Epidemiology and Public Health Intelligence

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> ***Epidemiology*** is the study of the distribution and determinants of health-related states or events in specified populations and the application of this study to the control of health problems.
>
> *From Last 2001—Dictionary of Epidemiology*

Abstract This chapter provides an introduction to epidemiology. It covers the key epidemiological concepts such as bias and confounding, as well as providing an overview of the nature, history and types of epidemiology. The main epidemiological study designs are described, including case series, ecological, cross-sectional, case–control, cohort, randomised controlled trial and systematic review. The advantages and disadvantages of each are summarised, and some of the ethical issues in doing research are considered. The 'hierarchy of evidence' framework is contrasted with an approach which recognises the most appropriate study design to answer different questions about population health. This chapter will examine the role of epidemiology in public health intelligence and develop students' or learners' knowledge and skills to carry out thorough, rigorous and meaningful research and investigation relevant to public health.

After reading this chapter you should be able to:

- Define epidemiology and differentiate between descriptive epidemiology and analytical epidemiology
- Describe the basic study designs, principles and methods used in epidemiology
- Explore key issues related to the design and conduct of studies
- Recognise the role of epidemiology in public health intelligence

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What Is Epidemiology?

Descriptive epidemiology is concerned with both the frequency and distribution of a health outcome (or health-related exposure). In other words, how common is it, and who does it affect? The first question can be answered using measures such as incidence and prevalence (see "Types of Data and Measures of Disease" chapter). The second can be framed in terms of TIME, PLACE and PERSON (see Fig. 1). For example, we may describe the distribution of health outcomes by age, population, geography or over time.

Descriptive epidemiological outputs are often presented graphically. Disease atlases and graphs showing trends over time are commonly used techniques to highlight disparities in health status between countries or areas within countries and to illustrate changes in health outcomes over time. These techniques are particularly important for highlighting inequalities according to not only geography, but also by age, gender, levels of deprivation, ethnicity and occupation. Many routine health reports present outcomes by quintiles of deprivation, and in New Zealand the Ministry of Health routinely reports on differences in health outcomes between the indigenous Maori population compared with the rest of the population (https://www.health.govt.nz/). It is quite common to see reported in the news maps showing outcomes such as life expectancy or quality of life for different regions or cities of the UK. Another important use of descriptive epidemiology is to monitor the incidence of new or rare diseases (examples include the global epidemics of bird flu and *ebola*). Maps (showing the number of cases recorded by region) and epidemic curves (plotting new cases against time) are tools often used in surveillance. See the "Public Health Surveillance" chapter for more information about health surveillance.

Analytical epidemiology, sometimes also known as aetiological epidemiology, considers the role of individual risk factors in the development of disease. In other words, investigating which factors are responsible for increasing or decreasing the risk of an outcome, and quantifying their effect. The key issue is to determine whether an exposure just happens to be associated with the outcome of interest, or whether it is causing the outcome (i.e. the association is causal). So while descrip-

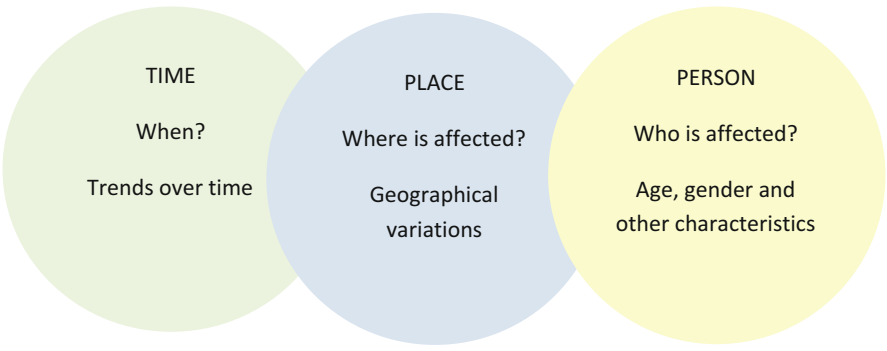

Fig. 1 Describing the distribution of disease

tive epidemiology may highlight a possible risk factor for a particular health outcome (e.g. suicide rates are increasing at the same rate as selective serotonin reuptake inhibitor (SSRI) prescribing, or immigrants are more likely to give birth to preterm babies than other women in the population), analytical epidemiology is used to determine what is actually causing the health outcome. Perhaps, for example, the rise in SSRI prescriptions has coincided with a decrease in funding for community mental heath services, and this is more directly related to suicide deaths. Or perhaps immigrant mothers are more likely to fall into age brackets associated with an increased risk of preterm birth, and this is the causal factor rather than immigrant status per se. These issues can be untangled through analytical epidemiology, with adequate control for confounding factors.

Confounding factors are those which are related to both the exposure and outcome of interest, and which distort the association being studied.

Rigorous analytical epidemiology can be summarised by the 5 Ws (see Fig. 2). The TIME, PLACE and PERSON of descriptive epidemiology translate into WHEN, WHERE and WHO, respectively. To these can be added WHAT and WHY, i.e. what is the health outcome of interest and why does it occur (e.g. what are the causes?)? The 5 Ws can be applied when considering any health condition in a population, whether it be norovirus aboard a cruise ship or asthma amongst school children.

Discussion Task
What are the key terms in the definition of epidemiology?

The Changing Nature of Epidemiology

In his treatise '*On Airs, Waters, and Places'*, Hippocrates (460BC–377BC) recognised the importance of the environment in the causation of disease. Epidemiology as a discipline developed in the area of infectious disease control, through the statistical analysis of routine data to quantify the risk associated with unsanitary environments (see, for example, the work of pioneer epidemiologists John Snow (1855) and William Farr (Ratcliffe 1974)). The epidemiology of communicable disease, and its application to Public Health, is sometimes also known as 'Health Protection' (something of a misnomer given that all epidemiology is about protecting health through identifying and limiting exposure to risk factors). Environmental epidemiology also includes, for example, studying the effect of pollution on the prevalence of asthma amongst children, and the health effects of environmental tobacco smoking. But

