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Exposure Assessment

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7.1. INTRODUCTION

'Exposure' is a substance or factor affecting human health, either adversely or beneficially. Exposure variables used in practice in epidemiology usually have to be regarded as approximations to the 'true' exposure of the subjects who are being studied. The accuracy and precision with which 'true' exposure is being approximated may vary widely from one 'surrogate' exposure variable to the next. Exposure misclassification and/or measurement error can lead to attenuation in health risk estimates and/or a loss of power. A simple example illustrates the potential effects of exposure misclassification and shows how important a good exposure assessment is. Let's assume a hypothetical example of a study with 2000 subjects, of whom 1000 are exposed to an environmental pollutant and the other 1000 are unexposed. In the exposed group, 200 have developed the disease, while only 100 have done so in the unexposed group (Table 7.1). The relative risk in this case is 2. However, the risk estimate would be only 1.5 if 20% of the subjects were misclassified (20% of the exposed become unexposed and vice versa; see numbers in brackets in Table 7.1). This example shows that even if the exposure misclassification is relatively minor (20%), the effect on the relative risk is considerable. Of course, this is a fairly simple example, and the effect of exposure misclassification/measurement error depends on other factors, including the type of error model (Classical or Berkson error; Nieuwenhuijzen, 2003).

7.2. INITIAL CONSIDERATIONS OF AN EXPOSURE ASSESSMENT STRATEGY

A major aim of epidemiological studies is to determine whether or not there is an association between a particular substance of interest, the exposure and morbidity and/or mortality. If there is an association, it is desirable to be able to show an exposure–response (or dose–response) relationship, i.e. a relationship in which the rate of disease increases when the level of exposure (or dose) increases. This will aid in the interpretation of such studies.

Over recent years there has been increasing interest in the field of exposure assessment causing it to develop rapidly. We know more than ever to what, where and how people are exposed and improvements have been made to methods for assessing the levels of exposure, its variability and the determinants. New methods have been developed or newly applied throughout this field, including analytical, measurement, modelling and statistical methods. This has led to a considerable improvement in exposure assessment in epidemiological studies, and therefore improvement in the epidemiological studies themselves.

In epidemiology, there are different study designs (e.g. cohort, case–control) to assess the association between exposure and disease (see Chapter 2). All the study designs require exposure estimates or exposure indices to be able to estimate the risk associated with the substance of interest, but they may differ depending on the study design. The design and interpretation of epidemiological...
studies is often dependent on the exposure assessment and therefore needs careful consideration. Quantification of the relation between exposure and adverse human health effects requires the use of exposure estimates that are accurate, precise, biologically relevant, apply to the critical exposure period and show a range of exposure levels in the population under study. Furthermore, there is generally also a need for the assessment of confounders, i.e. substances that are associated with both exposure and disease and may bias the study results. Assessment of confounders should be in similar detail to the assessment of exposure indices, since measurement error in confounders may also affect the health risk estimates (Nieuwenhuijsen 2003).

In epidemiology we often deal with large population sizes, with the population spread over large distances. This may make estimating exposure for the subjects in the study more difficult, for example in environmental epidemiological studies, since we cannot go out and visit each of the subjects. Therefore, one often relies on some form of modelling or surrogate of exposure (e.g. distance to a source). Small sample sizes, on the other hand, may allow for cruder exposure estimates, while smaller population sizes will require more refined exposure estimates to have similar statistical power. Armstrong (1996) has provided a general framework that can help individual researchers to decide which measures of exposure to include in their study in order to obtain maximum statistical power, and which validity and reliability substudies to include to assess the quality of the exposure assessment methods used in the full study.

The basic premise of Armstrong’s considerations is that it is better, but more expensive, to measure ‘true’ exposure than to measure ‘approximate’ exposure. When the correlation between the ‘approximate’ and the ‘true’ exposure variable is high, the loss of power by using the ‘approximate’ rather than the ‘true’ exposure variable is small. Therefore, if the cost per study subject of measuring ‘approximate’ exposure is clearly lower than the cost of measuring ‘true’ exposure, a study using the ‘approximate’ measure of exposure will be more efficient. Alternative study designs can be compared by calculating the so-called ‘asymptotic relative efficiency’ (ARE), defined as the ratio of the sample size necessary to achieve equal power to detect an association (Armstrong 1996). When \( r \) is the correlation between the ‘approximate’ and the ‘true’ exposure, \( C_i \) is the basic cost of including a subject in the study (e.g. related to assessment of disease status) and \( C_a \) and \( C_t \) are the cost of measuring ‘approximate’ and ‘true’ exposure, respectively, per study subject, then the ARE can be expressed as:

\[
ARE_{\text{opt}} = r^2 \left[ (C_t + C_i)/(C_a + C_t) \right]
\]

