable. Birds' faeces were found on rim of the storage tank, on pipes located above the tanks, and on the tarpaulin that partially covered the one tank that still contained some water.

If the drinking-water was the source of contamination, then the contamination probably occurred in the roof storage tanks. When the pump failure occurred, the water level in the tanks fell to the height of the effluent line (approximately 25-30 cm above the bottom of the tanks). These remaining 25 cm of water generally constitute a stagnant zone in which the water moves very little or not at all. Water in this zone would not normally become mixed with water in the zone above, and its chlorine concentration would be very low. This lower zone is therefore a probable area for biological growth. When the pump failure occurred, the tanks were drained to this level.

Box 10.1 (continued)

When the pump was turned back on, the new water coming into the storage tank doubtless mixed with the stagnant water that it still contained, with the result that the stagnant water became distributed throughout the building. The birds' faecal material, and use of the water by birds for drinking or washing, were possible sources of initial contamination.

The new water flowing into the storage tanks both flushed the tanks out and added fresh chlorine to the lower areas of the tanks. The flushing action and chlorine would have been sufficient to reduce the algae concentration in the tank so that the later sampling for algae was negative.

Additional studies

The following areas for additional sampling were recommended because they might provide verification of the hypothesized transient contamination. A water sample from a residential room that has been vacant 5 July might show contamination. Recent remodelling involved removal of a kitchenette. Plumbing if intact might also be an ideal place for water sampling. One of the water filters should be sampled to verify that they were not the source of the algae contamination.

Control and prevention

On 11 July the residents were advised not to drink the water in the residence hall until further notice. A bottled-water dispenser for drinking water was placed on each floor for use while the drinking-water ban was in effect.

The open loop system was replaced by a closed loop system. The filters, surge tank and the two roof storage tanks were replaced with a totally closed system. It was recommended that additional chlorination should be carried out once the new system had been installed, in order to clean the hall's water distribution system.

Communicate findings

The outbreak was reported in the Morbidity and Mortality Weekly Report (Vol. 40. No. 19).

10.3 Disease clusters

When disease occurrence is not uniform (for example, differences in the pattern of disease occurrence are observable between population groups, geographic regions, or over time periods), epidemiologists attempt to identify patterns of factors or events that may explain the observed distributions. Exploratory analyses using epidemiological data are often known in public health programmes as "cluster" studies. Many public health programmes have programmes for the reporting of disease clusters. The key to evaluating disease cluster reports is to determine whether case occurrence within a certain location is higher than would normally be expected. The spatial pattern of cases within a geographic area, the time pattern of the occurrence of cases, and, in some instances, the space-time pattern, are examined for evidence that the distribution of cases is not random and potentially the result of a hazardous environmental exposure.

A "cluster" investigation is not a distinct type of study design (see Chapter 6). Rather it refers to using epidemiological methods to explore whether there is an elevated incidence or prevalence of disease by time and location. A "cluster" investigation is differentiated from an "outbreak" investigation only in that the latter tends to involve sudden or acute changes in the health outcome incidence.

Most cluster studies are small area investigations involving a very small numbers of cases (Thacker, 1989). These small numbers make the data analyses very difficult. A variety of specialized statistical methods have been developed for disease cluster analysis (Aldrich et al., 1990; CDC, 1990). However, application of statistical techniques does not offer not a simple solution for assessing disease clusters. Biological reasoning must also be applied to interpretation of a cluster report. Statistical techniques may, however, help to decide which cluster reports should be investigated and in what order. Computerized statistical packages are available for statistical analysis (Aldrich & Griffith, 1993).

If clusters are investigated regularly, development of a protocol should be considered. This will help to ensure that all cluster reports are treated in the same manner. A protocol, when combined with statistical techniques, also can help to prioritize among reports. If disease cluster reports increase in number, a surveillance strategy should also be considered, which would consist of systematic monitoring of disease patterns to detect unusual case aggregations before they present themselves as a cluster report. Monitoring health events as sentinels of potential exposure to hazardous substances in the environment (Rothwell et al. 1991) has been suggested.

10.4 Specific investigations of health impacts of local pollution

Epidemiological investigations of populations are sometimes required at specific locations that are known to be contaminated with a specific pollutant or that are suspected of being so. (See Section 2.1 on page 17, which discusses the context for epidemiological investigations, as well as Section 8.7 on page 241, which discusses investigations in communities that are alarmed by environmental hazards.) They may be undertaken:

- to ensure or verify compliance with statutory programmes of epidemiological research;
- to dispel concerns expressed by a community or group that considers itself at risk, or to provide supporting evidence for those concerns;
- to advance scientific knowledge.

The exact nature of a site-specific environmental epidemiology investigation will be determined by the objectives of the investigators and the nature of the community's concerns. The design of such an investigation will be very different from that of a disease investigation, since it will start from the exposure rather than the disease. The investigator must include the following questions in the epidemiological protocol:

• What is currently known about the nature and extent of the environmental hazard experienced by the population of interest? For instance, if toxic exposures have occurred, what substances were released into the environment, at what levels of contamination, what environmental media were contaminated, and what is known about the health effects of the contaminants?

- Which population is at risk as a result of exposure to the environmental hazard? Are there any groups within this population that may be particularly susceptible (e.g. children)?
- Will it be possible to obtain estimates or measures of the levels of exposure to the environmental hazard of concern?
- How will the population or community at the site of concern be involved in shaping the
 epidemiological investigation? (A site-specific investigation must involve the population
 if it is to receive its support. Moreover, such involvement will enhance the credibility of
 any study findings.)
- Given the environmental conditions and the health concerns of the population at the site under investigation, what kind of study design (e.g. cohort, cross-sectional) would be most appropriate?

Evidently, determining whether a site should be or can be the subject of an environmental epidemiology investigation is not a simple matter. If multiple sites are being considered for study (as in a large programme that screens sites for potential investigation), the selection process becomes even more complex.

Public health assessments

In the USA, ATSDR has developed the concept of a "public health assessment" (ATSDR, 1992b). The Agency defines a public health assessment as the evaluation of data and information on the release of hazardous substances into the environment, undertaken to:

- assess any current or future impact on public health;
- develop health advisories or other health recommendations;
- identify studies or actions needed to evaluate and mitigate or prevent adverse human health effects.

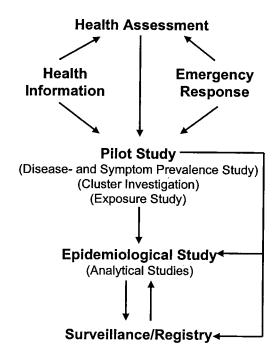
For ATSDR, a public health assessment represents the initial effort to categorize a hazardous waste site (ATSDR 1992b), but more generally, a public health assessment may be the first in a sequence of events leading to an epidemiological site investigation (see Figure 10.3). The various components of a public health assessment are shown in Fig. 10.4.

ATSDR public health assessments are currently based on three key sources of information:

- environmental contamination data (e.g. data on levels of contaminants in groundwater or air) or biological data (such as blood lead concentrations);
- health outcome data (e.g. tumour or birth defects incidence rates);
- information about community health concerns (e.g. information from local health care providers concerning unusual morbidity patterns).

Community health data can include valuable information about the baseline health status of persons living near specific sites. Although information about community health concerns may not contribute to determining causal relationships, it may indicate appropriate follow-up health actions.

Figure 10.3 A public health assessment may be the first in a sequence of events leading to an epidemiological investigation



Source: ATSDR, 1992b.

Categories of health hazard

In its public health assessments, ATSDR classifies the threats posed by an individual hazardous waste site according to the following five categories of health hazard and site (ATSDR 1992b):

- 1. Urgent public health hazard a site at which even short-term exposure would represent a serious health hazard.
- 2. Public health hazard a site at which long-term exposure would represent a health hazard.
- 3. Indeterminate public health hazard sites for which information is incomplete.
- 4. No apparent public health hazard sites at which human exposure to contaminated media is occurring or has occurred in the past, but at levels which do not represent a health hazard.
- 5. No public health hazard sites that do not pose a public health hazard.

A site is placed in one of these categories on the basis of judgement by a staff of environmental health professionals, using weight-of-evidence criteria. As such, the determination is not based on a formal, quantitative risk assessment methodology (ATSDR, 1992b). Classifying sites according to the human health hazard, they represent enables an agency or investigating team to direct programme resources and effort to where they are most needed.

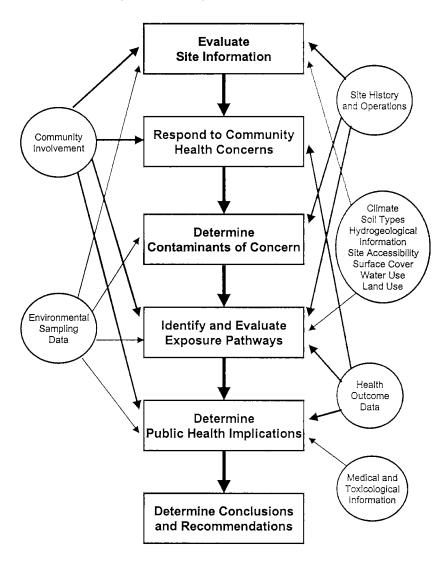


Figure 10.4. Various components of a public health assessment

Source: adapted from ATSDR, 1992b.

10.5 Importance of communication

Epidemiologists should communicate their findings to environmental managers and policy developers, as well as to the scientific community and the public. As discussed in Chapter 8, a report in accurate scientific language detailing the results of the epidemiological study must be prepared. The report should accurately describe the purpose of the investigation, the methods used, the findings and the interpretation of the findings. The report should be reviewed by the investigators' peers, before it is finalized, to ensure that the presentation is clear and scientifically

valid. The study design, data collection methods, statistical methods, etc., should already have been reviewed by colleagues and other experts at the planning stage (see Chapter 8).

Additionally, in order to create a permanent record of the study for future reference, epidemiologists should submit their findings to peer-reviewed journals, for publication. Published reports provide valuable information for national and international regulatory or health authorities who are responsible for establishing exposure standards or guidelines on specific environmental hazards. In this context, publication of not only those reports that describe statistically "positive" association between environmental hazards and human health outcomes, but also of those that describe "negative outlines", should be encouraged.

A simplified presentation of results that can be readily understood by policy makers, the public, and the mass media may also be required (IPCS, 1983). Since the latter presentation is intended for a non-technical audience and will therefore not include all the technical details of the study, the risk of misinterpretation is higher. Any material written for public dissemination should therefore be cleared by the scientists and epidemiologists who were involved in the study. Such a presentation may need to make explicit the limitations of the epidemiological approach, and the need to gather supplementary information from other studies, before finalizing conclusions.

Environmental managers and policy developers are increasingly called upon by legislative bodies and the public to control environmental hazards. The pressure to act is often enormous. Moreover, their decisions invariably impact human health in some way. Epidemiological findings, as described in peer-review reports prepared by a study's investigators, can make a substantial contribution to building a scientific base for the development of government regulations, guidelines, and policies relating to environmental hazards.

Communicating with the public

The epidemiological findings of studies of environmental hazards must be communicated effectively to the public. This is particularly important with respect to investigation involving communities who have expressed concern about alleged clusters of adverse health effects. Epidemiologists and scientists will need to establish a dialogue with such communities and with health and environment officials who are knowledgeable about the communities' conditions and concerns. Such contact can be developed by working with local media in order to make the presence of health investigators known.

The US Environmental Protection Agency (USEPA) has developed a set of "Cardinal Rules of Risk Communication" that could also be considered for adoption by investigators when initiating and implementing epidemiology investigations, and when presenting their findings (Table 10.2). An especially important rule, yet one that is often neglected, concerns the need to evaluate the effectiveness of a particular communication. For example, did the communication reach the desired audience and did it have the intended result? If not, why not?

An evaluation of the effectiveness of a particular health risk communication (i.e. how well the intended audience understood the message) can be carried out by means of a structured interview — by mail or telephone — of a sample of the persons who received the risk communication. A

structured interview can also be conducted with a "focus group" (i.e. a sample of the target audience). In this case, a sample of the target audience is brought together to be interviewed.

Table 10.2. Cardinal rules of risk communication

- accept and involve the public as a legitimate partner
- plan carefully and evaluate efforts
- listen to the public's specific concerns
- be honest, frank and open
- coordinate and collaborate with other credible sources
- meet the needs of the mass media
- speak clearly and with compassion.

Source: USEPA, 1988.