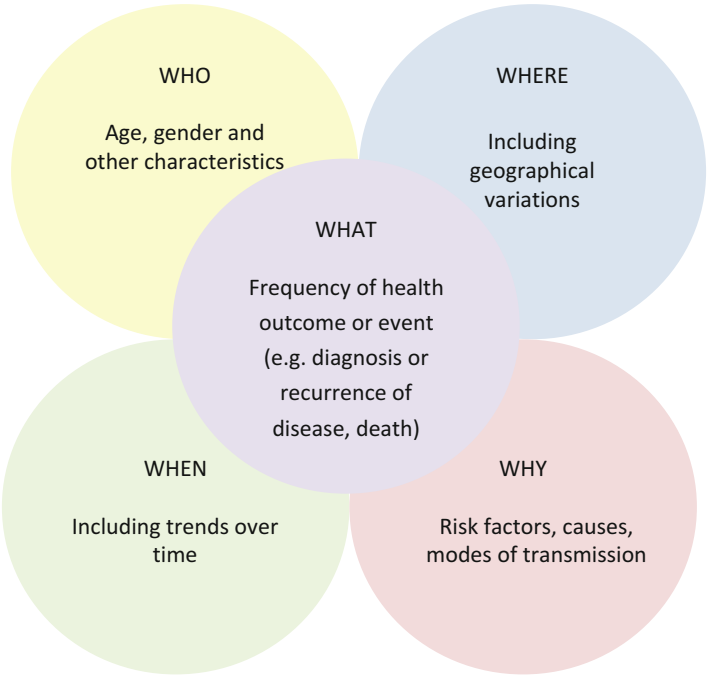

Fig. 2 The 5 Ws of analytical epidemiology

elucidating the causes of non-communicable diseases such as asthma, coronary heart disease and cancer is, by definition, harder than studying infectious diseases because there are a range of complex factors which may be causally related to the non-communicable disease in question, and possibly interactions between these factors.

One way to conceptualise epidemiology is as follows. Imagine you walk into a room; there is one switch on the wall, and you discover that this switch turns the light on and off. In the next room, there are several switches, but you find that only one of them controls the light. In a third room, there are also several switches, but none of them operates the light. You discover though trial and error that only a certain combination of these switches will turn the light on. In the final room, there are many switches on the wall and you find that *certain combinations* of switches will turn on the light, *some of the time*. In this scenario, the switches are the various exposures we are interested in (which may be environmental, genetic or behavioural), and the light is the disease outcome of interest. And so it is that we seek to understand the component causes of disease—why some people develop cancer and others not, why some children develop obesity and others not and why some people born into adversity have good health outcomes while others do not.

In the developed world, non-communicable disease has overtaken communicable disease as a priority. This is known as the *epidemiological transition*. The transition is partly due to the success of prevention measures put in place against infectious disease, and epidemiology still has an important role to play in providing evidence to support these measures (e.g. Madsen et al. 2002). Many developing countries going through the epidemiological transition are suffering a double burden, with high rates of infectious disease (e.g. malaria, HIV) and infant mortality due to preventable infectious disease, and at the same time a developing economy leading to more 'Westernised' lifestyles which brings with it increasing prevalence of non-communicable diseases such as cardiovascular disease and cancer. We note that despite our attempts to class diseases as being either communicable or non-communicable, we are increasingly discovering that conditions traditionally thought of as non-communicable can be associated, in part, with certain infections. Examples include *H. pylori* infection and coronary heart disease, hepatitis and liver cancer, and human papilloma virus and cervical cancer.

Just as a certain proportion of cancer cases can be attributed to infectious agents, other cases are due to genetic causes. *Genetic epidemiology* examines the role of genes in the development of diseases (e.g. breast cancer), and what are known as *gene–environment interactions*. This is when a certain combination of genetic predisposition and environmental exposure (e.g. to stress or a toxin) increase the risk of a certain health outcome occurring in an individual. *Epigenetic epidemiology* is concerned with environmental effects on the expression of genes rather than the DNA itself. We can think of genes being switched on or off by exposures experienced at critical periods (e.g. in utero or in the pre-pubertal slow growth period). For more about epigenetics, see '*The Epigenetics Revolution*' (Nessa Carey 2012). Epigenetic epidemiology takes us beyond the nature–nuture (gene–environment) dialogue and into a new dimension in which the environment can alter the expression of genes in such a way that the effects of environmental exposures on genes are passed down from one generation to the next. The discovery that our environment can have this effect on our genetic make-up, previously thought to be down to a roll of the dice at conception and then fixed, to be passed onto the next generation, emphasises the importance of environmental influences on health and well-being, and brings us full circle back to Hippocrates.

Epidemiological Study Designs

Epidemiological study designs can be categorised as being either observational (we study what is already happening, without intervening) or experimental (when we conduct a trial to assess the effects of an intervention on the health outcome of interest). In observational study designs, we want to quantify the effect of an exposure (e.g. environmental, genetic or behavioural) on the outcome, whereas in experimental study designs we are testing a potential intervention or treatment—in this case, the intervention is the exposure of interest. Since different terms are

sometimes used interchangeably, or by different disciplines to mean the same thing, Fig. 3 lists various terms that may be used when talking about exposures and health outcomes in epidemiological research.

Within the broad categories of observational and experimental, there are several different study designs. These are sometimes thought of in terms of a 'hierarchy of evidence'. Although this approach has somewhat lost favour as over-simplifying the situation, it is still a useful framework for describing epidemiological study designs. Figure 4 lists the main study designs which will be considered here, ranging from case series to systematic review. These can be classified according to whether they are observational or experimental study designs, and also according

Context	Exposure	Health Outcome
Observational designs	Exposure	(Health) Outcome
	Risk factor	
Experimental designs	Treatment	Disease
	Intervention	Condition
Statistical modelling	Independent variable	Dependent Variable
	Explanatory factor	
	x	y

Fig. 3 Alternative terms used for exposures and health outcomes

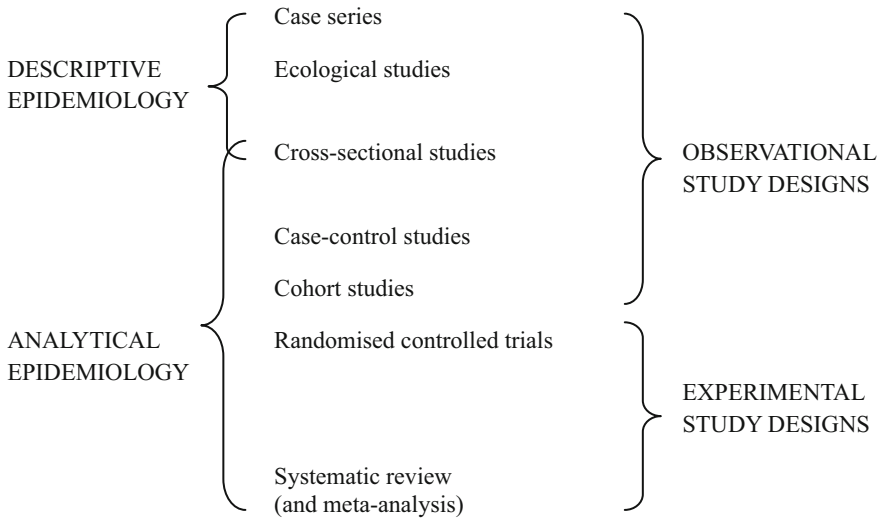

Fig. 4 The hierarchy of evidence showing the main epidemiological study designs, ordered from the least reliable (case series) up to the most reliable (systematic review)

to whether they are used for descriptive or analytical epidemiology. Of course, there are different versions of this framework, and other study designs could be included.