So, when the correlation between the ‘approximate’ and the ‘true’ exposure variable is equal to 0.5 \((r^2 = 0.25)\), then the use of the ‘approximate’ variable is more efficient than the use of the ‘true’ variable when the total cost of including subjects by measuring the ‘approximate’ variable is more than four times lower than the cost of including subjects in the study by measuring the ‘true’ exposure variable. Differences in cost of this or even a larger magnitude can easily occur when the choice is between doing personal exposure measurements on all subjects compared to collecting information on sources, habits and/or occupations by questionnaire, and when the ‘fixed’ cost of including study subjects \( C_i \) is not too high compared to the cost of making exposure measurements per se.

A decision to use ‘approximate’ exposure variables needs to be based on knowledge of the correlation between these variables and the ‘true’ exposure, and often, this information needs to be obtained in a pilot study preceding the full study. This adds to the cost of the total study, and Armstrong (1996) also provides guidance for the relative costs of exposure assessment during the main study.

Besides these considerations to be exposure a study are, and available particularl;e, many use routine subjects fation of res the subject or biom gek this case a of environ or little it may be in exposure, or difficult to often tendonal mor often not i for many informatic to rely on. A further individual approach, individual is the group app subpopul groups”, sure, and are obtain mental eq may be d absence or smoker exposed source (si as playin exposure. The unde each exp character:
The relative allocation of budget for pilot and the main study.

Besides sample size and costs, other considerations to be taken into account in designing a specific exposure assessment strategy for an epidemiological study are, for example, accessibility to the subjects and availability of tools and measurement methods, particularly for historical assessments. For example, many environmental epidemiological studies use routinely collected health outcome data from subjects for whom only postcode (or zip code) location of residence is available and no contact with the subject can be made. Questionnaires, personal or biomonitoring cannot be used or conducted in this case and one is often restricted to modelling of environmental concentrations at the location of residence. A further disadvantage of this is that no or little information is available where the subject spends his/her time outside the residence, which may be important for obtaining information on total exposure. Estimating past exposure of subjects is difficult and the tools available are sparse. Subjects often tend to recall only limited information and personal monitoring is not possible. Biomonitoring is often not informative because the biological half-life for many substances is too short to provide helpful information on past exposures, and therefore one has to rely on some form of environmental modelling.

A further consideration is whether to obtain individual or group estimates. In the individual approach, exposure estimates are obtained at the individual level, e.g. every member of the population is monitored either once or repeatedly. In the group approach, the group is first split into smaller subpopulations, more often referred to as ‘exposure groups’, based on specific determinants of exposure, and group or ecological exposure estimates are obtained for each exposure group. In environmental epidemiological studies, exposure groups may be defined, e.g. on the basis of presence or absence of an exposure source (such as gas cooker or smoker in the house), distance from an exposure source (such as roads or factories) or activity (such as playing sport or not); in occupational studies exposure groups are often defined by job title. The underlying assumption is that subjects within each exposure group experience similar exposure characteristics, including exposure levels and variation. A representative sample of members from each exposure group can be personally monitored, either once or repeatedly. If the aim is to estimate mean exposure, the average of the exposure measurements is then assigned to all the members in that particular exposure group. Alternatively, other exposure estimates can be assigned to the groups, e.g. data from ambient air pollution monitors in the area where the subjects live. Ecological and individual estimates can be combined, e.g. in the case of chlorination by-products, where routinely collected trihalomethane measurements providing ecological estimates are sometimes combined with individual estimates on actual ingestion, showering and bathing (Nieuwenhuijsen et al. 2000).

