EPIDEMIOLOGY, EVIDENCE-BASED MEDICINE AND PUBLIC HEALTH

Lecture Notes

Yoav Ben-Shlomo
Sara T. Brookes
Matthew Hickman

6th Edition

WILEY-BLACKWELL

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Epidemiology, Evidence-based Medicine and Public Health

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Preface

It was both an honour and a challenge to take on the revision of a 'classic' textbook such as *Lecture Notes in Epidemiology and Public Health Medicine* already in its fifth edition (originally written by Richard Farmer and David Miller, the latter author being subsequently replaced by Ross Lawrenson). Much has changed in the field of epidemiology, public health and the scientific world in general since the first edition was published almost 35 years ago. When the current editors sat down to plan this new sixth edition, we felt there was now a need to restructure the book overall rather than updating the existing chapters. In the intervening period, we have seen the rise of new paradigms (conceptual ideas) such as life course and genetic epidemiology and the advance of evidence-based medicine. The latter was first covered in the fifth edition by a single chapter. We felt the need to rebalance the various topics so this new edition has now got three main subsections: Epidemiology, Evidence Based Medicine (EBM) and Public Health. Whilst much of the epidemiology section will appear familiar from the previous edition, we have added a new chapter on genetic epidemiology and there is a whole chapter on causality as this is so fundamental to epidemiological research and remains an issue with conventional observational epidemiology. The new section on EBM is very different with separate chapters on diagnosis, prognosis, effectiveness, systematic reviews and health economics. The Public Health section is less focussed on the National Health Service and we now have a new chapter on global health; a major topic given the challenges of 'climate change' and the interrelated globalised world that we all now live in. We have also included a new chapter specifically on the difficult task of evaluating public health interventions, which presents unique challenges not found with more straightforward clinical trials. Inevitably, we have had to drop some topics but we believe that overall the new chapters better reflect the learning needs of contemporary students in the twenty-first century. We hope we have remained faithful to the original aims of this book and the previous authors would be proud of this latest edition.

In redesigning the structure of the book we have been guided by three underlying principles:

(1) To fully utilise our collective experience based on decades of teaching undergraduate medical students (Ben-Shlomo, 2010). We have therefore used, where appropriate relevant materials from the courses we run at the University of Bristol that have been refined over many years. We wish to thank the many students we have encountered who have both challenged, provoked and rewarded us with their scepticism as well as enthusiasm. We fully appreciate that some students are put off by the more statistical aspects of epidemiology (a condition we termed 'numerophobia (Ben-Shlomo *et al.*, 2004)). Other students feel passionately about issues such as global health and/or the marked inequalities in health outcomes seen in both developing and developed countries (see http://www.medsin.org/ for more information around student activities).

(2) The need to have a wide range of expertise to stimulate and inspire students. We therefore decided to make this new edition a multi-author book rather than relying on our own expertise.

(3) The desire to make our textbook less anglocentric and of interest and relevance to health professionals and students other than those studying medicine. We appreciate that the examples we have taken are predominantly from a developed world perspective but the fundamental principles and concepts are generic and should form a sound scientific basis for someone wishing to learn about epidemiology, evidence based medicine and public health regardless of their country of origin. It would be wonderful to produce a companion book that specifically uses examples and case studies that are more relevant to developing countries. But that is for the future.

As we work in the United Kingdom, our curriculum is heavily influenced by the recommendations of the UK General Medical Council and the latest version of *Tomorrow's Doctors* (GMC, 2009). We have tried to cover most of the topics raised in sections 10–12 of *Tomorrow's Doctors* though this book will be inadequate on its own for areas such as medical sociology and health psychology, covered in more specialist texts. We appreciate that students are usually driven by the need to pass exams, and the medical curriculum is particularly dense, if you forgive the pun, when it comes to factual material. We have, however, tried to go beyond the simple basics and some of the material we present is somewhat more advanced than that usually presented to undergraduates. This was a deliberate choice as we believe that the inevitable over-simplification or 'dumbing down' can turn some students off this topic. We feel this makes the book not merely an 'exam-passing tool' but rather a useful companion that can be used at a postgraduate level. We believe that students and health-care professionals will rise to intellectual challenges as long as they can see the relevance of the topic and it is presented in an interesting way. We have therefore also included further readings at the end of some chapters for those students who want to learn more about each topic.