Case Series

A case series is a report on a number of cases exhibiting a similar set of symptoms, possibly describing a new syndrome. It is compiled from individual case reports and may lead to formulation of a new hypothesis relating to risk factors and disease. However, since it does not involve a control group and provides no evidence of a causal relationship, it can only suggest possibilities for further research. Our first example of a case series is a report called 'Thalidomide and congenital abnormalities' (McBride 1961). The author had noticed a number of babies with abnormal limbs being born to mothers who had taken thalidomide for morning sickness, and suspected a connection. His paper was published in The Lancet, and soon other doctors around the world were responding that they had noticed similar cases amongst their patients. This enabled a rapid response to prevent the drug being given to more pregnant women. The second example is more infamous—that is the case series that suggested a link between the MMR vaccination and autism (Wakefield et al. 1998). The case series was based on only 12 children. In fact, the paper itself (now retracted by the Lancet) was relatively cautious and the title does not even mention the vaccination. The conclusion contained the following statements—'*In most cases, onset of symptoms was after measles, mumps and rubella immunisation*' and '*Further investigations are needed to examine this syndrome and its possible relation to this vaccine*.' The second of these statements is appropriate to the limitations of a case series, but the misinterpretation of the first and its effect on MMR immunisation rates in many countries is well-documented elsewhere (Tannous et al. 2014). What is probably less well known is that the hypothesis was subsequently investigated by large cohort studies which showed no evidence of a link between the MMR vaccine and autism (e.g. Madsen et al. 2002).

Cross-Sectional Study

The defining feature of a cross-sectional study is that it is carried out at one point in time. A sample is drawn from the population of interest, and data collection is often through self-completed survey but may be through interviewer-administered questionnaire. This study design is ideal for descriptive epidemiology, in particular for estimating the prevalence of a given health condition (the proportion of the population who have the condition), or indeed the prevalence of an important exposure (such as smoking), but cannot measure incidence (the number of new cases in a given time period such as a year). Its appropriateness for analytical epidemiology is very limited by the fact that exposures are measured at the same

time as disease outcomes, which creates a 'chicken and egg' problem. Imagine a survey that collects information on levels of physical activity and mental health, amongst other things. If there is a positive association between these variables, are we to conclude that physical activity improves mental health? Or might it be that people with better mental health are more likely to be motivated to take exercise? Other common problems with cross-sectional studies are low response rates which can lead to a non-representative sample (affecting the generalisability of the findings), and the measurement of exposure and outcome through self-report which can lead to reporting bias. For example, it is well known that people tend to under-report their tobacco and alcohol use, and a recent study found that men tended to over-report levels of physical activity (Dyrstad et al. 2013).

Bias is a systematic error in the measurement of the exposure or outcome variables.

Ecological Study

An ecological study is a cross-sectional study with the unit of analysis being a geographical area (e.g. a country, region or ward) rather than the individual (as is usual in epidemiology). Associations between potential exposures and the outcome of interest are often shown on a scatter graph, with each point representing a country (or other unit of analysis). Ecological studies suffer from the same drawbacks as other cross-sectional surveys when used for analytical purposes (confounding, exposure measured at the same time as outcome, bias in reporting of exposures and outcomes), but there is also the additional problem of the ecological fallacy. This means that associations that hold at a population level do not hold at an individual level. Take, for example, a study of average income and rates of coronary heart disease in capital cities of the world. This would show that those cities with the highest average income also had the highest rates of coronary heart disease, from which you might deduce that increased wealth is associated with increased risk of coronary heart disease. But, for Westernised societies at least, the opposite is true. If you look at individuals within wealthy cities such as London and Washington, it is the poorer people who have the highest rates of coronary heart disease. This is the ecological fallacy. However, ecological studies are often quick and easy to carry out since they can be conducted using routinely collected and often freely available data, and they are very useful for generating hypotheses to be tested in further more rigorous studies. For example, using dietary information from international studies and cancer incidence rates available by country from the WHO, you could carry out an ecological analysis to generate hypotheses about dietary risk factors for cancer. Another example of an ecological analysis is the *The Spirit Level* (Wilkinson and Pickett 2010), which examines income inequalities in a wide range of countries across the globe, and examines the association between this exposure and many health and social outcomes.

Case–Control Study

A case–control study (see Fig. 5) compares a group of people with a condition (the cases) with a similar group of people who do not have the condition (the controls). Cases and controls are drawn from the same population. The aim is to identify the risk factors which caused the condition, by comparing the exposure status of cases and controls. In order to ensure that any differences are not due to confounding factors such as age and gender, controls are usually selected to be similar to cases in these respects. This is called 'matching'. Other variables such as socio-economic status may also be matched upon. A case–control approach is particularly useful when we need to conduct a study quickly to ascertain the cause of a disease or health outcome. It could have been used, for example, following the thalidomide case series described above, to get more concrete evidence of the link, and it is also widely used to investigate infectious disease outbreaks.