Intuitively, it is expected that the individual estimates provide the best exposure estimates for an epidemiological study. This is often not true, however, because of within-subject variability in exposure and the limited number of samples on each individual. In general, in epidemiological studies, individual estimates lead to attenuated, although more precise, health risk estimates than ecological estimates. The ecological estimates, in contrast, result in less attenuation of the risk estimates, albeit with some loss of precision (Kromhout et al. 1996; Seixas and Sheppard 1996; Heederik et al. 1996; Nieuwenhuijsen 1997). These differences can be explained by Classical and Berkson-type error models. The between group, between subjects and within subject variance, can be estimated using analysis of variance (ANOVA) models and this information can be used to optimize the ability to detect an exposure-response relationship, e.g. by changing the distribution of exposure groups (Kromhout and Heederik 1995; Nieuwenhuijsen 1997; van Tongeren et al. 1997). In this case the aim is to increase the contrast of exposure between exposure groups, expressed as the ratio between the between group variance and the sum of the between- and within-group variance, while maintaining a reasonable precision of the exposure estimates of the exposure groups.

7.3. EXPOSURE PATHWAYS AND ROUTES

Generally there are a number of different pathways of exposure to a given contaminant, e.g. food, indoor and outdoor air, water, soil, workplace,
and these may all need to be considered to obtain estimates of total exposure for subjects. Furthermore, there are three possible exposure routes for substances: inhalation through the respiratory system; ingestion through the gastrointestinal system; and absorption through the skin. The exposure route(s) of a substance depends on e.g. the biological, chemical and physical characteristics of the substances, the location and the activities of the person. Inhalation and deposition of particles through the respiratory system depends on the particle diameter and the breathing characteristics of the person. Smaller particles are more often inhaled and penetrate deeper into the lungs. Furthermore, inhalation depends on the breathing rate of the subject; those carrying out heavy work may inhale much more air and breathe more deeply (20 l/min for light work vs. 60 l/min for heavy work).

Skin absorption can play an important role for uptake of substances such as solvents, pesticides and trihalomethanes. Trihalomethanes are volatile compounds that are formed when water is chlorinated and the chlorine reacts with organic matter in the water. In this context there are a number of possible exposure pathways and routes (Figure 7.1). The main pathway of ingestion is generally drinking tap water or tap water-based drinks (e.g. tea, coffee and squash). Swimming, showering, bathing, and dish washing may all result in considerable uptake through inhalation and skin absorption and, for the former three, ingestion to minor extent. Water standing or flushing in the toilet may lead to uptake by inhalation, through volatilization of the chloroform. The total uptake of trihalomethanes may be assessed using the concentration measured in exhaled breath or serum.

In the human body, the uptake, distribution, transformation and excretion of substances such as trihalomethanes can be modelled using physiologically-based pharmacokinetic (PBPK) models (Nieuwenhuijsen 2003). These models are becoming more sophisticated, although they are still rarely used in environmental epidemiology. They can be used to estimate the contribution of various exposure pathways and routes to the total uptake and model the dose of a specific target organ. For example, where ingested trihalomethanes may mostly be metabolized rapidly in the liver and not appear in blood, uptake through inhalation and skin increases the blood levels substantially. Furthermore, metabolic polymorphisms may lead to different dose estimates under similar exposure conditions.

7.4. EXPOSURE DIMENSIONS

The exposure to a substance can depend upon the following factors:

- Duration (e.g. in hours or days) or amount (kg/day ingested)
- Concentration (e.g. in mg/m³ in air or mg/l in water)
- Frequency (e.g. times/week)

It is important to recognize that there may be considerable variability in these factors, both temporally and geographically, which can be exploited by epidemiological studies. Any of these factors can be used as an exposure index in an epidemiological study, but they can also be combined to obtain a new exposure index, e.g. by multiplying duration and concentration to obtain an index of cumulative exposure. The choice of index depends on the health effect of interest. For substances that cause acute effects, such as ammonia (irritation), the short-term concentration is generally the most relevant exposure index, while for substances that cause chronic effects, such as asbestos (cancer), long-term exposure indices, such as cumulative exposure, may be a more appropriate exposure index.

7.5. EXPOSURE MEASURE

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7.5. EXPOSURE CLASSIFICATION, MEASUREMENT OR MODELLING

Different tools, such as questionnaires, monitors and statistical techniques, are available for classifying exposures. The methods are often divided into direct and indirect methods (Figure 7.2).