Community participation

Another important application of communication principles is to encourage and facilitate community involvement in health investigations. Investigators should consider setting up a local community assistance panel (CAP) to represent the interests of the community. The decision as to whether or to establish a CAP will be determined by such factors as the level of concern within the community, local political considerations, and the resources available. Creating and working with CAPs can be facilitated by following the rules for health risk communication presented in Table 10.2.

Typical community assistance panels include environmental activists, elected officials, local physicians, local health agencies, religious leaders, teachers and industry representatives. The panels provide a forum for the voicing of health concerns by local citizens, and for the communication of proposed study protocols and findings. When communicating with community panels, epidemiologists must guard against sharing information (e.g. via inappropriately designed survey questionnaires) that could bias the outcome of an investigation.

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Chapter 11

Environmental Epidemiology for Policy and Management

Learning objectives

- Understand the use of epidemiological information in environmental health policy.
- Be able to describe uses and major steps of a risk assessment.
- Understand how epidemiological information is used in environmental regulation and management.

11.1 Use of epidemiological information in policy and management

Chapter 1 began with a description of the role of epidemiology in environmental health policy and management because it is essential to understand the linkage between doing environmental epidemiology studies and using the information derived from the studies to prevent and manage environmental health conditions in society. To protect the population from the adverse effects of environmental pollution, environmental managers and regulators must have credible scientific information about the link between human exposures and environmentally induced disease. Epidemiology is the core scientific discipline that provides data upon which public health actions and decisions are based (IOM, 1988). For example, a major public and environmental health innovation of the 20th century is the disinfection of public drinking-water supplies. The adoption of this measure was the result of environmental epidemiology studies starting in the 1840s indicating that water is the principal vector of several life-threatening diseases. It was much later that microbes were discovered as the etiologic agents responsible for those diseases (the 1890s for bacteria and the 1950s for viruses). Similarly, environmental epidemiology studies implicated the consumption of fish in Minimata disease long before it was discovered that fish in Minimata Bay had become contaminated with methyl mercury (WHO, 1990). These two examples illustrate the importance of epidemiologic data in making management decisions.

An example of the importance of environmental epidemiologic data in shaping health policy is provided by the actions in the US to prevent children's exposure to lead in the environment. While the toxicity of lead at high exposures in adults and children has long been recognized, epidemiologic investigations in several countries during the period of the 1970's to the 1980's revealed that lead exposure at low levels, levels once thought to be without harm, in fact caused reduced intelligence, delayed cognitive development, and adverse effects on hearing, amongst other adverse effects, in young children (ATSDR, 1988). In addition, investigations showed maternal exposure to lead during pregnancy has an adverse effect on the fetus (ATSDR, 1988).

As these epidemiologic findings became known to policy makers, health policies had to be worked out in ways intended to reduce the exposure of young children to lead in the environment, ideally leading to prevention of exposure and lead toxicity. In the US, national legislation, supplemented by local regulations, developed as the direct result of epidemiologic

findings that low-level lead exposure is harmful to the health of young children and fetuses. These various laws and regulations include actions to remove lead from older houses that contain lead-based paint, screening and surveillance of children at high risk of lead toxicity, research on methods to measure lead absorption, and educational efforts to inform the public and medical providers about how to prevent lead toxicity in children. What has emerged is the health policy that lead toxicity must be prevented in young children as a matter of health promotion.

Epidemiological data provide direct evidence of human exposures and their subsequent health effects. A body of environmental epidemiologic data is used to determine whether an association is causal. This same body of data is then used to guide decision makers in developing preventive or remediation strategies, and finally epidemiologic data are used to evaluate the preventive or remediation policies implemented. Because data are obtained from people in real world situations, the findings are not subject to the uncertainties associated with animal studies, such as extrapolations from species to species, from high to low dose, or from acute to chronic effects. Moreover, evidence collected in humans has an innate directness and relevance that tends to insure its acceptance by a broad spectrum of constituencies. A body of epidemiologic data provides both qualitative and quantitative information to serve as a scientifically credible base for making environmental policy and management decisions.

Epidemiology has been used in some areas of health policy, such as in risk assessment and standard setting, which are described in the next two sections. However, epidemiology has had a more limited impact on environmental health policy than it could given the direct relevance of human studies described above. One reason is the vesting of responsibilities with environmental regulatory agencies (or similar ministries) for controlling or preventing environmental hazards. This leads to the establishment of environmental regulations that are based primarily on toxicologic-based risk data, sometimes in conjunction with a limited amount of epidemiologic data. The regulations are intended to limit human exposure to regulated hazards. What is often lacking when regulating hazards are epidemiologic data that represent a population-based estimate of health risk for the regulated hazard. From a public policy standpoint, this raises a number of important questions. For example, should regulatory activities be curtailed or delayed simply to collect epidemiologic data that would be useful for purpose of more precisely calibrating risk estimates and exposure levels? On the other hand, should regulatory standards ever be established in the absence of any epidemiologic data to support the presence of a presumed adverse health effect in a population? These are difficult questions whose answers ultimately get rooted in public policy.

Finally, it is becoming increasingly recognized that epidemiology can play an important role in evaluating the impact of current environmental health policies and programs, and predicting future environmental health impacts of proposed programs. Section 11.4 will discuss areas of growing or future applications of environmental epidemiology in policy and management.

11.2 Risk assessment

The 1970s was a period of heightened public concern about the effects of technology on the environment. Many governments were urged by their citizenry to regulate as scientific evidence emerged on various chemical and microbial substances that may cause health effects in humans. New government programs were established to identify and regulate these hazards to humans and

the environment. To aid in this decision-making the process of "risk assessment" was developed as a means for identifying health hazards and estimating the risks to human populations. The term "risk assessment" used for decades in public health took on a specific meaning in the environmental regulatory process. In the regulatory setting, risk assessment is the use of a factual base to define the health effects of exposure to pollutant of interest. This is separate from risk management which is the process of weighing policy alternatives and selecting the most appropriate regulatory action.

Overview of risk assessment

Risk assessment can be defined as "the characterization of potential adverse health effects of human exposures to environmental hazards" (Aldrich & Griffith, 1993). In other words, it develops a quantitative estimate of risk to humans of a specified hazard, based on the availability of exposure data. The four basic steps of risk assessment are hazard identification; dose—response assessment; exposure assessment; and risk characterization. The risk assessment process is shown in Figure 11.1, which is similar to Figure 1.1 on page 3.

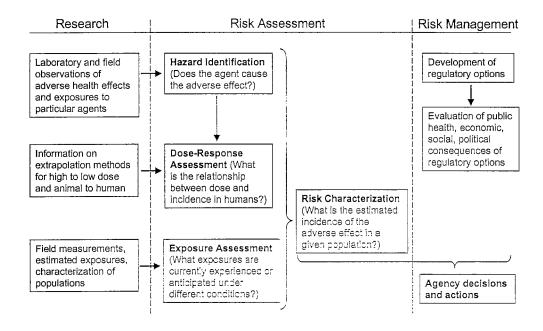


Figure 11.1 Role of epidemiological research in the risk assessment process

Source: NRC, 1983.

Hazard identification is the process of determining whether an exposure to an environmental agent is associated with an adverse health effect. Exposure assessment describes or estimates the magnitude, duration and route of exposure. Once a hazard has been identified, dose—response assessment determines whether the adverse effect increases with increasing exposure to the hazard. The risk is then characterized. This means that the incidence of an

adverse health effect that could be anticipated following exposure to the hazard is estimated. Risk characterization is performed by combining information from the dose–response assessment and the exposure assessment. For a detailed explanation of the above steps, see Canter, 1989; Aldrich & Griffith, 1993, and IPCS, 1994.

Uses of risk assessment

The US Environmental Protection Agency (1984) has outlined the major uses of risk assessment (Table 11.1). First, risk assessment enables managers to set priorities and to improve the decision-making process, thereby producing consistent risk reduction policies.

Second, risk assessment enables the scientific community to identify important data gaps. It can also contribute to the prioritizing of research agendas, and in so doing, strengthen a particular scientific discipline. For example, the use of pharmacokinetics and pharmacodynamics data for risk assessment, has increased research in both these areas. As a result, our understanding of chemicals has increased in ways that both benefit risk assessment and add to the knowledge about biological mechanisms associated with chemical exposures.

Table 11.1: Uses of risk assessment

Management uses risk assessment to:

- set priorities
- improve decision-making
- produce more efficient and consistent risk reduction policies.

Scientific uses of risk assessment include:

- identification of data gaps
- prioritizing research
- promoting development of new methods.

Epidemiological information and risk assessment

Epidemiological data can contribute to risk assessment. Yet most risk assessments rely solely on animal data. This is because it would be virtually impossible to obtain human data on even a small percentage of the 65,000 chemicals currently present in our environment, and because the endpoint of concern (e.g. cancer) often has a long latency period. However, epidemiological data are available for many agents and have been used in risk assessment. As with available animal data, these must first be evaluated qualitatively.

An example of criteria to qualitatively evaluate human data are those used by the International Agency for Research on Cancer (IARC). IARC uses four criteria when evaluating human data (IARC, 1991) for classification of compounds as carcinogens. The first focuses on the type of

study design. Analytic designs such as cohort or case—control designs are considered to be of more value than descriptive designs because of their specificity in hypothesis testing. The second criterion considers the quality of the studies; quality is determined by examining issues of bias, confounding and chance in interpreting the study results. The third criterion evaluates the relative risks and the absolute risks in the context of length of exposure and duration of exposure, and other temporal variables relating to exposure and disease. The final criterion concerns comparison of the entire body of epidemiological evidence with causal criteria in order to determine causality. Causal criteria include: strength of the association, consistency of the association, temporal relationship between exposure and effect; biological gradient of association; specificity of association; and biological plausibility (Beaglehole et al., 1993; Landrigan, 1994). (Causation is discussed further in Chapter 3, pp. 63).

Once epidemiological data have been evaluated qualitatively, they must be analysed quantitatively. This process may require extrapolating from high-dosage to low-dosage exposures. The epidemiological data under evaluation may have been collected in occupational settings involving high levels of exposure to the hazard of concern. The risk assessment may be interested in general exposures in the population which may be much lower than the exposures in occupational studies. Therefore, risk assessors must attempt to associate high-dosage effects (occupational studies) with low-dosage exposure (majority of population). The results of the risk assessment are often controversial in this situation because scientists disagree about the effects of high-doses on the metabolism, and the subsequent mechanisms of action (Canter, 1989). Another concern is that dose-response models developed at high-dose levels can produce very different results when extended to estimated low-dose levels. As Figure 11.2 shows, dose-response curves derived with different models diverge substantially in the low dose range. Thus, low-dose extrapolation must be more than a curve-fitting exercise, and considerations of biological plausibility must be taken into account.

Risk assessors work primarily on estimating cancer incidence in relation to environmental exposures. Since cancer is thought to arise from a single cell (Yunis & Hoffman, 1985), and the prevailing philosophy is that "each cellular injury works harm" (Meselson, 1980), risk assessors operate on the "no threshold" or zero-level concept, and therefore use a straight (linear) line, no threshold, extrapolation model. However, models can also be non-linear (based on pharmacokinetics and on the genetic capabilities of a cell).

The use of confidence bounds in the risk model must also be considered. Confidence limits are placed on each of the dose–response data points taken from animal data in order to reduce the uncertainty that results from use of small sample sizes. When the regression is performed, the upper 95% confidence limits are used; they are often very broad because of the small sample sizes. Setting 95% confidence limits on small study populations results in a steeper slope for the dose–response model, and their use is sometimes criticized since they produce a prohibitively conservative risk assessment (Aldrich & Griffith, 1993). Although human data can be used to reduce the potential for uncertainty that is associated with the extrapolation process, it is clear that the type of model chosen can have a significant impact upon a regulatory decision, and subsequently upon costs associated with compliance. It is also the case that the greater the number of epidemiological studies and the more varied the studies over different levels of exposure, the less uncertain the risk assessment.

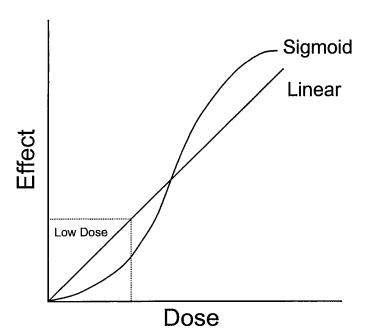


Figure 11.2. Models of low dose extrapolation

Advantages and disadvantages of risk assessment

The advantages of risk assessment have been discussed extensively elsewhere (USEPA, 1984; Canter, 1989). The main advantage is that the process defines the problem. During the risk assessment process the decision maker is required to analyse the problem and list all the major contributing factors that are known. This analysis identifies interactions and relationships that might exist and reduces the chance of omitting pertinent information.