A key aspect of this study design is that we are collecting exposure data retrospectively. This has disadvantages in terms of the reliability of that data, particularly if exposures are self-reported. The scale of the problem depends on what we are asking people to recall and the time that has elapsed since exposure. So if, for example, we were asking participants to report how many children they had given birth to, or whether they had been swimming in the previous week, we would hope that their memory of these exposures would be accurate. But if we ask participants to report how many tetanus vaccinations they had received before the age of 16, or how many coffees they had drunk in the last week, then this would be less reliably reported. Added to this general problem of less-than-perfect memories is recall bias which is usually the most serious drawback of using a case–control approach. It occurs because the exposures reported by cases and controls are biased by the very

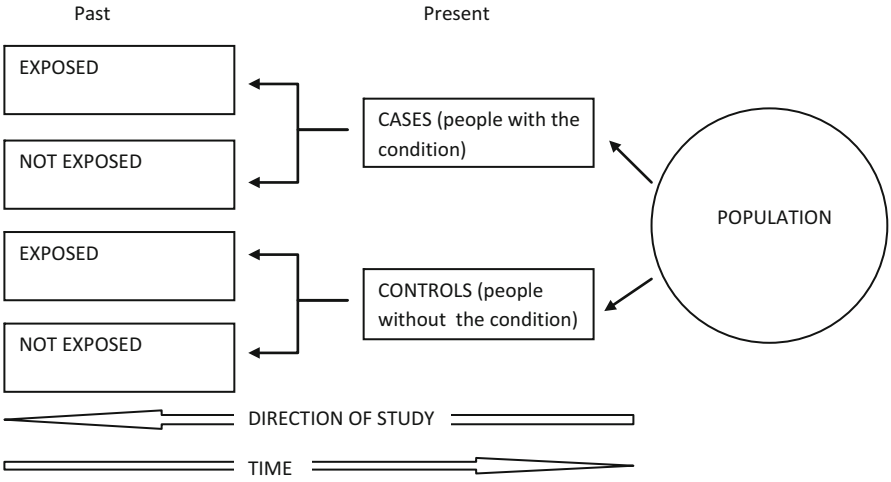

Fig. 5 Case–control study design

fact of being a case or control. People who have the health condition of interest may over-report potential risk factors, because they are trying to understand why they developed the condition, and looking to past exposures for reasons. Conversely, people who do not have the condition are likely to under-report exposures as they have no particular incentive to recall them, and their memory has faded with time. Of course, these are generalisations and the effect of recall bias will very much depend on the context and how the questions are asked, but recall bias is a very real phenomenon.

An example of this is a comparison between data on medical x-ray exposure obtained a) from medical records and b) from mailed questionnaires (Hallquist and Jansson 2005). In this case-control study of thyroid cancer, the authors concluded that both cases and controls underreported x-ray investigations, but that underreporting was of greater magnitude amongst the controls. The degree of underreporting was also found to differ according to age and gender. The authors concluded that recall bias was an important risk, if relying on self-report of x-ray exposure alone. Of course, if we are collecting data on exposures based on other data sources, such as medical records or other routinely available data, then recall bias is not a problem, but the suitability of the data for research purposes should be considered.

Cohort Study

A cohort study takes a group of people from the population of interest, measures exposures at the outset, and follows them up for a given period of time so that incidence of health outcomes can be ascertained (see Fig. 6). Many different exposures

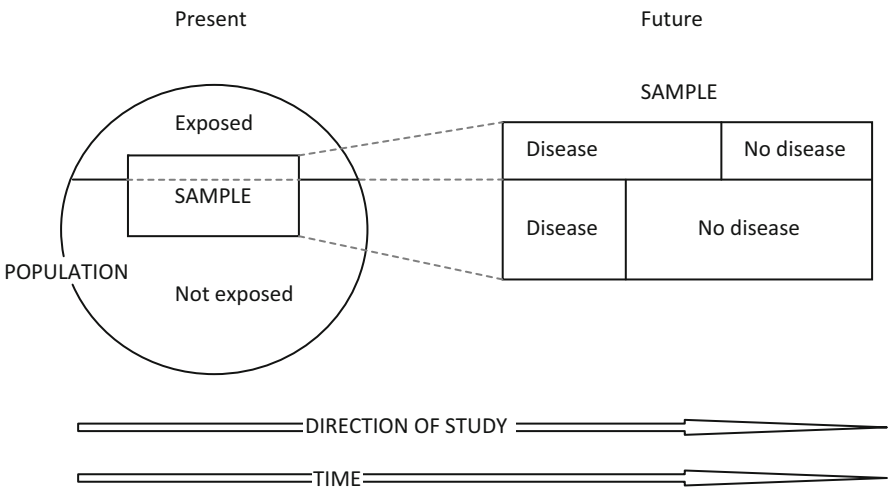

Fig. 6 Cohort study design

and outcomes can be considered. Exposure and outcome measurement may be through self-reported questionnaire, measured by observers (e.g. a research nurse at a clinic or during a home visit) or collected from existing data sources (e.g. educational or health records) through data linkage. Measurement of both exposures and outcomes may continue throughout follow-up.

Cohort studies can take many shapes and sizes. Some population-based studies follow up tens of thousands of participants for their entire lives. Data on a large number of exposures and outcomes may be recorded. Others follow more specific populations for shorter periods of time, and may be designed to answer a more focused research question. For example, a small cohort of patients with a rare condition might be followed up for 5–10 years to collect data on prognosis. If a cohort study is designed to investigate a particular exposure, the sample may be selected on the basis of exposure status, to ensure that sufficient numbers of participants who have experienced the exposure are included. This is particularly useful if the exposure is rare, e.g. exposure to asbestos.

An example of a large population-based cohort study is the Avon Longitudinal Study of Parents and Children (ALSPAC). Information was collected from approximately 14,000 women throughout their pregnancy. Data was also collected from the children from birth and is ongoing. ALSPAC is now a multi-generational study of immense value for answering all kinds of research questions. However, ALSPAC serves to illustrate a major drawback of cohort studies with reasonably long follow-up periods, which is drop-out over time. This occurs because participants move, die, become uncontactable, or simply do not wish to continue in the study. As well as reducing the sample size, this increases bias in the sample, because those who drop out are different to those who remain in the study. Twenty-five years after the study started, response rates to ALSPAC questionnaires are now approximately 50 %. Those who were still contributing data at age 16–18 were more likely to be female than those who had dropped out, more likely to be of white ethnicity and less likely to have been eligible for free school meals (Boyd et al. 2013).