We have provided a glossary of terms at the end of the book to help students find the meaning of terms quickly and also highlighted **key terms** in **bold** that may help students revise for exams. Finally we have included some self-assessment questions and answers at the end of each section that will help the student test themselves and provide some feedback on their comprehension of the knowledge and concepts that are covered in the book. We appreciate that very few medical students will become public health practitioners, though somewhat more will become clinical epidemiologists and/or health service researchers. However the knowledge, skills and '*scepticaemia*' that we hope students gain from this book, will serve them well as future doctors or other health care professionals regardless of their career choice. Improving the health of the population and not just treating disease is the remit of all doctors. As it states in *Tomorrow's Doctors:*

> *Today's undergraduates – tomorrow's doctors – will see huge changes in medical practice. There will be continuing developments in biomedical sciences and clinical practice, new health priorities, rising expectations among patients and the public, and changing societal attitudes. Basic knowledge and skills, while fundamentally important, will not be enough on their own. Medical students must be inspired to learn about medicine in all its aspects so as to serve patients and become the doctors of the future.*

Yoav Ben-Shlomo
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Part 1

Epidemiology

1

Epidemiology: defining disease and normality

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Learning objectives

In this chapter you will learn:

- ✓ what is meant by the term epidemiology;
- ✓ the concepts underlying the terms 'normal, abnormal and disease' from a (i) sociocultural, (ii) statistical, (iii) prognostic, (iv) clinical perspective;
- ✓ how one may define a case in epidemiological studies.

What is epidemiology?

Trying to explain what an epidemiologist does for a living can be complicated. Most people think it has something to do with skin (so you're a dermatologist?) wrongly ascribing the origin of the word to epidermis. In fact the Greek origin is *epidēmia* – 'prevalence of disease' (taken from the Oxford online dictionary) – and the more appropriate related term is epidemic. The formal definition is

> *'The study of the occurrence and distribution of health-related states or events in specified populations, including the study of the determinants influencing such states and the application of this knowledge to control the health problems' (taken from the 5th edition of the Dictionary of Epidemiology)*

An alternative way to explain this and easier to comprehend is that epidemiology has three aims (3 Ws).

Whether	To describe *whether* the burden of diseases or health-related states (such as smoking rates) are similar across different populations (descriptive epidemiology)
Why	To identify *why* some populations or individuals are at greater risk of disease (risk-factor epidemiology) and hence identify causal factors
What	To measure the need for health services, their use and effects (evidence-based medicine) and public policies (Public Health) that may prevent disease – *what* we can do to improve the health of the population

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Population versus clinical epidemiology – what's in a name?

The concept of a population is fundamental to epidemiology and statistical methods (see Chapter 3) and has a special meaning. It may reflect the inhabitants of a geographical area (lay sense of the term) but it usually has a much broader meaning to a collection or unit of individuals who share some characteristic. For example, individuals who work in a specific industry (e.g. nuclear power workers), born in a specific week and year (birth cohort), students studying medicine etc. In fact, the term population can be extended to institutions as well as people; so, for example, we can refer to a population of hospitals, general practices, schools etc.

Populations can either consist of individuals who have been selected irrespective of whether they have the condition which is being studied or specifically because they have the condition of interest. Studies that are designed to try and understand the causes of disease (**aetiology**) are usually population-based as they start off with healthy individuals who are then followed up to see which risk factors predict disease (**population-based epidemiology**). Sometimes they can select patients with disease and compare them to a control group of individuals without disease (see Chapter 5 for observational study designs). The results of these studies help doctors, health-policy-makers and governments decide about the best way to prevent disease. In contrast, studies that are designed to help us understand how best to diagnose disease, predict its natural history or what is the best treatment will use a population of individuals with symptoms or clinically diagnosed disease (**clinical epidemiology**). These studies are used by clinicians or organisations that advise about the management of disease. The term clinical epidemiology is now more often referred to as evidence-based medicine or health-services research. The same methodological approaches apply to both sets of research questions but the underlying questions are rather different.