Another advantage is that it serves as a guide for data collection. The development or choosing of a model for analysis defines the types of data needed. This saves time and resources by minimizing the collection of inappropriate or unneeded data. The risk assessment process provides a framework for assessing several environmental problems, thereby enabling decision-making to become more consistent. Since risk assessment is quantitative it lends itself to standard or guideline setting. Risk assessment provides a mechanism to predict responses to combinations of conditions that fall outside the range of the data used for the model calibration. The risk assessment models can be used to evaluate hypothetical situations such as those that may represent conditions associated with management controls or standard setting. Thus it can also be used to identify risk reduction goals as part of efforts to control pollutant levels.

The primary disadvantage of risk assessment is that the information on which decisions must be based is usually inadequate. Because the decision process cannot wait, the gaps in information must be bridged by inference and belief, and these cannot be evaluated in the same way as facts. These inferences inevitably draw on both scientific and policy considerations.

Another disadvantage of risk assessment is the probabilistic nature of the assessment. The unit of risk based directly on the slope of the model refers to the increased health risk per unit of exposure. And as already mentioned, the confidence limits around the estimate can lead to a very conservative estimate that may not be realistic. These estimates may even be below typical background levels or actual detection limits for measuring the agent in the environment.

Finally it must be understood that the result is not applicable to each individual. This is not necessarily a disadvantage but merely a misapplication of the result. Risk assessment is estimating risks in populations. Since epidemiology population based; it is relevant to the risk assessment process (Aldrich & Griffith, 1993).

Case study: environmental tobacco smoke

The US Environmental Protection Agency (USEPA) released a risk assessment for respiratory effects associated with environmental tobacco smoke (also known as passive smoking) (USEPA, 1992a). Most of the evaluated information was epidemiological data. Several health outcomes were evaluated in the risk assessment, but for this case study only the analysis concerning lung cancer is presented.

Exposure assessment

Several studies have shown that environmental tobacco smoke (ETS) is a major source of indoor air contaminants (NRC, 1986). Personal monitoring studies have measured the levels of nicotine and respiratory suspended particles (RSP) found in ETS and in a variety of indoor environments (Muramatsu et al., 1984; Coultas et al., 1990). The results of these studies clearly demonstrate that exposure to ETS, even if of low frequency, duration and magnitude, can lead to RSP and nicotine values that exceed background levels. Cotinine in saliva, blood and urine is a biomarker of ETS exposure (National Research Council, 1986) (see Table 2.3 on page 26). Studies that compared exposure measured by questionnaire with exposure as measured by continine in urine found that a significant number of individuals who reported no exposure via questionnaire had actually experienced exposure as measured by cotinine in urine (Riboli et al., 1990).

Hazard identification and dose-response

Hazard identification was carried out in two phases. The first phase evaluated the relationship between smoking and lung cancer. The USEPA report concluded that there was an unequivocal causal association between tobacco smoking and lung cancer in humans with dose—response relationships extending down to the lowest observed exposure. It also cited the corroborative evidence of animal bioassays and *in vitro* studies of the carcinogenicity of main-stream smoke and ETS as establishing the plausibility that ETS is also a human lung carcinogen. Furthermore, biomarker studies verified that for non-smokers passive smoking results in a detectable uptake of tobacco smoke constituents (see exposure assessment). Substantial epidemiological evidence demonstrates the increased risks of lung cancer in non-smokers who are exposed to ambient levels of ETS (Table 11.2). There was no need to extrapolate from high-dose animal bioassays, or to extrapolate from high-level occupational human exposures in order to estimate the human risk of environmental exposure levels. The epidemiological data alone were sufficient for evaluating the health risk of ETS exposure.

Table 11.2. Statistical measures by individual study and pooled by country, correction for smoker misclassification and tier evaluation

Location (Author) ¹	Power	p-value effect	p-value trend	RR	Confidence interval	Tier
Greece (Kalandidi) 1990	0.39	0.02	0.04	1.92	(1.13, 3.23)	1
Greece (Trichopoulos) 1981	0.45	0.01	<0.01	2.08	(1.31, 3.29)	2
Greece - ALL	<u> </u>	<0.01		2.00	(1.42, 2.83)	
Hong Kong (Chan) 1982	0.43	0.5	*	0.74	(0.47, 1.17)	2
Hong Kong (Koo) 1987	0.43	0.06	0.16	1.54	(0.98, 2.43)	2
Hong Kong (Lam T.) 1987	0.73	<0.01	<0.01	1.64	(1.21, 2.21)	3
Hong Kong (Lam W.) 1985	0.39	<0.01	*	2.51	(1.49, 4.23)	4
Hong Kong ALL		<0.01		1.48	(1.21, 1.81)	
Japan (Akiba) 1986	0.42	0.05	0.03	1.50	(1.00, 2.50)	2
Japan (Hirayama) 1984	0.75	0.04	<0.01	1.37	(1.02, 1.86)	2
Japan (Inoue) 1988	0.17	0.07	<0.03	2.55	(0.90, 7.20)	3
Japan (Shimizu) 1988	0.37	0.39	*	1.07	(0.70, 1.67)	3
Japan (Sobue) 1990	0.66	0.01	*	1.57	(1.13, 2.15)	4
Japan ALL		0.01		1.43	(1.20, 1.71)	
USA (Brownson) 1987	0.15	0.28	*	1.50	(0.48, 4.72)	1
USA (Buffler) 1984	0.17	>0.5	*	0.70	(0.34, 1.43)	2
USA (Butler) 1988	0.18	0.17	*	2.01	(0.61, 6.73)	2
USA (Correa) 1983	0.22	0.09	0.01	1.90	(0.86, 4.15)	2
USA (Fontham) 1991	0.93	0.04	0.04	1.26	(1.01, 1.58)	2
USA (Garfinkel) 1985	0.60	0.15	<0.02	1.24	(0.88, 1.76)	2
USA (Garf - cohort)	0.92	0.19	*	1.15	(0.88, 1.51)	3
USA (Humble) 1987	0.20	0.10	ns	1.98	(0.81, 4.95)	3
USA (Janerich) 1990	0.44	>.50	*	0.78	(0.51, 1.16)	3
USA (Kabat) 1984	0.17	>.50	*	0.74	(0.28, 1.90)	3
USA (Wu) 1985	0.21	0.29	ns	1.31	(0.58, 2.92)	3
USA ALL		0.02		1.19	(1.04, 1.35)	

Location (Author) 1	Power	p-value effect	p-value trend	RR	Confidence interval	Tier
Scotland (Hole) 1989	0.09	0.26	*	1.97	(0.34, 11.67)	1
England/Wales (Lee) 1986	0.20	0.50	*	1.01	(0.47, 2.15)	2
Sweden (Pershagen) 1987	0.45	0.22	0.12	1.17	(0.75, 1.87)	2
Sweden (Svensson) 1989	0.24	0.32	*	1.19	(0.62, 2.35)	3
W. Europe ALL		0.21		1.17	(0.84, 1.64)	
China (Gao) 1987	0.66	0.19	0.29	1.19	(0.87, 1.62)	3
China (Geng) 1988	0.32	0.01	<0.05	2.16	(1.21, 3.84)	4
China (Liu) 1991	0.18	>0.5	*	0.77	(0.35, 1.68)	4
China (Wu-Williams) 1990	0.89	>0.5	*	0.78	(0.63, 0.96)	4
China (All)		>0.5		0.95	(0.80, 1.12)	

^{1.} First author of reference. See bibliography in USEPA, 1992a.

The second hazard identification phase entailed a review of 30 studies of ETS and lung cancer. The studies were evaluated for confounding, bias and association due to chance. The following confounding variables were considered: history of lung disease, family history of lung disease, heat sources for cooking or heating, cooking with oil, occupation, and dietary factors. Other than studies in China, there were no indications that confounding could account for the association between lung cancer and ETS. In China, the use of smoky coal in the home for cooking was considered a confounder in the interpretation of those studies.

The statistical inferences for each of the 30 studies were evaluated for power, effect and trend. A summary of the studies is presented in Table 11.2. To increase power, the studies were combined by country or geographic region. The results of the combined studies were compared with the results of the individual studies and it was concluded that the number of statistically significant epidemiological effects and trends were not attributable to chance alone.

The major concern regarding bias was the possible misclassification of exposure status, particularly with respect to comparisons of non-smokers with smokers. Previous exposure assessment suggested that some misclassification was highly likely based on questionnaires. The net effect of a smoker versus non-smoker bias would be that any association between non-smokers and ETS could be partly accounted for by current or former active smoking by some subjects. Studies were therefore adjusted for bias due to smoker misclassification. Adjustment on an individual study basis for potential bias due to smoker misclassification resulted in slightly lower relative risk estimates but did not affect the overall conclusion.

The potential for bias in relation to diagnosis of cases, selection of the control group in case—control studies, collection of data in cohort studies and type of analysis used, was also examined. The studies were categorized based on quality of study into one of four tiers. Tier 1 studies had the highest quality and Tier 4 studies were not included in further analyses.

Analysis by tiers provided a method for evaluating studies both qualitatively and quantitatively. As a result of this exercise, the report concluded that other types of bias did not have a significant effect on the results.

In addition, study findings were evaluated by using seven criteria for causality similar to those mentioned in Chapter 3 (temporal relation, consistency, strength, dose-response, specificity, biologic plausibility and coherence) (USEPA, 1989a). It was considered that the cohort studies — which formed the majority — met the temporal relation criterion. This applied especially to those studies in Tiers 1 and 2. Having adjusted for bias, and evaluated for confounding, the consistency of a significant association was clearly evident for the studies in Tiers 1 and 2. The strength of the observation is limited by the small relative risk, but the pooling of studies either by country or by tier improved the statistical significance. Of the 14 studies reporting various dose levels, the statistical test for trend was significant (0.05) for eight of them. This strengthens dose—response because it is unlikely that it would be a result of bias or confounding. Specificity does not apply to ETS nor does it apply to many environmental agents studied (which is why it is not included in Table 3.4, page 64). Because ETS is a product of main-stream tobacco smoke, it is biologically plausible that ETS is also a lung carcinogen. The coherence of the results from the analysis of the studies and the lack of significant arguments to the contrary support the causal association between ETS and lung cancer.

Risk characterization

The report concluded that ETS is a cause of lung cancer in humans. The next step was to assess the magnitude of the health impact on the US population. The investigators used increased relative risk of lung cancer for women who had never smoked but who were married to smokers, to extrapolate to the general population. The total number of lung cancer deaths in US females from all causes was segmented according to: causes that were unrelated to tobacco smoke; background ETS; spousal ETS, and ever-smoking. The cause that was unrelated to tobacco smoke was defined as the baseline risk and all risk ratios were converted in order to take this into account. The estimated lung cancer mortality from ETS in women who had never smoked is therefore 1,500 (1,030 from background + 470 spousal ETS). Additional estimates for males who had never smoked and former smokers of both sexes were combined, to produce a total of 3,060 lung cancer deaths (Table 11.3). These calculations were based on numerical estimates which were subject to uncertainty. Additional calculations revealed that the range was 2,500 to 3,300. The report concluded that this was a reasonable range. The confidence in these results was judged medium to high because of the large amount of data available from various studies of human exposures to actual environmental ETS levels.

11.3 Standards setting

One of the most important fields for which epidemiological information is used is that of standard setting. But it must be emphasized that epidemiological data represents only one of the many factors that must be taken into account when developing standards. For any standard under consideration for implementation, it is likely that the scientific information available from all sources, including toxicological research, clinical studies, epidemiological surveillance and environmental monitoring, will not be sufficient to derive a perfect exposure—effect relationship. And even if such a relationship can be constructed, the standard setting process must resolve political, societal and economic issues before a standard can be proposed. Moreover, in setting

a standard, the societal acceptance of an appropriate risk level and the national resources for ensuring compliance with the standard must be evaluated (de Koning, 1989).

Any value judgments — to be made on the basis of information available — are the responsibility of policy decision-makers, and not of scientists in their professional roles. The role of an epidemiologist is to provide the best data and exposure—effect relationships possible and, in interpreting them, to indicate clearly where their confidence limits lie.