The main aim of an exposure assessment is generally to obtain accurate, precise and biologically relevant exposure estimates in the most efficient and cost-effective way. As discussed before, the cost of the exposure assessment generally increases with increasing accuracy and precision, and therefore the assessment is often a balancing act between cost on one side and accuracy and precision on the other (Armstrong 1996). The choice of a particular method depends on the aim of the study and, more often, on the financial resources available.

Subjects in an epidemiological study can be classified to a particular substance on an ordinal scale, for example as exposed:

- Yes/no
- No, low, medium, high

This can be achieved by:

- **Expert assessment.** A member of the research team decides, based on prior knowledge, whether the subject in the study is exposed or unexposed, e.g. lives in an area with highly contaminated soil or not. Some environmental epidemiological studies have used simple proxies, e.g. distance from a (point) source, such as a factory (Dolk et al. 1999), radio and TV transmitters (Dolk et al. 1997), incinerators (Elliott et al. 1996), emissions from roads (Livingstone et al. 1996; English et al. 1999; Hoek et al. 2002) or landfill (Elliott et al. 2001), while others have categorized exposure by industrial sources, land use or urban zone (Barbone et al. 1995).

- **Self-assessment by questionnaire.** The subject in the study is asked to fill out a questionnaire in which he/she is asked about a particular substance, e.g. pesticides. Questionnaires are often used to ask a subject whether he/she is exposed to a particular substance and also for an estimation of the duration of exposure. They are also often used in nutritional epidemiology, in the form of food frequency questionnaires or diaries.

Questionnaires can be used not only to ask the subject to estimate his/her exposure but also to obtain information related to the exposure, such as where people spend their time (time micro-environment diaries), work history, including the jobs and tasks they carry out, what they eat and drink, and where they live. These variables could be used as exposure indices in epidemiological studies or translated into a new exposure index, e.g. by multiplying the amount of tap water people drink and the contaminant level in the tap water to obtain the total ingested amount of the substance.

Expert and self-assessment methods are generally the easiest and cheapest, but can suffer of a lack of objectivity and knowledge and may therefore bias the exposure assessment. Both experts and subjects may not know exactly what the subjects are exposed to or at what level, and therefore misclassify the exposure, while diseased subjects may recall certain substances better than subjects without disease (recall bias) and cause differential misclassification, leading to biased health risk estimates.

A more objective way to assess the exposure is by measuring the level of the contaminant in air, water or food. Here are some examples of such measurements:

- **Levels of outdoor air pollution** can be measured by ambient air monitors (Dockery et al. 1993; Katsouyanni et al. 1995; Dockery and Pope 1997).
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These monitors are placed in an area and measure the particular substance of interest in this area. Subjects living within this area are considered to be exposed to the concentrations measured by the monitoring station. This may or may not be true, depending on, for example, where the subject in the study lives, works or travels. The advantage of this method is that it could provide a range of exposure estimates for a large population. Nowadays there are many monitors that are routinely monitoring air pollutants for regulatory purposes, particularly in cities in the developed world but also elsewhere.

- **Levels of air pollution** can be measured by personal exposure monitors (Magnus et al. 1998; Krämer et al. 2000; Magari et al. 2002; Brant et al. 2005). These monitors are lightweight devices that are worn by the subject in the study. They are often used in occupational studies and are becoming more frequently used in environmental studies. The advantage of this method is that it is likely to estimate the subject’s exposure better than, for example, ambient air monitoring. The disadvantage is that this method is often labour intensive and expensive and can often only be used for relatively small populations. However, personal monitoring is ideal for validation studies, e.g. of modelled exposure estimates.

- **Levels of water pollutants and soil contaminants** can be estimated by taking water samples and soil samples, respectively, and analysing these for a substance of interest in the laboratory. Often these need to be combined with behavioural factors, such as water intake, contaminated food intake or hand-to-mouth contact, to obtain a level of exposure (Nieuwenhuijsen et al. 2000).