Another major problem with cohort studies is that of confounding. Imagine a cohort study designed to test a possible association between alcohol consumption (exposure) and risk of lung cancer (outcome). A simple approach would be to take a sample from the population and collect data on alcohol consumption at the outset. The follow-up period would have to be long enough for sufficient numbers of cases of lung cancer to be diagnosed. Then, based on a naïve analysis which ignores confounding factors, you may conclude that there is a positive association between alcohol consumption and lung cancer. However, this apparent association is actually due to smoking status (which is associated with both alcohol consumption and risk of lung cancer). If this confounding factor is also measured and taken into account in the analysis, then the association between alcohol consumption and lung cancer can be explained. This simple example illustrates the point, but the reality is that there are many confounding factors leading to spurious associations between exposures and outcomes in observational epidemiological studies. Some are obvious and easy to understand (e.g. age, gender), others less so (e.g. educational status). Data must therefore be collected on all potential confounders so that they can be taken

into account during analysis. There are often many confounding factors that we have not even thought of, so cannot measure. And there are those that we are aware of but are difficult to define and measure (e.g. socio-economic status, adverse childhood circumstances). In this situation, we attempt to capture the confounding factor (through use of a deprivation index, for example) but since this is imperfect there will be 'residual confounding' that we have not managed to control for.

Discussion Task
What are the advantages and disadvantages of observational study designs?

Randomised Controlled Trials

The randomised controlled trial (RCT) is thought of as the 'gold standard' of research designs. It is the most reliable way to test the effectiveness of a treatment or intervention. Interventions can be classed as primary prevention (to reduce the risk of exposure) or secondary prevention (therapeutic interventions to alleviate symptoms, prevent recurrence or decrease risk of mortality). An example of primary prevention would be a smoking cessation intervention. An example of secondary prevention would be chemotherapy for breast cancer.

A trial is any experiment to test an intervention. So you give a group of patients a new treatment, and they get better. Can you claim that the treatment is a success? Maybe they would have got better anyway (the body often heals itself with time). So we need a control group, and a trial which compares patients on the new treatment with another group of patients receiving either standard treatment (if there is one) or no treatment. Now, if the patients on the treatment get better more rapidly than those in the other treatment group, then the new treatment appears to be a success. But someone might argue that this was because the patients in the new treatment group were somehow different, and more likely to do well. Perhaps their disease was less severe, or they were younger, or they had better access to healthcare? This is the reason for randomising participants to the two groups. If they are allocated to the two groups on a completely random basis, then factors that might influence the success of the intervention (such as age, gender, disease severity) are evenly distributed between the two groups by the play of chance. Now, any difference in outcome between the two groups is not down to confounding factors, so must be due to the actual treatment. The key advantage of RCTs over observational study designs is that by randomising participants we are comparing two groups who should be similar in terms of all confounding factors, even those we are unaware of. The process of conducting an RCT is described in Fig. 7.

But could the observed treatment effect be, at least in part, due to the placebo effect? The patients receiving the new intervention know they are getting the latest treatment. They expect to feel better, and they do feel better (the mind plays an important role in these matters). So, if possible, we need to conduct a trial in which

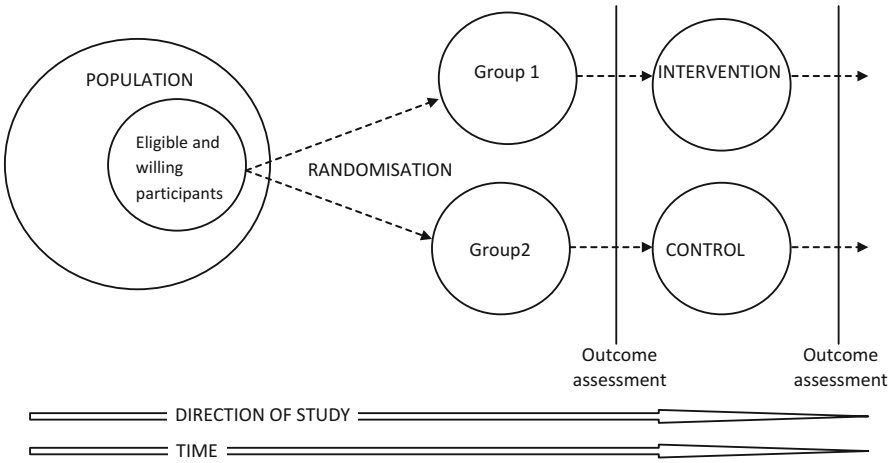

Fig. 7 Randomised controlled trial design

the participants do not know which treatment group they are in. This is known as 'blinding'. The participants in the study are 'blinded' to their treatment group. Then any self-reported outcomes, such as pain or quality of life, are not biased by knowledge of treatment group. Outcomes assessed by an observer (e.g. function scored by a physiotherapist) are also subjective and prone to bias, so observers should also be blinded. It is not always possible to blind participants and observers, depending on the intervention in question, but it should be attempted wherever possible. Having a 'placebo', that is something that looks like the treatment but is in fact inactive, makes it easier to blind a study. The theory and practice of RCTs developed in the very medical context of drug therapy. In this case, it is easy to make a pill that looks like the new drug but isn't. It has taken a long while for many surgical procedures to be subjected to the same rigorous assessment, partly because it is so difficult to blind the patient as to whether they have been operated on or not. However, there have been attempts to compare traditional surgery with keyhole surgery for a particular procedure, giving both groups of patients the same dressings. The fact that blinding has been attempted in such unlikely circumstances demonstrates the importance of blinding to the validity of an RCT. The issue of blinding becomes harder when you are comparing two quite different approaches to alleviate a condition. Depression may be treated with antidepressants. We might want to know whether alternatives, such as free gym sessions on prescription, or cognitive behaviour therapy, work just as well or better. In a trial that compared these approaches, it would be obvious to the participant which of these alternatives they were receiving. This applies to many Public Health interventions, making blinded RCTs of non-medical interventions difficult.

There are other challenges with conducting trials on Public Health interventions. Imagine you were interested in increasing levels of physical activity amongst teenage girls, and had identified a dance programme as an intervention to be tested.

Delivering this intervention through a school would seem a good way to reach the population of interest. If you randomised a sample of girls in the school to be offered extra dance sessions or not, you would find that some girls within each class were in the intervention group, while others were not. Some girls within particular friendship groups would be in the intervention group, while others would not. As well as being logistically challenging to organise, you may get a certain amount of 'contamination'. That is, girls receiving the intervention may influence their peers not receiving the intervention, so that the intervention increases physical activity levels in both the intervention and control group. One solution is to randomise groups of participants (classes or schools in this case) rather than individuals. This approach is commonly used in Public Health, and often makes the organisation of trials simpler. The unit of randomisation may be school, clinic, GP surgery, or nursing home, for example. A recent trial randomised wards within a hospital to a smoking cessation intervention, compared with usual practice (Murray et al. 2013). It would have been harder logistically to give individual patients on the same ward different smoking cessation services. This example also illustrates one of the problems with cluster randomisation—randomisation resulted in the wards in the two arms of the trial being quite different in terms of specialty and patient characteristics. This is a particular problem if the number of clusters to be randomised is small.