Table 11.3. Estimated female and male lung cancer mortality by attributable ETS sources for United States, 1985, using the pooled relative risk estimate from 11 U.S. studies

				Lung CancerMortality			ity
Smoking status	Sex	Exposed to spousal ETS	Number at risk (x 10 ⁶)	Back- ground ETS	Spousal ETS	Total ETS	Total ETS by sex and smok- ing status
Non- smoker	F	No	12.92	410		410	1500
Non- smoker	F	Yes	19.38	620	470	1090	
Non- smoker	M	No	9.93	320		320	500
Non- smoker	M	Yes	3.13	100	80	180	
Former smoker	F	No	2.0	60		60	430
Former smoker	F	Yes	6.7	210	160	370	
Former smoker	M	No	8.8	280		280	630
Former smoker	M	Yes	6.2	200	150	350	(FS,M)
Total			69.07	1,030	860	3060	3060

Source: USEPA, 1992a.

Factors in setting standards and guidelines

The first step in standard setting is to compile the available data. This is usually accomplished through a risk assessment process. While many standards are based primarily on animal data, risk assessments based on epidemiologic data have fewer limitations and uncertainties. It is the perception that few regulations are based on epidemiologic data. However, an evaluation of environmental regulation by the USEPA produced a sizable list of regulations based primarily on human data (Table 11.4).

Table 11.4. Pollutants regulated by USEPA based on data provided by epidemiology studies

Pollutant			Health Effect	Agency Action		
Arsenic			Carcinogenic	A, C, F, R, T, W		
Asbestos			Carcinogenic	A, C, R, W, X		
Benzene			Carcinogenic	A, C, F, R, W		
Benzidine			Carcinogenic	A, C, R		
Bis (chloro	methyl e	ther)	Carcinogenic	A, C, R		
Chloromet	hyl ether))	Carcinogenic	A, C, R		
Chromium			Carcinogenic	A, C, R, W		
Coke oven	emissio	ns	Carcinogenic	Α		
Environme	ntal toba	cco smoke	Carcinogenic	Α		
Nickel			Carcinogenic	A, C		
Vinyl chlori	ide		Carcinogenic	Α		
Cadmium			Renal	C, F, I, R, W		
Carbon mo	onoxide		Cardiovascular	N		
Chlordeco	ne		Neuro & Repro	F		
Chlorpyrifo	s		Neurological	C, F, I, R		
Dibromoch		ane	Reproductive	P		
Ethion			Neurological	F, I, R		
Fluorine			Osteosclerosis	I, R, W		
Lead			Neurological	Ć, Ń, R, W		
Malathion			Neurological	F, I, R		
Methyl mercury			Developmental	C, I, R		
Nitrate			Haematological	C, I, W		
Ozone			Pulmonary	N		
Piriniphos-	methyl		Neurological	F, I		
PM10 (par			Pulmonary	N		
Sulfur diox			Pulmonary	N		
Silver			Dermatologic	C, I, R		
A	=	Class A carcinoge				
C	=	Ambient Water Quality Criteria for Human Health				
F	=	Registered, use limited or cancelled under FIFRA				
1	=	Reference dose in IRIS based on human data				
N	=	Regulated as a National Ambient Air Quality Standard				
R	=	Reportable Quantity for Accidental Release under CERCLA				
Т	=	Listed as a Hazardous Air Pollutant				
W	=	MCL set under the Safe Drinking Water Act				
Х	=	Use either limited or specified under TSCA				

Once the scientific stage has been completed the political or management stage begins. This involves:

- **Determination of acceptable risk** problem is not scientific but rather one of opinion.
- **Determination of public to be protected** identifies and considers population groups who are at extreme risk or highly susceptible to the pollutant to be regulated.
- Consideration of human ecology sees man in balance with his environment.
- Choice of control technology requires both formulation of strategy and selection of appropriate control techniques.
- Legislation or standards considers legal framework and identifies necessary legal strategies.
- **Economics** strikes a balance between cost and benefits.

The process as outlined appears to be linear. In practice it is cyclical. This is because all standards should be periodically reviewed. Frequently, epidemiological studies do not provide the unequivocal evidence required by decision-makers. Nevertheless, they may form the basis of interim measures to reduce or limit exposures while further studies are pursued. Since adverse effects may become manifest only after a long induction period, interim standards for new or newly-introduced substances must sometimes be maintained for extended periods, while appropriate epidemiological data are collected.

The need for epidemiological data for standard setting will continue to be of high priority for environmental managers. As countries expand their industrial base and their environmental laws mature, regulations will be scrutinized as to their uncertainties particularly in the face of rising costs to industry associated with regulation.

Case study: lead

Lead is a ubiquitous toxic metal. It has been used for several thousand years and has no known beneficial biological effects. Humans are exposed to lead through inhaled air, dusts, food (the primary route) and drinking water. Industrial and auto emissions are primary sources of lead, although lead-based paint is also a significant source. Young children are exposed to lead by both their normal mouthing behavior and pica, and many other persons are exposed by smoking. Exposure to lead is indicated by measuring blood lead levels.

Baseline human exposure to lead is 35-50 micrograms per day (µg/day), with children exposed more than the average adult, and adult males exposed more than adult females. As a result, children have higher estimated blood lead levels than adults and men have higher levels than women (USEPA, 1986). Exposure also varies according to urbanization, age, sex, and socioeconomic status. Epidemiologic studies have pointed out that humans are not equally affected by lead. Lead may adversely affect the physical and neurobehavioral development in children, and cardiovascular function in adults. A number of animal studies involving lead exposure and neurological effects have been reported in the literature. Approximately 50 such studies have provided evidence of learning impairment in rodents and primates; however, their usefulness is limited because of the danger in generalizing these findings to humans.

Human studies have noted cardiac abnormalities in persons with overt lead intoxication since the 1960's (USEPA, 1986). More significantly, at least 25 epidemiologic studies have reported, as long ago as 1886, an association between high blood lead levels and increases in blood pressure (USEPA, 1990). Conclusive findings have emerged from more than a dozen epidemiologic studies evaluating lead and cancer. While most of the studies have methodological limitations which prohibit establishing any causal relationship, the findings from these studies are "suggestive" of lead being a human carcinogen (USEPA, 1989b).

Lead in air: WHO guidelines for the European community

An estimated 80 to 90% of lead in ambient air derives from the combustion of leaded motor fuels. The degree of pollution depends on traffic density, and the lead content of motor fuels. European urban air lead levels currently range from 0.5 to 3.0 $\mu g/m^3$; the annual average urban air lead level has been decreasing over time. Most of the lead in air is in the form of submicron size particles. These are inhaled and retained in the respiratory system. Most of this lead is absorbed into the body. Based on the dose-response relationship for haematological and neurological parameters in adults, the observed effect level has been found to be 0.2 $\mu g/ml$ in blood. In order to ensure that blood lead levels remain below 0.2 $\mu g/ml$, WHO recommends that the annual mean lead level in ambient air should not exceed 0.5–1.0 $\mu g/m^3$.

Lead in drinking-water, standards for the United States

In the United States, lead is regulated under five different federal environmental protection laws (Table 11.5). The maximum permissible contaminant level (MCL) for drinking-water is 5 μ g/ml, but the maximum contaminant level goal (MCLG) is zero. This goal is based on:

- The occurrence of a variety of health effects for which it is currently difficult to identify threshold exposure levels below which there is no risk of adverse health effects.
- The USEPA's goal to reduce the lead content of drinking-water to the maximum extent possible, thereby reducing total lead exposures.
- The classification of lead by USEPA as a probable human carcinogen.

Table 11.5: Lead regulatory actions in the United States

Regulatory act	Standard or guideline	Standard
Clean Air Act	Standard	1.5 µg/m³ calendar quarter average
Safe Drinking Water Act	Standard	5 μg/l
Clean Water Act	Guideline	50 μg/l
Superfund	standard	1 pound accidental release

The health literature on lead has been summarized in the *Air Quality Criteria Document* (USEPA, 1986) and in its 1990 supplement (USEPA, 1990). Based on this review, the USEPA concluded that blood lead levels at or below $10-15~\mu g/dL$ were of concern. The contribution of lead in water to blood lead levels was evaluated for infants, older children and adults. For infants, the Lacey study (1985) was used to give a slope of $0.26~\mu g/dL$ blood per $\mu g/L$ water at water lead levels below 0.015~mg/L and $0.04~\mu g/dL$ blood per $\mu g/L$ water at water lead levels above 0.015~mg/L. For older children, USEPA used a study of Hawaiians exposed to lead in drinking-water across a wide range of levels (Maes et al., 1991). The slopes were $0.12~\mu g/dL$ blood per $\mu g/L$ water at water lead levels below 0.015~mg/L and $0.06~\mu g/dL$ blood per $\mu g/L$ water at water lead levels above $0.015~\mu g/L$. For adults, a slope of $0.06~\mu g/dL$ blood per $\mu g/L$ water lead was used (Pocock et al., 1983). Based on this information, and the relative source contribution of water to total lead intake (estimated 20%), an MCL of $5~\mu g/L$ in water was set (Federal Register, 1991).

11.4 Potential roles of epidemiology in policy and management

Epidemiology has the potential to make other substantial contributions to environmental health policy and management. Human data that can quantify the relationship between environmental hazards and health effects can be used to estimate the potential impact of new programs or facilities, as well as to evaluate the impact of current policies. In most instances, the full potential of environmental epidemiology in these areas has yet to be realized.

Health component of environmental impact assessment

Environmental impact assessment (EIA) began in 1970 with the passage of the National Environmental Policy Act in the United States. Since then, over 50 countries have adopted EIA requirements and developed associated procedures. Potential health effects of projects should be analysed as part of the EIA process, and some have suggested that the overall process could be called the environmental health impact assessment (EHIA) process. The goals of EHIA are to predict and assess the impacts of a development on environmental health factors. An example of an EHIA would be estimation of increases in levels of malaria-carrying mosquito populations as the result of construction of water dams. By predicting future changes in environmental factors, it is possible to indicate the potential changes in health which may be caused by a development. These indications may then be used by local health experts, in conjunction with other considerations, to assess future changes in morbidity and mortality (Canter, 1989).

Giroult (1984) listed the following steps in the EHIA process:

- 1. Assessment of primary impacts on environmental parameters.
- 2. Assessment of secondary or tertiary impacts on environmental parameters resulting from the primary ones.
- 3. Screening of impacted environmental parameters of recognized health significance (requires epidemiologic data).
- 4. Assessment of the magnitude of exposed populations for each group of environmental health factors.

- 5. Assessment of the magnitude of risk groups included in each group of exposed population.
- 6. Computation of health impacts in terms of morbidity and mortality.
- 7. Definition of acceptable risks or of significant health impacts.
- 8. Identification of efficient mitigation measures to reduce significant health impacts.
- 9. Final decision.

Predicting environmental health impacts

There are two principal means of estimating future environmental health changes: observational description and analysis of past and current information, and estimation of trends. Trends can be estimated by using epidemiological measures of potential impact and developing models of environmental health scenarios that might result following specific interventions. There are several approaches to observational description and analysis of past and current information that can be used to estimate future environmental health changes.

- Descriptive epidemiological data can be used to create a "picture" of the distribution and possible environmental determinants of a disease. If ecological epidemiology studies can be developed from these records, some predictions can be made concerning the shortand medium-term situation.
- Analytical epidemiology studies conducted on a specific environmental problem can be
 used as evidence of the association between environmental hazards and health effects.
 Epidemiological effect measures such as relative risk, attributable risk percentage and
 population attributable risk percentage, can then serve as the basis for making a
 quantitative estimate of any change in effects, following adoption of control measures.
- Risk assessment is another means of predicting the various risks of an environmental agent. Risk characterization will indicate the level of risk for exposed populations. By analysing actual exposure and by considering a prediction of how conditions affecting exposure could vary in the future, a possible risk can be estimated.
- It is also possible to use environmental epidemiology surveillance to predict the impact of control and preventive activities. Surveillance of trends in emissions of environmental pollutants, environmental dynamics and concentrations of pollutants, and of related health effects, as well as of the effectiveness of control programmes are all relevant here.

Economic analysis

In the health care field, epidemiological data is used routinely to determine the economic impact(s) of various diseases and treatment of them. But this use of epidemiological data is not yet widespread among environmental health policy-makers; assigning monetary values to a health endpoints has proved to be a major obstacle. Many economic analyses simply ignore the health costs and/or benefits of regulations and environmental policies. Estimates of the number of lives saved or work years gained are calculated, but they are not often assigned a monetary value. Given the importance of sustaining the environment while encouraging economic development, these types of analyses are becoming more and more necessary.