- **Levels of uptake of the substance into the body** can be estimated by biomonitoring, e.g. for lead (Bellinger and Schwartz 1997; Nieuwenhuijsen 2003). Biomonitoring consists of taking biological samples, such as urine, exhaled breath, hair, adipose tissue or nails, e.g. the measurement of lead in serum. The samples are subsequently analysed in a laboratory for the substance of interest or a metabolite. Biomonitoring is expected to estimate the actual uptake (dose) of the substance of interest, rather than the exposure. Biomonitoring can be very informative, particularly for substances that have multiple pathways and routes. A major drawback is often the fairly short biological half-life of many substances, which makes this method only useful for estimating current exposures/doses. However, infectious disease epidemiology has extensively employed exposure biomarkers. In the case of infections and cancer, developmental work to establish validated laboratory assays for antibodies to viral or bacterial antigens, e.g. hepatitis viruses, human papilloma virus and *Helicobacter pylori*, has been central to understanding the aetiological role of these agents in epidemiological studies. Furthermore, the more recent emphasis on DNA and protein adducts has undoubtedly contributed substantially to establishing the biological plausibility of exposure–disease associations. Examples include investigations of the association between genotypes for carcinogen-metabolizing enzymes and adduct levels; or the use of biomarkers as modifiable end points in short-term intervention studies (Groopman et al. 1999). In contrast, the application of exposure biomarkers of this nature to aetiological studies is far more limited. Aflatoxin is perhaps the prime example in which the exposure biomarker permitted categorization of this environmental agent as a human carcinogen (Qian et al. 1994; Wang et al. 1996), others include polycyclic aromatic hydrocarbon–DNA adducts in lung cancer (Tang et al. 2001) and arylamine–haemoglobin adducts in bladder cancer (Gan et al. 2004). Further developments are envisaged (Wild et al. 2005).

The measurement of exposure is generally expensive, particularly for large populations, and, as mentioned above, can be restricted due to inaccessibility to subjects or the need for a historical assessment of exposure, rather than assessment of current exposure. It may be very useful for validation purposes.

Modelling of exposure can be carried out, preferably in conjunction with exposure measurements, either to help to build a model and/or to validate a model. It is in particularly important that the model estimates are validated.
Modelling can be divided into:

- **Deterministic modelling** (i.e. physical), in which the models describe the relationship between variables mathematically on the basis of knowledge of the physical, chemical and/or biological mechanisms governing these relationships (Brunekreef 1999; see Box 7.1).

- **Stochastic modelling** (i.e. statistical), in which the statistical relationships are modelled between variables. These models do not necessarily require fundamental knowledge of the underlying physical, chemical and/or biological relationships between the variables. Examples are regression and Bayesian modelling.

For regression modelling, a statistical regression model can be constructed, expressed in the form:

\[ \ln(C_{ij}) = \beta_0 + \beta_1 \text{var}_1 + \beta_2 \text{var}_2 + E \]

in which \( \ln(C_{ij}) \) denotes the log-transformed exposure concentration, \( \beta_0 \) the background level, \( \text{var}_x \) the potential determinant of exposure, \( \beta_x \) the regression coefficient of \( \text{var}_x \), providing the magnitude of the effect, and \( E \) a random variable with mean 0, often called the error term (for examples, see Boxes 7.2 and 7.3).

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**Box 7.1 Deterministic modelling**

Hodgson *et al.* (2006) used an atmospheric dispersion modelling system (ADMS) to assess mercury dispersion in Runcorn in north-western England. ADMS uses algorithms that take account of stack height and diameter, volume flow rate, temperature and emission rates of pollutants, as well as meteorology, local geography, atmospheric boundary layer and deposition parameters, to calculate concentrations of pollutants at ground level. Three authorized processes were included in the model, a chloralkali plant, an associated multi-fuel power station, and a coal-fired power station. Compared to using distance as a proxy for exposure, the model identified a much smaller exposed population (Figure 7.3).

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**Figure 7.3** Comparison of modelled exposure output (average 1998–2001) to exposure analysis based on distance as a proxy for exposure for a study of mercury in the north-west of England
Box 7.2 Regression modelling