Discussion Task
Is an experimental study design always superior to an observational study design?

Systematic Review

A systematic review provides an overview of primary research to answer a particular research question. The aim is to identify, select, synthesise and appraise all high quality research evidence relevant to answering the question. Reviews on particular topics have long been published by experts in the field, but these are prone to selective reporting and bias. The key thing about a systematic review is that it minimises bias by using explicit, systematic methods. This approach was championed by Archie Cochrane (2009). Cochrane reviews (http://www.cochranelibrary.com/) are internationally recognised as the highest quality systematic reviews to support evidence-based healthcare. Access to a reliable review of the current evidence to answer a particular research question becomes increasingly important as the amount of information available increases—it is very difficult for any professional to keep up with all the individual reports published in their field.

A systematic review starts with a clearly defined question. The next step is to identify all relevant research. This requires an appropriate search strategy and knowing the right databases for the topic. The search strategy should be transparent and reproducible. It is also important to search for unpublished research, through

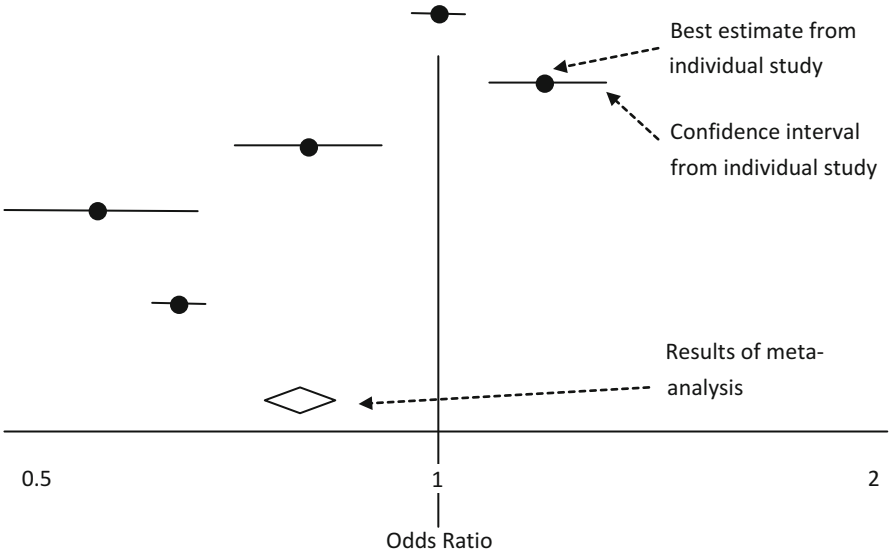

Fig. 8 Forest plot showing results of a systematic review

trial registers, for example. From the studies identified by the search strategy, those that are actually relevant to answering the question of interest need to be selected. Once those that should be included in the review have been agreed on, then each should be quality assessed (using a critical appraisal checklist or the Cochrane Risk of Bias Tool, for example). Studies of lower quality may be excluded at this stage. The next stage is to extract the results from each paper, using a standardised form to ensure consistency. Finally, the results of the individual studies can be compared. If the studies are sufficiently similar to one another (heterogeneous) in terms of the exact intervention delivered, the population of interest, and the follow-up time, then it may be appropriate to combine the results of the various studies.

This statistical analysis is called a meta-analysis. Essentially, it averages the results across studies, weighting by the size of the study. If a meta-analysis is performed, then the overall results are shown by a diamond at the bottom (see Fig. 8). In this graph, each black circle represents an individual study, and the horizontal lines through each show the confidence intervals. Sometimes, the studies are shown by squares proportional to the size of the study, and it is clear that larger studies tend to have narrower confidence intervals. The width of the diamond denotes the confidence interval around the overall result. This demonstrates one of the major advantages of a systematic review—combining several small studies with relatively wide confidence intervals can result in an overall estimate that is considerably more precise and therefore much more useful for informing practice.

One of the major disadvantages of a systematic review is the problem of 'publication bias'. This arises because the direction and statistical significance of research results will affect the likelihood of it getting published. This form of bias starts

with the researchers themselves, who are less likely to write up and submit for publication the results of a study if it does not show something new and interesting. It extends to journal reviewers, who are likely to be more impressed by significant findings regardless of the study quality, and to journal editors who want to carry exciting research 'stories', much like newspaper editors. This is a serious problem when we try to combine all the evidence on one subject. We might find six studies saying that music therapy reduces severe depression, but what if there were another six studies which found no benefit at all (or even a negative effect), and these were not published? Then, our systematic review would draw a very erroneous conclusion. One way of testing for the existence of publication bias in a review is to plot the results of the various studies in what is called a 'funnel plot'. This identifies whether there appear to be any studies missing from the general pattern of results, but this approach only works when there are a good number of studies under consideration. A thorough search of the 'grey literature'—that is research not published in the peer-reviewed literature—is the best way to minimise publication bias. This might involve looking for Ph.D. theses and conference proceedings, internal reports of relevant organisations and talking to experts in the field.

Discussion Task
How can systematic reviews contribute to Public Health Intelligence?

Which Is the Most Appropriate Study Design?

An awareness of the hierarchy of evidence is useful for judging the reliability of research evidence. And while it is usually preferable to seek out a systematic review of all available evidence to answer a particular question, rather than relying on a single study, we cannot say that an RCT is always the best study design to use. It is more helpful to think about different study designs suiting different situations. Consider the following questions pertaining to tobacco smoking. If you wanted to answer the question 'What is the prevalence of smoking in this population, and how does it differ according to ethnicity?', then a cross-sectional study would be the most appropriate way to address this question. If you wanted to know how life-long smoking affects the risk of coronary heart disease and cancer, then a cohort study would enable you to answer this. But if the question was 'What is the most effective treatment to quit smoking?', then an RCT comparing various treatments would give the best quality evidence to answer this question. Finally, going beyond the traditional epidemiology discussed in this chapter, if you wanted to know why people continue to smoke, even when it is known to be harmful to health, then a qualitative approach would be best (i.e. talking to people to understand their decisions). Decisions about the most appropriate study design, therefore, depend upon an appreciation of the advantages and disadvantages of each (see Fig. 9).