Environmental equity

Environmental equity is a societal goal, defined as the provision of adequate protection from environmental toxicants for all people, regardless of age, ethnicity, gender, health status, social class, or race (Sexton & Anderson, 1993). Although there is debate about the extent to which society can achieve this goal, there is widespread consensus that fairness and equality should be inherent in society's commitment to safeguard people from the harmful consequences of exposures to environmental agents. Issues of environmental equity (sometimes referred to environmental justice) have been reviewed in several documents (ATSDR, 1992c; Lee, 1992; USEPA, 1992b; Sexton & Anderson, 1993; Sims, 1994). A major impediment to evaluating environmental equity has been the lack of data that would enable policy makers to distinguish the environmental component of many diseases in the general population; there are even fewer data that would enable us to examine the role of the environment in diseases and disorders that may be more prevalent in disadvantaged populations (USEPA, 1992b). Epidemiologic data whether through the design and conduct of studies or surveillance can provide an evaluation of environmental equity in a community or geographic region.

Evaluation of intervention and policies

Epidemiology can be thought of as having two fundamental levels of investigations. The first is an understanding of hazard-health effect relationships and the second is management or intervention. Intervention does not always require an extensive understanding of the disease process, as the examples on microbial and methyl mercury contamination of water at the beginning this chapter illustrated. Environmental epidemiology is an important tool to identify appropriate risk reduction strategies and subsequently evaluate the benefit to society of those management strategies.

There are several examples where various reductions in environmental pollution resulted in some measurable health benefit to the population. In the United States, lead was removed from gasoline used to fuel automobiles. Subsequent blood lead monitoring programs noted a precipitous drop in blood lead levels as did air lead monitoring programs (see Figure 6.4 on page 152). In Chile, the air pollution from motor vehicles was considered a major cause of respiratory morbidity and mortality. The government removed old buses that did not meet certain exhaust standards. Within weeks, many health clinics reported a decline in a variety of respiratory conditions. Chlorination or other disinfectants in drinking water has virtually eliminated typhoid fever, cholera and diarrhea as a major cause of morbidity and mortality in many countries.

Evaluations of such management decisions are done through two major types of epidemiology. The most prevalent use of epidemiology for evaluation is through monitoring and surveillance systems. The other epidemiologic method is specific studies aimed at specific populations. These studies are discussed in Chapter 6. In environmental epidemiology, these types of studies are rarely done and yet from a policy point of view these studies can provide direct input to the costs and benefits of management decisions, regulations and policy. The investment in epidemiology can often save a government many times the cost of the research itself by evaluating a risk reduction/prevention policy. This is particularly crucial in this era of making economic growth compatible with preserving the environment.

11.5 Role of epidemiology in environmental health decision- making

The ultimate goal of environmental health and epidemiology is to prevent needless morbidity and mortality by protecting people from unnecessary exposure to environmental hazards (Kjellström & Schwartz, 1994). Unfortunately, despite the large and expanding literature, relatively few people have reaped the potential health benefits identified by environmental epidemiology. This situation is worse in many developing countries where environmental and occupational exposures exceed national and international guideline levels by a considerable amount, but very little is done to rectify these trends. To reverse this trend, data from environmental epidemiologic studies must be translated from theory into public health practice more efficiently. This process requires the epidemiologist to be involved in the process of addressing the solutions to the problems they study.

There are many factors that influence actions towards decision-making. Some of these are:

- Value placed on health, human life extension & environmental protection, concern for future generations
- Strength of data, extent of documentation
- Public understanding of data and perceptions (acceptability) of risk
- Costs of intervention; are they affordable?
- Leadership: ability to persuade/motivate, negotiate, resolve conflicting goals or competing interests
- Process that provides a forum for debate and permits input into setting public policy
- Emphasis on planning for the future, government responsibility for protecting public from future harms
- Degree of collaboration: government/business/NGOs
- Regulatory process
- Judicial process
- Seriousness of the outcome
- Involvement of mass media
- Targeted message for decision-makers

Decision-making is not a simple process. A decision-maker must choose between competing alternatives, and may face uncertainties at every step. These difficulties, however, are no excuse for lack of action. There is a clear gap between the sophistication in public health research and that of decision-making in public health and environmental issues (Schwartz, 1994). One option to rectify this gap is to involve epidemiologists in the process of addressing the solutions to the problems they study. Certainly, increasing evidence about a potential health problem would aid the decision making process, but waiting for more evidence implies that someone has to endure the suffering in the meantime (Sandman, 1991).

As noted by Bradford Hill in 1965, "All scientific work is incomplete - whether it be observational or experimental. All scientific work is liable to be upset or modified by advancing knowledge. That does not confer upon us a freedom to ignore the knowledge that we already have, or to postpone the action that it appears to demand at a given time."

Agenda for the Future in Environmental Epidemiology: Research, Practice, and Teaching

Learning objectives

- Be able to develop a plan to further develop your knowledge and skills in environmental epidemiology.
- Be aware of the breadth of information sources available in environmental health and know how they can be accessed.
- Know how to plan and conduct a workshop in basic environmental epidemiology.
- Understand the possible future directions that environmental epidemiology might take.

12.1 Continuing your education in environmental epidemiology

This textbook is intended to go beyond the scope of an introductory textbook in environmental epidemiology. Its goal is to help prepare health and environmental professionals for participating in epidemiological investigations. Nevertheless, more information needs to be acquired than could be included here. Even the most seasoned epidemiologists agree that there is a need to continually update their knowledge and share points of view with colleagues in epidemiology and of in the allied environmental health professions. There are a variety of ways in which this can be accomplished:

- by critically reading the literature in environmental epidemiology;
- by advanced reading of textbooks and monographs;
- by enrolling in short courses or degree programmes in environmental epidemiology

Further reading

The literature in environmental epidemiology continues to grow at a rapid pace. Textbooks and journals with a speciality in related fields are listed in Annex 12.1. The World Health Organization Programme in Environmental Health also has published numerous relevant documents in the last several years. Students should feel free to contact the WHO Environmental Health Programme in Geneva if they wish to be informed about the newest publications.

Government departments of health statistics, health, and the environment also publish material relevant to local or regional environmental epidemiology situations which can be useful to draw experience from. Also nongovernmental organizations such as disease-specific foundations, environmental action groups, and others also publish material which can be useful and is often free of charge.

Further training

Numerous courses designed for professionals with a variety of educational backgrounds are available for postgraduate training. Universities and other nongovernmental agencies, WHO's regional offices, and professional societies operate short courses, ranging in length from days to weeks, on various topics. Commercial short courses are also widely available in North America and Europe. Many of the available programmes offer a broad content of material as well as opportunities targeted at more specific interests within environmental epidemiology. A list of training courses is available from the Office of Global and Integrated Environmental Health, WHO, 1211 Geneva 27, Switzerland.

12.2 Sources of information

There are numerous potentially useful sources of information that can be consulted on nearly every aspect of environmental epidemiology. They include:

- the large and growing environmental epidemiology literature published regularly in the form of national and international journals;
- the WHO Global Environmental Epidemiology Network (GEENET) (which comprises more than 1000 environmental epidemiologists, many of whom are willing to assist fellow epidemiologists)
- a number of international and national professional societies such as the International Society of Environmental Epidemiology (ISEE), the International Commission on Occupational Health (ICOH), the International Epidemiology Association (IEA) and the Society for Epidemiologic Research (SER).

In addition, numerous annual scientific meetings are held at which information on a wide range of current environmental epidemiology topics can be sought.

The information resources of WHO's Global Environmental Epidemiology Network (GEENET) are often a good place to start searching for environmental epidemiology information. For example, GEENET maintains numerous inventories of useful information, including a bibliography of relevant articles known as the environmental health resource collection, as well as compilations of environmental epidemiology newsletters, training courses, funding sources and research projects.

Generally, environmental epidemiologists seek information in the form of advice or relevant articles from the literature or data. A literature review is often the first step in an investigation into a specific environmental health problem. Information on how to access the literature can be found in the Appendix. Additionally, advice regarding methodology, analytic tools, or practical considerations can often be obtained from fellow professionals. Contacts can be fostered through:

- GEENET
- universities
- governmental/nongovernmental agencies
- national/international meetings: e.g. ISEE, IEA and SER.

Reference ranges for exposure data, can serve as a good screening tool when planning research or evaluating the need for interventions. Many international and national criteria documents contain summary information about the human health effects of specific hazards, including in some instances, information about human levels of exposure to specific environmental hazards. Epidemiological findings, when available, are key data in these documents because they are directly applicable to human health concerns. Examples of criteria documents that contain epidemiological findings and human exposure data are given in Table 12.1.

Table 12.1. Examples of criteria documents that contain epidemiological findings

Document	Agency or source
Environmental health criteria documents	International Programme on Chemical Safety
Monographs on the evaluation of carcinogenic risk to humans	International Agency for Research on Cancer
Toxicological profiles	Agency for Toxic Substances and Disease Registry (United States)
Environmental assessment and criteria documents	Environmental Protection Agency (United States)
Criteria for recommended standards	National Institute for Occupational Safety and Health (United States)
ECETOC monographs	European Chemical Industry Ecology and Toxicology Centre
Chemical toxicity data profiles on radioactive substances	Organisation for Economic Co-operation and Development
BUA reports	Beratergremium für Umweltrelevante Altstroffe der Gesellschaft Deutscher Chemiker (Germany)
Monograph series	Rijksintituut voor Volksgezondheid en Milieuhygiene (Netherlands)

If basic information about the chemical constituents or toxicity of a substance is sought, it may be worthwhile referring to Material Safety Data Sheets (MSDS). These can be obtained from the manufacturer, supplier or seller of the particular substance of interest. Toxicity data found in MSDS generally relates to acute effects and can be useful in emergency situations. Poison Control Centers can also be a good source of basic clinical information for early treatment of acute poisonings.

Existing information

In addition to the information sources discussed above, it is possible to obtain existing data that may be used to plan or conduct an epidemiological study. A substantial amount of data on environmental exposures and health outcome occurrence is collected on a routine basis. Most countries have some system for recording and processing mortality data (WHO/CEC, 1989). A wide range of routine morbidity statistics, such as rates of congenital abnormalities and infectious diseases, is also available in many countries. Also in many countries, it is possible to examine rates of cancer incidence, rather than just mortality, by using case registries which carry out ongoing population—based cancer reporting surveillance. Several European countries maintain national record linkage systems that are particularly useful for epidemiological analysis using existing demographic and health outcome records. Additional information may be obtainable from periodic population surveys, such as the National Health and Nutrition Survey conducted in the United States. Many of these global and regional statistics are compiled by the WHO.

There are comparatively fewer sources of environmental exposure data and the quality of much of it is not adequate for epidemiological studies. Nevertheless, these data may be useful in deciding whether an epidemiological study should be done and in planning for new environmental monitoring data collection. Examples of environmental monitoring data include lists of industries containing estimates of the levels of pollutants discharged by geographic area; public health monitoring of water or commercial food products; and data collected during legally mandated monitoring of lead, pesticides, or other toxic substances in air or water. The Global Environmental Monitoring System, sponsored by the WHO, collects information on air, water and food monitoring.

Investigators typically examine existing data to decide whether to proceed with an epidemiological study. On the other hand, existing data are sometimes used as the basis for a study. Several examples are provided in Chapter 6 – e.g., investigators who used data from the National Health and Nutrition Examination Survey conducted in the US to examine hypothesized associations for children between blood lead concentration and stature (Schwartz et al., 1986) and between air pollution and lung function (Schwartz, 1989); and the investigation of the association between arsenic and cancer mortality that was conducted in the endemic area of Blackfoot Disease in Taiwan is an example of an ecological study (Chen & Wang, 1990).

Libraries

A large number of libraries participate in the Global Environmental Library Network (GELNET). They serve as repositories of WHO environmental health publications and are accessible to the public during regular working hours. Information on GELNET can be obtained from the Office of Global and Integrated Environmental Health, World Health Organization, 1211 Geneva 27, Switzerland.

National and international organizations

A vast amount of information on prior studies and data on potential environmental health hazards is available through regional, national, and international organizations. It is becoming more and more feasible even for persons in relatively remote locations to access this information electronically via telephone and the Internet.

Databases containing information that could be useful in an environmental epidemiology investigation are maintained by numerous international organizations including ILO, UNEP, UNESCO, WHO and the World Bank. For example, ILO operates the International Occupational Safety and Health Hazard Alert System, which is able to disseminate information on newly—discovered or suspected occupational health hazards rapidly. The Hazard Alert System is linked with the International Register of Potentially Toxic Chemical (IRPTC) of the United Nations Environment Programme. Additionally, the ILO's International Occupational Safety and Health Information Center (CIS) maintains a database on literature published since 1974. In the US, the National Institute of Occupational Safety and Health maintains the Registry of Toxic Effects of Chemical Substances (RTECS) which contains toxicity data on more than 30,000 substances.