Harris et al (2002) measured 2,4-d (2,4-dichlorophenoxyacetic acid), mecopop [2-(4-chloro-2-methylphenoxy)propionic acid, MCPPI] and dicamba (3,6-dichloro-o-anisic acid) in urine (two consecutive 24 h periods) collected from a group of 98 professional turf applicators from 20 companies across south-western Ontario. The group also filled out questionnaires to acquire information on all known variables that could potentially increase or decrease pesticide exposure to the amount handled, to build models for epidemiological studies. They used linear regression to assess the relationship between the concentrations of the substances in urine and the questionnaire data. They found that the volume of pesticide (active ingredient) applied was only weakly related to the total dose of 2,4-d absorbed ($R^2 = 0.21$). Two additional factors explained a large proportion of the variation in measured pesticide exposure, the type of spray nozzle used and the use of gloves while spraying. Individuals who used a fan-type nozzle had significantly higher doses than those who used a gun-type nozzle. Glove use was associated with significantly lower doses. Job satisfaction and current smoking influenced the dose but were not highly predictive. In the final multiple regression model, it was concluded that approximately 64% of the variation in doses could be explained by the small number of variables identified (Table 7.2). Biological monitoring in this case was important to be able to determine the true effect of wearing protective equipment, such as gloves. This study provided extremely useful information for epidemiological and health risk assessment studies, which could focus on obtaining information on these particular variables in a larger population.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Estimate</th>
<th>SE</th>
<th>$p$ Value</th>
<th>Partial $R^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>-1.09</td>
<td>0.01</td>
<td>0.29</td>
<td></td>
</tr>
<tr>
<td>Log spray</td>
<td>0.96</td>
<td>0.12</td>
<td>0.001</td>
<td>0.44</td>
</tr>
<tr>
<td>Nozzle</td>
<td>1.37</td>
<td>0.23</td>
<td>0.001</td>
<td>0.29</td>
</tr>
<tr>
<td>Glove wear</td>
<td>-1.50</td>
<td>0.25</td>
<td>0.001</td>
<td>0.29</td>
</tr>
<tr>
<td>Satisfaction</td>
<td>-0.39</td>
<td>0.17</td>
<td>0.021</td>
<td>0.06</td>
</tr>
<tr>
<td>Smoke</td>
<td>0.51</td>
<td>0.22</td>
<td>0.02</td>
<td>0.06</td>
</tr>
</tbody>
</table>


Box 7.3 Modelling using sparse data

Trihalomethane (THM) concentrations were used as the marker for chlorination by-products in a study of chlorination by-products and birth outcomes. In the UK, where the study was conducted, water samples are routinely collected and analysed from each water zone (population up to 50 000 people), using random samples at the tap (an average of four measurements per zone). Because of the small number of THM measurements in some water zones, the need for quarterly (3-monthly) estimates (to allow for trimester-weighted exposure estimates) and the problem of measurements below the limit of detection, it was necessary to model the raw THM data to obtain more robust estimates of the mean THM concentration in each zone. This was done using a hierarchical mixture model in the software WinBUGS (Bayesian inference using Gibbs sampling) (Spiegelhalter et al. 1996), as described in detail elsewhere (Whitaker et al. 2005). A three-component mixture model was fitted, in which zones were assumed to belong to one or some mixture of three components, which were labelled ‘ground’, ‘lowland surface’ and ‘upland surface’ waters (the components may not strictly correspond to these three water sources.
types, and simply aimed to group waters with similar THM profiles, which are more likely to be shared among water of the same source type; Figure 7.4). The hierarchical model was assigned over the zone-specific mean individual THM concentrations, enabling zones to ‘borrow’ information from other zones with the same water source type. This resulted in more stable estimates for zones where few samples were taken. Seasonal variation was taken into account by estimating a quarterly effect common to all zones supplied by the same source type. The modelling provided estimates of exposures for various seasons (Figure 7.5). The modelled exposure estimates provided a better exposure–response relationship than when using estimates based on the mean of the raw THM concentrations for each zone.

Figure 7.4  Hierarchical mixture model to estimate the water zone means of THMs by water source, using tap water samples and applying a common seasonal effect

Figure 7.5  Modelled THM levels by water zone, using Bayesian mixture modelling
A problem in exposure assessment is that often few routinely collected measurements are available to model exposure estimates and therefore more sophisticated statistical techniques need to be used, as was demonstrated in a study of chlorination by-products (see Box 7.3).

In recent years, in environmental epidemiology many of the modelling methods have been greatly strengthened by the use of geographical information system (GIS) techniques (Nuckols et al. 2004; Briggs 2005). Looked at simply, GISs are computerized mapping systems. GISs, however, can do more than simply map data. They also provide the capability to integrate the data into a common spatial form and to analyse the data geographically. It is these capabilities that give GISs their special power in relation to exposure assessment. However, there are often some problems in acquiring the data needed to carry out geographic methods of exposure assessment. Also, a GIS requires that all data be georeferenced. Various GIS and geostatistical techniques have been used to model local pollution patterns, on the basis of the monitored data, e.g. using inverse distance weighting, kriging or focal sum methods. These essentially fit a surface through the available monitored data, in order to predict pollutant concentrations at unmeasured sites. It is an approach that has been greatly facili...