Study Design	Advantages	Disadvantages
Case series	Quick, based on existing case notes	No control group, hypothesis generating only
Ecological study	Uses existing data sources	Depends on quality of data, ecological fallacy
Cross-sectional study	Good for descriptive statistics e.g. prevalence. Can collect data on a range of exposures and outcomes	Exposure and outcome measured at the same point in time Bias associated with poor response rates
Case-control study	Good for rare outcomes Can investigate multiple exposures Can be quick (e.g outbreak investigation)	Not good for rare exposures Recall bias Appropriate selection of controls Cannot estimate incidence
Cohort study	Good for measuring incidence Exposure measured before outcome. Can collect data on a range of exposures and outcomes Can investigate rare exposures if sample selected accordingly	Takes longer to collect data Drop-out over time leads to bias Difficult to control for confounding
Randomised Controlled Trial	Controls for confounding through randomisation Can collect data on multiple outcomes	Takes longer to collect data Can only compare 2 (or sometimes 3) interventions
Systematic review	Provides a summary of all available evidence Systematically addresses quality of individual studies	Prone to publication bias There may be heterogeneity between studies (in terms of population, intervention and

Fig. 9 Advantages and disadvantages of different study designs

Ethical Issues

A key ethical issue with all research designs involving primary data collection from human participants is consent. All participants should give consent to participate before they enter the study, in full knowledge of what this involves and understanding that they have the right to withdraw from the study at any point. There should be no coercion or pressure to take part. There are procedures in place for parents or guardians to give consent for children. Consent is also required to gain data on study participants through data linkage. When it comes to using anonymised secondary data, then access to the data will depend what purpose the data was collected for in the first place, and what consents if any have been obtained already for its use.

The sample size should be large enough to detect a difference or association if one really exists; otherwise, it is a waste of resources and unfair to the participants who are contributing to a study that has not been properly designed. Sample size calculations must take into account likely response rates and anticipated dropout over the course of follow-up. Studies should however not normally include more participants than is necessary, particularly if the research in invasive or particularly onerous for the participants.

Expenses incurred through being part of a study (e.g. travel) should be reimbursed. Participants may also be recompensed for their time, but incentives to take part are generally thought to be more problematic ethically. Nevertheless, the use of incentives can be very effective in improving response rates (Edwards et al. 2009), and might be approved by ethics committees when weighing up the benefits of achieving an adequate sample size.

Another ethical issue is what should be done if, during the course of a research study, a serious health condition or a high level of risk is discovered (e.g. dangerous drinking behaviour or suicidal thoughts). Protocols to deal with this situation must be agreed in advance. Although it is good practice to feed back the overall results of the study to participants, researchers need to decide whether to feed back any of the individual results. Participants of large cohort studies in the United States, for example, are often incentivised to take part by what they see as ‘free health checks’, whereas this type of individual feedback is less common in similar studies in the UK. Any potentially harmful effects of the research on the participants must be considered. These may be physical or mental. If asking questions about deliberate self-harm or drug misuse for example, it would be good practice to signpost relevant sources of help and information, and even to include a hotline number.

A key ethical issue in RCTs is whether it is appropriate to randomise at all. Although to epidemiologists the reasons for randomising are clear and we think of this as being the only sure way to test an intervention, it is much harder to convince the general public and even other professionals that randomising patients to receive a treatment or not is a good idea. There is a fear that this will lead to an apparent ‘postcode lottery’ with some people in an area receiving an intervention and others not. (One way round this problem is to use a cluster RCT, as described above.) An RCT is appropriate when there is what we call ‘clinical equipoise’. That means that we genuinely don’t know whether the new treatment to be tested is more (cost-)

effective than the standard treatment or, more generally, whether the intervention works. This applies whether we are talking about a new drug to treat cancer or a social policy intervention such as offering free nursery places to preschool children, or free school meals to all school children. Although there has traditionally been more acceptance of carrying out RCTs for medical interventions, and they are generally easier to organise than randomised trials of social interventions (which tend to be more complex and evolving), there is a growing trend to assess the effectiveness of policy decisions through the same rigorous approach as has long been applied to medicine.

Discussion Task
Explore some general ethical issues related to the design and conduct of epidemiological studies.

The Relevance of Epidemiology to Public Health Intelligence Today

Epidemiological information is used to investigate patterns of ill-health, generate and test hypotheses for the causes of ill-health, take action to prevent illness and promote health, and finally to evaluate existing health services and Public Health interventions. The role of epidemiology in Public Health practice is further discussed by Brownson (2011, p. 1).

The following examples of recent public heath news stories illustrate the application of epidemiology in practice: (1) an inner-city neighbourhood's concern about the rise in the number of children with asthma (*patterns of ill-health*), (2) findings published in a leading medical journal of an association between workers exposed to a chemical agent and an increased risk of cancer (*testing hypotheses*), (3) the revised recommendations for who should receive influenza vaccinations (*action to prevent illness*), and (4) the extensive disease-monitoring strategies being implemented in a city recently affected by a massive hurricane (*to enable evaluation of the disaster response*). In each case, the story relies on analysis and collation of Public Health intelligence. Identifying relevant data of the highest possible quality, understanding its limitations and interpreting it as useful information to help with Public Health planning and decision-making is the remit of Public Health Intelligence. London Health Observatory (2006) considers Public Health intelligence as 'The use of population information which has been analysed, interpreted and presented in clear and accessible form to inform proposed improvements to health services or to those factors which determine health, and which allow later examination to assess success'. This role has gained increasing importance with the shift towards evidence-based practice in Public Health (Killoran and Kelly 2009) which has followed the evidence-based medicine movement (Sackett et al. 1996).

Another recent trend is the need to include economic evaluations of Public Health interventions and health services, as well as evaluations of their efficacy and effectiveness. Public Health Economics is an area in which the Public Health workforce requires further training and capacity development. It includes techniques such as Social Return on Investment, which aims to capture all costs and benefits to society of a particular course of action, rather than those which are immediate, direct and easy to measure.

Many Public Health interventions are complex, spanning both health and social care and the anticipated benefits to society are often long term. In a climate of limited resources with a perpetual threat of funding cuts, the ability to capture data to accurately measure the return on investment in this way is clearly a priority for Public Health teams.