The International Commission on Occupational Health (ICOH) publishes the *International Directory of Databases and Data Banks in Occupational Health*. The directory includes 170 databases on a variety of topics and can be obtained from ICOH at 10 Avenue Jules-Crosnier, CH-1206, Geneva, Switzerland.

Literature searches

In the United States, the National Library of Medicine maintains more than 30 biomedical databases. *Medlars* (Medical literature analysis and retrieval system) or *MEDLINE* (Medlars on-line), is the best known of these databases, and contains over 20 years of bibliographic data from over 3600 major medical journals that are routinely abstracted. The database now contains more than 7 million references, and 8000 new entries are made each week. Medline can be accessed "on-line" through libraries or agencies. A CD-ROM version of Medline is also available on subscription. It is updated and mailed monthly. (CD-ROM stands for "compact disc read-only memory".) In many countries, it is now possible to access the Medline database through the Internet.

Toxline is a toxicology database containing more than 800,000 references to human and animal toxicity studies, including the health effects of environmental chemicals. Other useful databases include: the *Hazardous Substances Data Bank* (HSDB), the *Environmental Teratology Information Center* (ETIC), the *Chemical Carcinogenesis Research Information System* (CCRIS), *Chemical Dictionary on Line* (CHEMLINE) and *Cancer Literature* (CANCERLIT).

Electronic access: Internet

The Internet is a "network of networks" that reaches millions of people worldwide. Originally connecting educational, research and non-commercial institutions, it now spans nearly all sectors of society, including industry, hospitals, non-profit organizations and private individuals.

Electronic mail (E-MAIL) and bulletin boards are the most common uses of the Internet. An electronic bulletin board can be a very efficient means of communicating information to numerous individuals. A user (often called a subscriber) can post messages that can be viewed by other subscribers according to author, subject or other classification.

Other projects currently being planned or considered for the Internet include:

- a Global Health Network for connecting public health workers;
- an Internet School of Public Health for public health training;
- an on-line environmental epidemiology journal for rapid dissemination of epidemiological information.

Additionally, the US Public Health Information and Surveillance System plans to provide information regarding health outcomes (e.g. vital statistics), risk factors (e.g. survey data) and surveillance data for specific diseases. This system will build on the current Wonder/PC (Wide-ranging Online Data for Epidemiologic Research) communication and information system, to enable the US Centers for Communicable Diseases, and public health practitioners, to link up with one another by using a computer, modem and toll-free telephone number.

Access to electronic communications requires a computer, modem and communications link. The communications link may be a direct connection to access the Internet or a telephone connection that provides remote access. Access is generally obtained via universities, research facilities, governmental agencies or private telecommunications services. Private "Internet service providers" (ISP) can provide access to the Internet through a connection called a "gateway". The charges for access through private providers may be based on the type of access and the amount of connection time accumulated each month.

The amount of information available through the Internet has grown explosively during the past few years. At the same time, it has become much easier to gain access to the Internet.

The software needed to access the Internet information (known as "browsers") are available for free as a component of most personal computers operating systems or can be downloaded and distributed at no cost by someone who already has access to the software. Once on the Internet, various programs known as "search engines" are readily available to assist the user in locating the desired information.

12.3 Teaching environmental epidemiology

"A good teaching programme is one that is geared to its student's needs, capacity, interests, preferences and exploits the capacity of various teaching situations and techniques to provide learning opportunities that will achieve the educational objective" (Abramson, 1992).

A separate Teacher's Guide for Environmental Epidemiology will be published as a comparison volume to this text. The following provides a summary of ideas and suggestions for the prospective teacher.

In common with other disciples, there are no firm rules that guarantee effective epidemiology teaching. Each teaching situation presents a unique set of challenges, linked to factors such as the level of interest and sophistication of the learners, their cultural attitudes and beliefs, the amount of teaching time available, and the capabilities and skills of the teacher (Weiner & Bower, 1982). Consider, for example, the wide range of knowledge and skills that might be

taught to meet the epidemiologist's needs as a researcher (designing, implementing, and analyzing studies), writer (e.g. grant writing), manager/administrator (e.g. of an epidemiological investigation), communicator (e.g. to fellow professionals, community groups, students or on the evening news) and decision-maker. Consider too the depth of understanding that might be attainable during a full one-year graduate degree programme for researchers, as compared to during a one-week introductory course for field workers.

Epidemiology has traditionally been taught to a highly specialized group of professional students in schools of medicine and public health. More recently, however, a broad range of students, ranging from liberal arts undergraduates to engineers have been successfully taught how to undertake basic epidemiology (Fraser, 1987). For example, one—week basic environmental epidemiology workshops have been organized through the World Health Organization's Global Environmental Epidemiology Network (GEENET) in more than 25 countries since 1988 (WHO, 1994a). Typical participants in these workshops have included:

- public health and medical officers (at the national or provincial level);
- environmental protection officers or policy makers;
- researchers in environmental health engaged in field studies;
- teachers of public health, environmental health or epidemiology.

Empowerment education

"Adults retain information best when they are actively involved in problem-solving exercises and hands-on learning. They remember 20% of what they hear, 40% of what they hear and see, and 80% of what they see, hear and do" (WHO - Approaches to university curricula in environmental health)

Adult education experts report that adults retain information best when they are actively involved in problem-solving exercises and hands-on learning. Education is less effective when people passively receive information, as through lectures for example. Wallerstein & Weinger (1992) suggest using participatory or interactive methods to foster empowerment skills which include critical thinking and social action skills.

Wallerstein (1993) notes that "empowerment education" aims to involve people in group efforts to identify their own problems, to critically analyze the cultural and socioeconomic roots of the problems, and to develop strategies to effect positive changes to resolve them. This approach also emphasizes the importance of team work by encouraging social contact in class through working in small groups. In addition, considerable attention is paid to two-way dialogue to provide reinforcement and to generate feedback. Ideally, students and teachers become "co-learners", sharing ideas and working together to produce solutions.

What makes a great teacher?

Most of us can recall particular teachers who excelled in their ability to provide a rewarding educational experience. Among their particular qualities, it is more than likely that they had a better-than-average command of the subject matter they taught. However, technical competence

as a research worker or a practitioner does not by itself guarantee excellence in teaching (Lowe & Kostrzewski, 1973). Most teachers of environmental epidemiology, indeed, probably the vast majority of teachers of health science students, have received little instruction in how to develop and teach a successful course. Most teachers learn by doing. In the long term, this may lead to an exciting and well-received course, but in the short term, teachers and students alike will probably be frustrated and disappointed.

Rotem & Abbatt (1982) note that teaching involves a set of skills that can be developed and improved. These skills include:

- Planning and organizing a course to decide what and how students should learn, and subsequently to evaluate whether the teaching has been successful.
- Communicating by a variety of methods including telling, explaining, advising, listening, demonstrating or by using audio/video presentations, role play or other interactive techniques.
- Providing opportunities and/or resources for enriching the learning experience such as field trips, books, journals, access to local experts and computers and software.

Planning and implementing training

The following aspects should be considered when planning and organizing an epidemiology course or workshop.

Know your audience

It is crucial to know the number, interests and current level of knowledge of the participants. Obviously the needs of undergraduates will differ vastly from those of graduates. Similarly, the needs of health professionals will differ from those trained in other disciplines. And even among health professionals, teaching requirements will vary markedly depending on whether those taught comprise mainly nurses, medical students, researchers, or students of public health administration or policy.

Ideally, participants should share a similar level of knowledge of epidemiology and environmental health principles. This helps to avoid a situation whereby newcomers are quickly lost or those with previous training become bored. Potential participants can be required to provide evidence of successful completion of previous training or of a specified level of epidemiological knowledge or skills. Alternatively, a qualifying or entrance test can be devised to screen applicants.

The number of participants should be limited, otherwise personal interaction between participants and teachers will not be possible. Moreover, if a group is too large there will not be sufficient time to respond to participants' questions. However, the group must be large enough for team learning. Thus the number of participants for a GEENET one—week basic environmental epidemiology workshop is generally between 20 and 30 participants.

The following information can be collected by a questionnaire:

- demographics;
- current job;
- background and experience;
- language skills;
- expectations;
- interests and concerns.

Information regarding local concerns can also be sought by interviewing local epidemiologists or by reviewing relevant research studies or reading the reports of previous teachers or experts.

Determine what students should learn

Determining what students should learn requires formulating training objectives for the proposed course and for each teaching session. Various types of objectives to be considered include:

Knowledge of epidemiological principles or methods. This might include the types of study designs, health effects of specific environmental exposures, analytic methods. The breadth and depth of knowledge to be gained must also be determined.

Behavioural skills such as the ability to practice or teach epidemiology. This could include the ability to critically evaluate the literature, develop a questionnaire, perform a risk assessment, use EPI-INFO, and design a study.

Developing sufficient expertise to be able to form an ad hoc committee to undertake studies, or, for example, to secure the participation of community representatives in the risk assessment or evaluation of a cancer cluster.

Determining teaching or training objectives will depend on a variety of factors including the stated or assessed needs, the participants' level of knowledge, the time available and the ability of the teachers.

Develop the curriculum

Developing a curriculum includes determining its content and selecting teaching methods. Specific learning objectives should be developed for each course and for each session. A timetable should be devised to schedule topics and teaching methods. Consideration should be given to the amount of time needed to cover each topic and the potential benefit of employing a variety of teaching methods. Each session should be outlined to determine the material to be covered. A sample timetable and curriculum for a one—week environmental epidemiology workshop can be found in WHO, 1994a. Olsen and Trichopoulos (1992) have also described methods for teaching a broad range of epidemiology topics.

It should be recognized that no single curriculum can meet the needs of all students. The keys to success are flexibility and relevance. Ideally, a curriculum can be modified as required and focused on topics and examples of interest to the participants.

Deliver the course

A variety of teaching methods are suggested. The goal is to maintain the participants' interest and involvement, encouraging them to take an active role. This can be accomplished by employing a variety of interactive techniques noted below (see Wallerstein & Rubenstein (1992) and Wallerstein & Weinger (1992)).

Lectures are the most common method of teaching. Lectures can be used to convey a basic body of knowledge. However, they are a one-way form of communication and should therefore be combined with participatory exercises, if possible. Because listener concentration does not usually extend beyond a period of 10-15 minutes, lectures should be brief. Lectures should include examples, make use of audiovisual aids and encourage questions from participants.

Small group activities can be used to encourage students to draw on their own experiences and to apply new information to answer questions. "Triggers" or "discussion starters" can be used to provoke critical thinking, stimulate participation, overcome anxiety and foster group interaction. For example, in buzz groups participants are paired and asked to compile a list of ideas on an issue. Similarly, in a brain storm, the whole group is asked to come up with as many ideas as possible on a given issue.

A worksheet questionnaire is a means of introducing a lecture through a series of questions that cover the lecture's main points. Students are asked to complete the answers by themselves or in pairs before the lecture (and to make calculated guesses if they have no or little idea as to the answers). The lecturer can then ask for answers, which can be used as the basis of discussion, thus fostering the group's interaction.

Problem-solving exercises and simulations can be used to practice the use of various skills (formulation of questions, collection of information, application of new knowledge). For example, participants can be given a problem (to be completed within a certain time) that requires them to track down information in the library, contact the appropriate agency or use computer tools. (A set of problem-based training exercises for environmental epidemiology is available from WHO (WHO, 1992b; Markowitz, 1998).

Case studies can be used to promote group learning. For example, small groups of participants are each presented with a case study and asked to analyze it. The findings of each small group should be reported to the whole group during **report-back** sessions. These sessions provide a means for each small group to share information with the whole group. The individual groups can be asked to 'defend' their conclusions (Wallerstein & Rubenstein, 1992).

In **role-play**, a problem situation is acted out rather than simply described. Role play encourages participants to apply their knowledge and to develop their communication skills.

Computer exercises can be used to introduce software tools. For example, EPI-INFO is a public domain software package that can be used for word processing, data entry, statistical calculations, and more complex epidemiological analysis (Dean et al., 1990). Tutorials are included in the package and learning modules are available as noted below.

Participants can be taken on a brief field project or field trip to witness the application of epidemiological methods (e.g. conduct of a survey) or particular environmental or occupational

conditions. For example, a visit to a local factory could include a walk-through survey, a meeting with the factory's medical and industrial hygiene staff, and discussions with workers and management. Following the trip a discussion (perhaps a panel discussion) can be held to discuss the adequacy of the factory's health and safety programmes.