Box 7.4. GIS-based regression modelling

Regression techniques were used as part of the (SAVIAH) study, for example, to model exposures to NO$_2$ (as a marker for traffic-related air pollution) in four study cities (Briggs et al. 1997). Data from 80 monitoring sites were used to construct a regression equation, using information on road traffic (e.g. road network, road type, traffic volume), land cover/use, altitude and monitored NO$_2$ data. The results showed that the maps produced extremely good predictions of monitored pollution levels, both for individual and for the mean annual concentrations, with $r^2 = 0.79$--$0.87$ across 8--10 reference points, although the accuracy of the predictions for individual periods was more variable (Figure 7.6). Subsequently it was shown that regression models developed in one location could be applied successfully, with local calibration using only a small number of sites, to other study areas or periods (Briggs et al. 2000). More recently, the same approach has been further developed to assess exposures to particles in a number of different cities as part of the TRAPCA study (Brauer et al. 2003), and to model traffic-related air pollution in Munich (Carr et al. 2002).

$$C = 38.5 + 0.003705 \times \text{Traffic} + 0.232 \times \text{Land} - 5.673 \times 10^{-9} \times \text{Alt}$$

where:

- Traffic = 18 $\times$ Vold40 + Vold40-300
- Land = 8 $\times$ HDH0-300 + Ind0-300

Figure 7.6 Modelled NO$_2$ levels in Huddersfield, using the SAVIAH approach
greatly facilitated through the development of GIS (Bayer-Oglesby 2004).

The approach appears to work well in areas where there is relatively gentle variation in air pollution and/or where the density of the monitoring network is high; conditions that are often not fulfilled. In other situations, it is helpful to supplement the available monitoring data through the use of covariates, i.e. variables that correlate with monitored concentrations and can be more readily obtained than quantitative measurements (Bayer-Oglesby 2004). Both cokriging and regression methods enable this (see Box 7.4).

People typically move about during the day and this mobility can greatly affect exposure. The importance of this was clearly shown by a study in Helsinki (Kousa et al. 2002), which used dispersion modelling to predict nitrogen dioxide concentrations across the city at different times of the day. These were then overlaid onto data showing where people were at different times, in order to build up a picture of exposure variations throughout the day. An interesting development in this area is that it is possible to track people through their environment using global positioning systems (GPS) with enough resolution to be useful for this type of study (Phillips et al. 2001; Elgethun et al. 2003). There are some restrictions as a result of the limitations in the technology, e.g. reception of the satellite signals can be adversely impacted by shielding from buildings of certain materials (concrete, steel), electrical power stations, and to some extent vehicle body panels. However, combining pollution maps with information on where people spend their time may greatly improve the exposure estimates if further improvements to the technology can be made.

All these different approaches are not exclusive and often are combined to obtain the best exposure index. It is often difficult or impossible to measure the exposure to the actual substance of interest and therefore exposure to an ‘exposure surrogate’ is estimated. The National Research Council (NRC) in the USA came up with a ranking of exposure data and surrogate measures around point sources, such as landfill sites (Table 7.2). The data at the top of the hierarchy shown in this table provide some fairly good information on the exposure of the subjects, while those at the bottom may not be helpful in the interpretation of exposure levels in an epidemiological study. Of course, there are still other issues that are important in the ranking, e.g. many area measurements may still be better than a few personal exposure measurements if exposure arises from a general source in the area.

7.6. RETROSPECTIVE EXPOSURE ASSESSMENT

A special challenge in epidemiological studies is studying disease with a long latency time, e.g. cancer; in such cases it is not the current exposures that are of most interest, but those that occurred in the past. A reconstruction of historical exposure, often referred to as retrospective exposure assessment, is therefore needed, and often involves some extensive modelling and specific expertise. Retrospective exposure assessment is difficult because there are often many changes occurring over time.