Discussion Task
Why is epidemiology the foundation and core principle of Public Health and Public Health intelligence?

Conclusion

Epidemiology is the cornerstone of Public Health. It employs rigorous methods and a quantitative approach to study the health of populations rather than individuals. Epidemiological methods are used to identify the causes of poor health, measure the strength of association between risk factors and disease, and evaluate interventions and monitor changes in population health over time. In short, epidemiology provides the necessary information for Public Health actions and decisions to be taken (see Carneiro and Howard 2011).

The main epidemiological study designs have been described, along with their strengths and limitations. In Public Health, interventions are often complex, and the exposures of interest are often known to be harmful in some way, or difficult to randomise for some other reason. In this situation, it is sometimes possible to conduct a natural experiment, but very often we have to rely heavily on observational study designs. Given that these are prone to bias and confounding, a pragmatic approach to identifying and quantifying likely biases is advisable. For a warning about the scale and implications of these biases, one needs only look at the contrasting evidence from cohort studies and randomised controlled studies on topics such as vitamin supplementation (Hooper et al. 2001; Egger et al. 2008).

Although the nature of epidemiology is changing, the key concept—that of assessing associations between potential risk factors and diseases or other health outcomes—remains the same. Developments in computing power make it ever more easy to model these relationships statistically, controlling for confounding, and assess the role of chance. The challenges of myriad forms of bias, and residual confounding, and the critical question of whether a relationship is causal are still very current.

References

Boyd, A., Golding, J., Macleod, J., Lawlor, D. A., Fraser, A., Henderson, J., et al. (2013). Cohort profile: The 'children of the 90s'—The index offspring of the Avon Longitudinal Study of Parents and Children. *International Journal of Epidemiology, 42*(1), 111–127.

Brownson, R. C. (2011). Epidemiology in Public Health practice [review of the book, by Haveman-Nies, A., Jansen, S., van Oers, H. and van 't Veer, P.]. *American Journal of Epidemiology, 174*(7), 871–872.

Carey, N. (2012). *The epigenetics revolution: How modern biology is rewriting our understanding of genetics, disease and inheritance*. London: Icon Books Ltd.

Carneiro, I., & Howard, N. (2011). *Introduction to epidemiology*. Maidenhead, England: McGraw-Hill Education.

Cochrane, A. L. (2009). *One man's medicine: An autobiography of Professor Archie Cochrane* (2nd ed.). Cardiff, England: Cardiff University.

Dyrstad, S. M., Hansen, B. H., Holme, I. M., & Anderssen, S. A. (2013). Comparison of self-reported versus accelerometer-measured physical activity. *Medicine and Science in Sports and Exercise, 46*(1), 99–106.

Edwards, P. J., Roberts, I., Clarke, M. J., Diguiseppi, C., Wentz, R., Kwan, I., et al. (2009). Methods to increase response to postal and electronic questionnaires. *Cochrane Database of Systematic Reviews, 8*(3), MR000008.

Egger, M., Davey, S. G., & Altman, D. G. (2008). *Systematic reviews in health care: Meta-analysis in context* (2nd ed.). London: Wiley-Blackwell.

Farr, W. (1974). Report on the mortality of cholera in England, 1848-9. In H. Ratcliffe (Ed.), Mortality in 19th century Britain. London: Gregg. Retrieved September 9, 2015, from http://johnsnow.matrix.msu.edu/work.php?id=15-78-12A

Hallquist, A., & Jansson, P. (2005). Self-reported diagnostic X-ray investigation and data from medical records in case-control studies on thyroid cancer: Evidence of recall bias? *European Journal of Cancer Prevention, 14*(3), 271–276.

Hooper, L., Ness, A. R., & Davey Smith, G. (2001). Meta-analysis of effect of high vs low vitamin E intake on cardiovascular mortality for observational and intervention studies (letter). *Lancet, 357*, 1705.

Killoran, A., & Kelly, M. P. (2009). *Evidence-based Public Health: Effectiveness and efficiency*. Oxford, England: Oxford University Press.

Last, J. M. (2001). *A dictionary of epidemiology* (4th ed.). Oxford, England: Oxford University Press.

London Health Observatory. (2006). Summary-mapping health intelligence in London. Retrieved August 24, 2015, from http://www.lho.org.uk/viewResource.aspx?id=10898

Madsen, K. M., Hviid, A., Vestergaard, M., Schendel, D., Wohlfahrt, J., Thorsen, P., et al. (2002). A population-based study of measles, mumps, and rubella vaccination and autism. *New England Journal of Medicine, 347*(19), 1477–1482.

McBride, W. G. (1961). Thalidomide and congenital abnormalities. *Lancet, 2*, 1358.

Murray, R. L., Leonardi-Bee, J., Marsh, J., Jayes, L., Li, J., Parrott, S., et al. (2013). Systematic identification and treatment of smokers by hospital based cessation practitioners in a secondary care setting: Cluster randomised controlled trial. *British Medical Journal, 347*, f4004.

Sackett, D. L., Rosenberg, W. M. C., Gray, J. A. M., Haynes, R. B., & Richardson, W. S. (1996). Evidence-based medicine: What it is and what it isn't. *British Medical Journal, 312*, 71–72.

Snow, J. (1855). *On the mode of communication of cholera* (2nd ed.). London: Churchill.

Tannous, L. K., Barlow, G., & Metcalfe, N. H. (2014). A short clinical review of vaccination against measles. *Journal of Royal Society of Medicine Open, 5*(4), 1–6.

Wakefield, A. J., Murch, S. H., Anthony, A., Linnell, J., Casson, D. M., Malik, M., et al. (1998). Ileal-lymphoid-nodular hyperplasia, non-specific colitis and pervasive developmental disorder in children. *Lancet, 35*, 637–641.

Wilkinson, R. G., & Pickett, K. (2010). *The spirit level: Why equality is better for everyone* (2nd ed.). London: Penguin Books.

Recommended Reading

Bhopal, R. (2008). *Concepts of epidemiology* (2nd ed.). Oxford, England: Oxford University Press.

Bonita, R., Beaglehole, R., & Kjellström, T. (2006). *Basic epidemiology* (2nd ed.). Geneva, Switzerland: World Health Organization.

Centre for Disease Control and Prevention. (2006). *An introduction to applied epidemiology and biostatistics*. Atlanta, GA: CDC.

Gordis, L. (2014). *Epidemiology* (5th ed.). Oxford, England: Elsevier Saunders.