There is some indication that self-taught epidemiology packages are better received, than lectures or seminars (Gehlbach et al., 1985). These packages allow individuals to set their own pace of learning, to focus on topics of interest, and to study where and when they choose. Self-taught packages either consist of written modules, or are computer-based. For example, the US Centers for Disease Control has used written modules on epidemiology for field workers, but has also developed a computer-based module to demonstrate an approach to outbreak investigations ("Pharyngitis in Louisiana"). Other modules are being developed. Self-taught introductory computer modules for EPI-INFO have been developed by WHO and the London School of Hygiene (Huttly & Sterne, 1993; Corvalán et al, 1996). EPITROP, a computer—assisted course in epidemiology and biostatistics, is intended to serve as a refresher course for students who have already completed epidemiology courses but who may have forgotten much of what they learned (Liefooghe, De Muynck & Van der Stuyft, 1993). In addition, both audio- and video-taped instruction have been used to enhance teaching programmes and provide continuing education.

Other extramural or distance learning methods have also proved successful (Ostbye, 1989). Communication connections have been used to establish telephone and computer conferencing as well as satellite television links.

Evaluation and follow-up

The purpose of evaluating training is to determine the extent to which the training objectives have been met. Feedback is elicited from participants to evaluate the process, content and effectiveness of the training.

For example, student feedback can be obtained on:

- the extent to which workshop objectives or personal expectations were met;
- whether presentations were useful or interesting;
- the appropriateness of training materials with respect to language, content, level and length;
- the organization and administrative aspects of the workshop (e.g. were books distributed sufficiently in advance, was the meeting room adequate, was enough time allowed for breaks and questions).

An evaluation of the knowledge and skills acquired by participants can be carried out by examination. GEENET workshops, for example, use pre- and post-test evaluations to determine the participants' ability to explain 20 environmental epidemiology and environmental health concepts (WHO, 1994a). An evaluation questionnaire was developed with EPI-INFO software and the replies can be entered into a data file on the final day of the workshop as a way of demonstrating the software's utility. The results can be used in a group evaluation session, as a basis for discussing the strengths and weaknesses of the workshop, and for proposing possible modifications for future workshops.

It is difficult to determine how best to evaluate the long-term effectiveness of training. Follow-up evaluations can be undertaken to determine whether participants applied their new knowledge and skills in their work (for example, by implementing new studies) or were motivated to seek more advanced training.

Knowledge and skills are quickly lost if not used. An effort should be made to encourage the application of skills. Follow-up in terms of workshops or via periodic contact (mail, phone, e-mail) can help to sustain the level of interest and skills.

Practical advice

Experienced teachers of the GEENET workshops contributed a wealth of practical advice to the *Teacher's guide for one-week training workshop: basic environmental epidemiology* (WHO, 1994a).

It is stressed that teachers should:

- know their audience;
- make advance preparations regarding space, time, logistics;
- distribute books and materials in advance;
- provide feedback let the students know how they are doing;
- encourage students to ask questions;
- be enthusiastic and avoid speaking in a monotonous voice;
- change the pace of speaking, but without speak too quickly or slowly;
- be entertaining through use stories and examples;
- use a variety of teaching methods and presenters;
- allow sufficient time for questions;
- be inspirational, taking into account the qualities of a role model
- determine the need for translators
- pay attention to presentation skills.

Overhead transparencies, slides and flip charts are visual triggers that can help to focus the audience's attention, stimulate interest in the topic being discussed and illustrate factors that are hard to visualize. Overhead transparencies can be overlaid to add or dissect components of complicated graphics. (Note that a set of tables and graphs suitable for making overhead transparencies is included in *Teacher's guide — 2nd edition — for basic epidemiology* (WHO, 1994a). Each visual should present one key point only, should be big enough to see or read easily and should contain no more than approximately 36 words (or six lines). If visual aids are used, care should be taken to talk to the audience, not to the visual aids.

Conclusion

The uninitiated, reluctant or inexperienced teacher of epidemiology is encouraged to expand his/her horizons beyond the research environment. Few epidemiologists are born excellent teachers. Teaching skills can be developed, however, if one is willing to commit time, effort and practice.

Adopting an empowerment approach to epidemiology teaching will ensure that public health problems are addressed not only as research questions but also as social problems that may require social remedies. This the teacher will gain satisfaction from the fact that he or she is contributing to the process whereby unanswered environmental epidemiology research questions of today will be appropriately addressed both in the laboratory and in the community by the next generation of well—trained epidemiologists.

12.4 Future directions of environmental epidemiology

Environmental epidemiology will continue to be driven by new analytic tools, newly-emerging hazards and the public's perception of the risks posed by environmental hazards. The Earth Summit in Rio de Janeiro in 1992 identified a number of planetary environmental concerns that will, in time, be the subject of additional epidemiological investigations. These concerns include air pollution, depletion of tropospheric ozone, contamination of drinking—water supplies, dumping of hazardous waste, electromagnetic radiation, and agricultural practices that have adverse environmental effects. The environmental epidemiologist will be called upon increasingly to assess the impacts of combined environmental exposures. Advances in how such investigations are conducted will require development of more rigorous epidemiological tools and more sophisticated reliance on statistical models. Moreover, further investigation of the more subtle and "non-cancer" health endpoints, such as learning deficits, is needed. To date, these types of endpoints have mostly lain outside the mainstream of epidemiological investigation. In particular, epidemiologists face the challenge of identifying early indicators of disease (Cohen & Gordis, 1993).

Planetary overload — potentially arising from population growth and ecological degradation — could threaten the very life—support systems that sustain the global environment (McMichael, 1993). In addition, the introduction of new technology and the increasing use of potentially hazardous technologies, such as agrochemical production, create conflict between desired technological or economic development, and the preservation of environmental quality. This may be particularly so in developing countries where well—established methods of environmental hazards control may not be applied because of awareness of the hazards themselves may be very limited.

Annex 12.1: Books and journals in environmental epidemiology

Environmental epidemiology books

Topics in environmental epidemiology.

Steenland K & Savitz D (1997) New York: Oxford University Press.

Environmental epidemiology.

Kopfler FC & Craun GF, ed. (1986) Chelsea, Michigan: Lewis Publishers.

Introduction to environmental epidemiology.

Talbott E & Graun G (1995) Boca Raton: Lewis Publishers.

Environmental epidemiology.

Leaverton PE, Mass TL & Simches SO (1982) New York: Praeger.

Environmental epidemiology and risk assessment.

Aldrich T & Griffith J (1993) New York: Van Nostrand Reinhold.

Environmental epidemiology: epidemiologic investigation of community environmental health problems.

Goldsmith JR, ed. (1986) Boca Raton, Florida: CRC Press.

Environmental epidemiology. Volume 1: public health and hazardous wastes.

Committee on Environmental Epidemiology, Board on Environmental Studies and Toxicology, Commission on Life Science, National Research Council (1991) Washington, DC: National Academy Press.

Environmental epidemiology: exposure and disease.

Bertollini R et al., ed. (1996) Boca Raton: CRC Press/Lewis Publishers.

Occupational/environmental health books

Chemical hazards of the workplace, 4th edition.

Proctor NH & Hughes JP (1996) New York: Van Nostrand Reinhold.

Encyclopaedia of occupational health and safety, 4th edition.

Stellman JM, ed. (1998) Geneva: International Labour Office.

Environmental and occupational medicine, 3rd edition.

Rom WN (1998) Philadelphia: Lippincott-Raven Publishers.

A practical approach to occupational and environmental medicine, 2nd edition.

McCunney RJ (1996) Boston: Little, Brown and Company.

Occupational and environmental medicine, 2nd edition.

LaDou J (1997) Stamford: Appleton & Lange.

Textbook of clinical occupational and environmental medicine. Rosenstock L & Cullen M, ed. (1994) Philadelphia: Saunders.

Principles and practice of environmental medicine. Tarcher AB (1992) New York: Plenum Medical Books.

Toxicology books

Casarett and Doull's toxicology: the basic science of poisons, 5th edition. Klaassen CD, Amdur MO & Doull J, ed. (1996) New York: McGraw-Hill.

Hamilton and Hardy's industrial toxicology, 4th edition. Finkel AJ (1983) Boston: Wright PSG, Inc.

WHO Environmental health criteria series.

Now consists of more than 150 publications regarding the toxicity of various agents. Geneva: International Programme on Chemical Safety (IPCS).

WHO *IARC monographs on the evaluation of carcinogenic risks to humans*, Now consists of more than 70 publications on the carcinogenicity of various agents. Lyon: IARC (International Agency for Research on Cancer).

Relevant journals

American journal of epidemiology
American journal of industrial medicine
American journal of public health
Archives of environmental health
British journal of industrial medicine
Environmental health perspectives
Journal of exposure analysis and environmental epidemiology
Journal of occupational medicine and environmental medicine
International journal of epidemiology
Scandinavian journal of work, environment and health
WHO bulletin



Key Terms

Chapter 1

- Environmental epidemiology the study of the distribution of health-related states or events in specified populations in relation to determinants/hazards in the living environment of these populations, and the application of this study to the control of such hazards.
- **Effect** any change in health status or body function that can be shown to be due to exposure to an environmental hazard.
- Effect measure epidemiological variables that describe changes in population experience.
- **Exposure** the concentration of an agent in the environment that comes into contact with the external portion of the human body.
- Hazard a qualitative term expressing the potential that an environmental agent can harm health.
- **Risk** a quantitative probability that a health effect will occur after a specified exposure to a hazard.
- Sustainable development development that meets the needs of the present without compromising the ability of future generations to meet their own needs.

- **Biological marker (biomarker)** any measurable biochemical, physiological, or other biological parameter obtainable from human tissue, fluids, or expired gases, that is associated with exposure to an environmental pollutant.
- **Cluster** a spatial and temporal pattern of a health effect incidence or prevalence that is higher than would be expected in the population.
- **Dose** the amount of an environmental agent that enters the body.
- **Dose-response** relationship (generally drawn as a curve) between increasing dose and risk of health effect in the exposed population.
- **Exposure** the concentration of an agent in the environment that comes into contact with the external portion of the human body.
- Hazard a qualitative term expressing the potential that an environmental agent can harm health.
- **Informed consent** duty to inform each potential participant in a study of the possible benefits and harms of participating in the study.
- Latency time interval between onset of disease process and the clinical manifestation of the disease in epidemiology, generally measured as the time interval between onset of exposure and the development of clinical disease.
- **Risk** a quantitative probability that a health effect will occur after a specified exposure to a hazard.
- **Risk assessment -** quantitative process of estimating (present or future) risk in a population using information derived from animal, experimental, or other population studies.

- Target organ dose the amount of an agent that reaches the susceptible organ or tissue within the body.
- Utilitarianism ethical theory that an action should be based upon the principle of securing the greatest amount of good for the greatest number of people.

- **Blind** measurement taken when either the study subject or the study staff is unaware of the exposure or disease classification of the person being studied.
- Confounder an independent risk factor for disease occurrence that is distributed differently among exposed and non-exposed, and which produces a bias in the exposure-disease effect estimate if it is not controlled.
- Cumulative incidence synonym for incidence proportion.
- **Disease frequency** quantification of the occurrence of disease involving a count of the affected individuals.
- **Double-blind** measurement taken when both the study subject and the study staff are unaware of the exposure or disease classification of the person being studied.
- Effect estimate the estimate of the effect of a factor on the occurrence of disease or injury, e.g. the risk ratio, rate ratio, or odds ratio.
- **Effect modification** modification of the estimate of effect of one risk factor by exposure to another risk factor.
- Incidence proportion the proportion of a defined population which develops the disease under study during some specified time interval.
- Odds the ratio of the number of people in a group who have experienced an event to the number in the same group who have not experienced the event.
- Odds ratio the ratio of two odds.
- **Population at risk** that part of a population which is "at risk" of a disease; this is usually the entire source population, excluding those who already have the disease.
- **Precision** the stability of an effect estimate, as reflected in the width of its confidence interval.
- **Prevalence** the proportion of a defined population that have the disease under study at a specified time.
- Rate number of newly-occurring cases of disease divided by the person-time of observation.
- Rate difference difference in disease rates between two groups.
- Rate ratio ratio of disease rates in two groups.
- Relative risk a general term to denote the rate ratio, risk ratio, or odds ratio.
- Risk the probability of developing the disease under study during some specified time interval. Risk is measured in a population using the incidence proportion (cumulative incidence).
- Risk difference difference in average (disease) risk between two groups.

- Risk ratio ratio of average disease risk between two groups, i.e. ratio of two risks.
- **Source population** the specific population at risk, from which the study population is sampled.
- **Study population** the population that is being studied after sampling from the source population. The study population is synonymous with the source population in a cohort study. The study population is a sample of cases and non-cases from the source population in a case-control study.