A good recent example of retrospective exposure assessment is provided by the study of air pollution and lung cancer in Stockholm, where the investigators used emission data, dispersion models and GIS to assess historical exposures to air pollutants and compared these estimates with actual measurements (Bellander et al. 2001). For NO2 they used a detailed regional database, which included information on approximately 4300 line sources related to traffic and 500 point sources, including major industries and energy plants as well as small industry and ferries in ports. Limited diffuse emission sources, e.g. air traffic and merchant vessels in commercial routes, were treated as area sources, and several population density-related sources, such as local heating, were mapped as grid sources, as were work machine emissions. They collected information on the growth of urban areas, the development of district heating, and the growth and distribution of the road traffic over time. They used the Airviro model, together with population data, to derive population-weighted average exposures during 1955–1990. In the case of traffic-related NO2 exposures were seen to increase over this period from about 15 μg/m3 in 1955 to about 24 μg/m3 in 1990, showing the effect of increasing traffic
**Table 7.3. Hierarchy of exposure data and surrogates for fixed source contaminants**

<table>
<thead>
<tr>
<th>Type of data</th>
<th>Approximation to actual exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Quantified personal measurement</td>
<td>Best</td>
</tr>
<tr>
<td>2. Quantified area measurements in the vicinity of the residence or sites of activity</td>
<td>Best</td>
</tr>
<tr>
<td>3. Quantified surrogates of exposure (e.g. estimates of drinking water use)</td>
<td>Worst</td>
</tr>
<tr>
<td>4. Distance from the site and duration of exposure</td>
<td>Worst</td>
</tr>
<tr>
<td>5. Distance or duration of residence</td>
<td>Worst</td>
</tr>
<tr>
<td>6. Residence or employment in the geographical area in reasonable proximity to the site where exposure can be assumed</td>
<td>Worst</td>
</tr>
<tr>
<td>7. Residence or employment in a defined geographical area (e.g. a county) of the site</td>
<td>Worst</td>
</tr>
</tbody>
</table>

Adapted from NRC (1991).

volumes. In contrast, modelled SO2 exposures fell from > 90 µg/m³ to < 20 µg/m³ as a result of improvements in fuel technology, emission controls and a shift to district heating.

### 7.7. VALIDATION STUDIES

In epidemiological studies it is often not possible to obtain detailed exposure information on each subject in the study. For example, in a large cohort study it is generally not feasible to take measurements on each subject and administer a detailed exposure questionnaire. In this case it is desirable to carry out a small validation study on a subset of the population that is representative of the larger population. Ideally this will be carried out before the main study starts and can make use of information from the literature. Questions in the questionnaire could be validated with measurements and exposure models could be constructed. The exposure assessment in the whole population could focus on key questions that have a large influence on the exposure estimates and thereby reduce the length of the questionnaire. Information on key determinants will also provide a better understanding of the exposure and how it may affect exposure–response relationships in epidemiological studies. Besides assessing the validity of the exposure surrogates, the reproducibility of the surrogates can also be evaluated in the subsample.

### 7.8. QUALITY CONTROL ISSUES

A well-designed and well-thought-out exposure assessment strategy carried out by well-trained personnel is essential for a successful exposure assessment. Issues such as cost, feasibility, accuracy, precision, validity, sample size, power, sensitivity, specificity, robustness and reproducibility always need to be addressed (e.g. during sampling, storage and analysis), while feasibility and pilot studies always need to take place before the actual study. Any form of bias (e.g. bias in sampling, selection, participation, monitoring, information, measurement error and exposure misclassification) should be avoided where possible, or if it takes place it should be clearly described.

Clear protocols for sampling, storage and analysis, including quality control should be written and be available at any time and researchers in the study should be properly trained. Potential sources of bias should be addressed at every stage.

Control measurement, e.g. air pollution filters that are not exposed but are otherwise treated as exposed filters, should be included (5–10% of total samples) particularly where measurements are close to the detection limit.

Samplers can measure with different accuracy, e.g. over- or under-sampling the true level, and this should be addressed when different samplers are used in order to reduce or avoid bias. This can be easily done by comparative sampling and adjusting for any difference observed.
References


Spiegelhalter D, Thomas A, Best N et al. 1996. BUGS 0.5; Bayesian inference using Gibbs sampling. Manual, Version ii. Available at: http://www.mrc-bsu.cam.ac.uk/bugs