- **Additive exposure** a combined exposure to more than one hazard which may cause an effect greater than that due to either hazard alone.
- **Ambient air pollution** the general outdoor air pollution.
- **Biologically effective dose** the dose at the target organ that is directly related to the biological effect of an absorbed hazard.
- **Biological marker** (biomarker) any measurable biochemical, physiological, or other biological parameter obtainable from human tissue, fluids, or expired gases, that is associated with exposure to an environmental pollutant.
- **Combined exposure** exposure to more than one environmental hazard that cause a particular health effect.
- **Contaminants (pollutants)** any potentially harmful environmental agent, generally referring to a chemical, physical or biological agent.
- **Detection limit** the minimum amount (concentration) of an environmental hazard that can be reliably detected using a specific measuring instrument.
- **Deterministic model** a model describing the relationship between (exposure) variables based on knowledge of the physical, chemical and/or biological mechanisms governing these relationships.
- **Dose** the amount of an environmental agent that enters the body.
- **Duplicate diet study** study in which exact duplicates of all foods and beverages consumed by subjects are collected and analysed for contaminants.
- **Emission** the release of an environmental hazard (pollutant) from a source into the environment.
- Environmental media the media through which environmental hazards may be transmitted, such as air, water, food or soil.
- **Exposure** the concentration of an agent in the environment that comes into contact with the external portion of the human body.
- External exposure same as exposure, generally used to refer to presence of a radionuclide (chemical that emits ionizing radiation) in media outside of the body.
- **Hybrid model** a model describing the relationship between variables using a combination of the deterministic model and stochastic model approaches.

- Indoor air pollution presence of potentially toxic contaminants to air within buildings or homes.
- Integrated exposure model a model to estimate total exposure to a contaminant by combining time-activity pattern variables and microenvironment measurement data.
- Internal exposure (term used for ionizing radiation) for the concentration of a radionuclide that has entered the body (lungs or intestines) through inhalation or ingestion, but has not been absorbed into the body.
- **Internal dose** the quantity of an environmental substance that is actually absorbed across the lining of the lungs or gastrointestinal tract.
- **Macro-environment** the overall environment in a community, region or nation.
- Market basket study study in which food samples of the principal diet constituents, based on community or national consumption data, are prepared and analysed for contaminants and possibly nutritional value.
- **Micro-environment** the environment at a specific place and time through which a person may be exposed to an environmental hazard.
- Outdoor air pollution presence of potentially toxic contaminants in the outdoor air.
- **Personal exposure measurement** quantitative individual measurement of an environmental exposure.
- Stochastic model a model expressing the statistical relationship between a determinant of exposure, and exposure itself, inferred from data collected in similar situations.
- Surrogate variable a variable that correlates with a contaminant concentration and may be used as an alternative to estimate exposure to the contaminant.
- **Time-activity pattern** a record of a person's activities and location recorded by time periods.
- **Total exposure (integrated exposure)** the sum of all exposure to an environmental hazard via multiple exposure pathways and in different spatial and temporal patterns.
- **Toxico-kinetic (pharmaco-kinetic)** a model of the movement and biotransformation of an model absorbed hazard within the body, including factors such as absorption, metabolism, distribution, storage, and excretion.

- Acute health effects health effects occurring in a time frame within minutes to days following an exposure.
- Case definition a set of criteria for deciding whether an individual should be classified as having the condition of interest.
- Chronic diseases diseases with non-repairable tissue damage which are compatible with a health compromised life.
- Coefficient of variation (percentage standard deviation) a measure of the variation in a continuous variable equal to the standard deviation divided by the mean value.

- **Dose–response** the relationship between dose of a toxic agent and the proportion of persons exposed at the dose who develop a specific health outcome.
- **Hyperreactive**—sensitive individuals who develop the same effect as expected in other persons, but the effect is quantitatively increased, or the effect occurs at a lower dose than in the majority of the population.
- Hypersensitive persons who develop an allergic reaction to a certain substance (allergen).
- **Incubation** the period of time between exposure and the manifestation of disease; in epidemiological studies, the same as the incubation period and latency; generally used to refer to infectious diseases.
- **Induction** the period of time between the causal exposure and the initiation of disease; in epidemiological studies, the same as the incubation period and latency.
- **Latency** the period of time between disease initiation and the manifestation of disease, generally used to refer to chronic diseases.
- Primary data data collected specifically for a study or investigation.
- Reportable disease (notifiable disease) a condition or disease that must be reported to a public health or governmental authority, which may vary from jurisdiction to jurisdiction.
- Secondary data data which was collected for other purposes (e.g., clinical or regulatory), but is used for a study or investigation.
- **Sub-clinical toxicity** physiological or pathological effect that does not manifest as clinical disease.
- Susceptibility at higher risk than the general population of developing a health outcome following an exposure, often due to a genetic predisposition.
- **Toxicity** the capacity of an agent to produce injury in an organism at a minimum effect level.

- **Age-standardized** analytical adjustment when comparing two or more populations to account for differences in the population age structures.
- **Aggregate measures** variables that indicate population characteristics, such as average exposure to an environmental hazard, rather than individual characteristic.
- **Case-cohort sampling** sampling of controls in a case-control study from the source population at the beginning of the risk period.
- Case-control (case-reference) study epidemiological study in which cases who have developed the health outcome under study and non-cases are sampled from the risk period (person-time experience) of a source population.
- **Census sampling** random sampling of the source population without regard to exposure or health outcome status.

- Cohort study epidemiological study in which individuals at risk of developing the health outcome under study are sampled from the source population and followed over time (the study period) to measure the health outcome occurrence.
- Community trial experimental study in which communities or similar population groups are allocated to treatment (exposure) and control groups.
- Comparison group (reference group) the group to which the treated, exposed or case group is to be compared generally, a nonexposed group in a cohort or cross-sectional study. In a case-control study, the comparison group is generally referred to as the control or referent group.
- Cumulative sampling sampling of controls in a case-control study from the source population at the end of the risk period.
- **Density sampling** sampling of controls in a case-control study from the source population concurrent with case incidents during the risk period.
- Ecological bias bias in which the group-level associations do not accurately reflect individual-level associations.
- Experimental study a study in which the investigators determine who will be exposed or treated.
- External comparison group a comparison group selected from a broader source population than that which yielded the exposed study population in a cohort study.
- Hospital-based cases (and controls) use of hospital patients or medical records as the sampling frame to select subjects for a case-control study.
- **Historical (retrospective) studies** timing of a study in which the study data are collected after the events (exposure and health outcomes) have occurred.
- Internal comparison group a comparison group selected from the same source population as that which yielded the exposed study population in a cohort study.
- **Panel study** cohort study in which the temporal association between a variable exposure and a variable health outcome is observed over time.
- **Period of observation (follow-up) (study period)**—the time during which the study population in a cohort study is kept under observation.
- Period prevalence the number of existing (prevalent) cases during a defined interval of time (equal to the prevalent cases at the beginning of the interval plus the incident cases during the interval).
- Point prevalence the number of existing (prevalent) cases during a defined point in time.
- **Population-based cases** use of an entire population (generally in a defined geographical region) as the sampling frame for cases in a case-control study.
- Proportionate mortality (morbidity) study epidemiological study in which the distribution of health outcomes (or exposures) is compared to the distribution of those same outcomes (or exposures) in another population without obtaining information on the characteristics of the source population.

- **Prospective studies** timing of a study in which the study data are collected as the events (exposure and health outcomes) are occurring.
- Randomized controlled trials experimental study in which the subjects (or groups) are randomly assigned to the treatment and comparison groups.
- Survey sampling see census sampling.
- **Time-series study** ecological (group) or cohort (individual) study in which the temporal association between a time-varying exposure and time-varying health outcome are observed over time.
- Unit of analysis observation unit at which exposure and health outcome are measured and analysed generally either group (ecological study) or individual (e.g. cohort, case-control or cross-sectional study).

Chapter 7

- Categorical data nominal or ordinal variables.
- **Confidence interval** a range of values for the effect estimate within which the true effect is thought to lie, with the specified level of confidence.
- **Confounder** a risk factor for disease that produces a bias in the effect estimate of an exposure if it is not controlled.
- **Discrete distribution** a distribution that can have specific (non-continuous) values.
- Effect modifier a factor that modifies the effect of a risk factor.
- **Effect modification** this occurs when the effect estimate is modified by the level of another risk factor.
- **Effect estimate** the estimate of the effect of a factor on disease, e.g. the risk ratio, rate ratio, or odds ratio.
- Exposure odds ratio ratio of the odds of exposure in one group (generally those with a health outcome) to those in another group (generally those without the health outcome).
- **Exposure-response curve (dose-response curve)** a visual graph showing a measure of health outcome occurrence (e.g. disease rate) according to different levels of exposure.
- Incidence odds ratio ratio of the odds of developing a health outcome in one group (generally the exposed) to the odds of developing the health outcome in another group (generally the non-exposed).
- **Logistic regression** a mathematical model in which the log odds is modeled as a linear combination of a set of risk factors; used in analysis of case-control studies.
- Measure of variability an estimate of the amount of variation in a measurement, due to chance alone, if the measurement is repeated many times.
- **Multicollinearity** instability of an effect estimate resulting from a strong correlation between one or more variables.

- **Poisson regression** a mathematical model in which the log of the incidence rate is modeled as a linear combination of a set of risk factors; used in analysis of cohort studies.
- **Precision** the stability of an effect estimate, as reflected in the width of its confidence interval.
- Standard error the estimate of the standard deviation of the mean; calculated as the standard deviation divided by the square root of the number of data points.

Standard deviation – a measure of the variability of the data.

Chapter 8

- **Data cleaning** procedures to ensure that study variables have been correctly recorded and entered into a computer data base.
- **Feasibility assessment** process to evaluate whether it is feasible to undertake a proposed study considering the availability of the study population and study logistics.
- **Human subjects protocol** a written protocol describing the participation of human subjects in the study, making clear the potential benefits and harm, and the procedures that will be used to safeguard the subjects' interests.
- **Informed consent** a written (although sometimes verbal) consent form used to convey information about the proposed study to each participant.
- Main study the collection study data, often requiring study personnel to work in the "field" or community.
- **Multi-centre study** study involving several populations and research centres collaborating on a common study protocol and pooling the data for analysis.
- **Pilot study** a small study undertaken using the full study methods to evaluate the feasibility and appropriateness of the proposed study.
- **Preparatory stage** initial stage of a study during which study methods are finalized, generally includes staff training, pretesting study instruments and planning field survey logistics.
- Protocol written document describing study methods, personnel, budget, and organization.
- Quality assurance the process of ensuring the accuracy and precision of study measurements and overall conduct of the study.
- **Timetable** graphical or table listing of study activities according to time of implementation during a study.

Chapter 9

Meta-analysis – quantitative analysis of the combined results of several individual studies on a related topic, undertaken in order to reach a summary interpretation.

Chapter 10

- Case definition a standard set of criteria for deciding whether an individual can be classified as at risk from the exposure of interest, or as having contracted the disease of interest.
- **Disease cluster** the occurrence of a disease (health outcome) by spatial and temporal pattern is higher than would normally be expected.
- **Environmental monitoring**—a systematic programme to measure environmental concentrations of agent(s) of concern, as well as related factors that may influence exposures.
- Exposure registry a system for collecting and maintaining information to document environmental exposure to specific hazardous substances for defined populations.
- **Public health assessment** a process to evaluate data and information on the release of hazardous substances into the environment in order to assess current or future public health impacts; develop health recommendations; and identify studies or actions needed to evaluate or prevent adverse human health effects.
- Public health surveillance ongoing, systematic collection, analysis and interpretation of health data essential to the planning, implementation, and evaluation of public health practice, closely integrated with the timely dissemination of these data.

Chapter 11

- Environmental Health Impact Assessment (EHIA) an analytical process to predict and assess the impacts of a development (proposed activity) on environmental health factors.
- Environmental equity (environmental justice) a goal to provide adequate protection from environmental hazards for all persons, regardless of age, ethnicity, gender, health status, social class, or race.
- **Hazard identification** process of determining whether an exposure to an environmental agent is associated with an adverse health effect.
- **Risk assessment** use of a factual base to characterize potential adverse effects of human exposure to environmental hazard.

Chapter 12

- **Empowerment education** education that aims to involve people in group efforts to identify their own problems, to critically analyse the cultural and socioeconomic roots of the problems, and to develop strategies to effect positive changes to resolve them.
- **GEENET** Global Environmental Epidemiology Network world-wide network of environmental epidemiologists coordinated by the World Health Organization.

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