One of the classical studies in epidemiology is known as the Framingham Heart Study (see http://www.framinghamheartstudy.org/about/history.html). This study was initially set up in 1948 and has been following up around 5200 men and women ever since (prospective cohort study). Its contribution to medicine has been immense, being one of the first studies to identify the importance of elevated cholesterol and high blood pressure in increasing the risk of heart disease and stroke. Subsequent randomised trials then went on to show that lowering of these risk factors could importantly reduce risk of these diseases. Furthermore the Framingham risk equation, a prognostic tool, is commonly used in primary care to identify individuals who are at greater risk of future coronary heart disease and to target interventions (see http://hp2010.nhlbihin.net/atpiii/calculator.asp).

Regardless of the purpose of epidemiological research, it is always essential to define the disease or health state that is of interest. To understand disease or pathology, we must first be able to define what is normal or abnormal. In clinical medicine this is often obvious but as the rest of this chapter will illustrate, epidemiology has a broader and often pragmatic basis for defining disease and other health-related states.

What is dis-ease?

Doctors generally see a central part of their job as treating people who are not 'at ease' – or who in other words suffer 'dis-ease' – and tend not to concern themselves with people who are 'at ease'. But what is a disease? We may have no difficulty justifying why someone who has had a cerebrovascular accident (stroke), or someone who has severe shortness of breath due to asthma, has a disease. But other instances fit in less easily with this notion of disease. Is hypertension (high blood pressure) a disease state, given that most people with raised blood pressure are totally unaware of the fact and have no symptoms? Is a large but stable port wine stain of the skin a disease? Does someone with very protruding ears have a disease? Does someone who experiences false beliefs or delusions and imagines her/him-self to be Napoleon Bonaparte suffer from a disease?

The discomfort or 'dis-ease' felt by some of these individuals – notably those with skin impairments – is as much due to the likely reaction of others around the sufferer as it is due to the intrinsic features of the problem. Diseases may thus in some cases be dependent on subjects' sociocultural environment. In other cases this is not so – the sufferer would still suffer even if marooned alone on a desert island. The purpose of this next section is to offer a structure to the way we define disease.

A sociocultural perspective

Perceptions of disease have varied greatly over the last 400 years. Particular sets of symptoms and signs have been viewed as 'abnormal' at one point in history and 'normal' at another. In addition, some sets of symptoms have been viewed simultaneously as 'abnormal' in one social group and 'normal' in another.

Examples abound of historical diseases that we now consider normal. The ancient Greek thinker Aristotle believed that women in general were inherently abnormal and that female gender was in itself a disease state. In the late eighteenth century a leading American physician (Benjamin Rush) believed that blackness of the skin (or as he termed it 'negritude') was a disease, akin to leprosy. Victorian doctors believed that women with healthy sexual appetites were suffering from the disease of nymphomania and recommended surgical cures.

There are other examples of states that we now consider to be diseases, which were viewed in a different light historically. Many nineteenth-century writers and artists believed that tuberculosis actually enhanced female beauty and the wasting that the disease produces was viewed as an expression of angelic spirituality. In the sixteenth and seventeenth centuries gout (joint inflammation due to deposition of uric acid) was widely seen as a great asset, because it was believed to protect against other, worse diseases. Ironically, recent research interest has suggested a potential protective role of elevated uric acid, which may cause gout, for both heart and Parkinson's disease.

In Shakespeare's time melancholy (what we would now call depression) was regarded as a fashionable state for the upper classes, but was by contrast stigmatised and considered unattractive among the poor. The modern French sociologist Foucault points out that from the eigtheenth century onwards those who showed signs of what we would now call mental illness were increasingly confined in institutions, as tolerance of 'unreason' declined. Whereas previously 'mad' people had often been viewed as having fascinating and desirable powers (and were legitimised as holy fools and jesters), increasingly they were seen as both disruptive and in need of treatment. Other examples exist of the redefinition of socially unacceptable behaviour as a disease. Well into the second half of the last century single mothers were viewed as being ill and were frequently confined for many years in psychiatric institutions.

As some diseases have been accepted as part of the normal spectrum of human behaviours so new ones have been labelled. Newly recognised diseases include alcoholism (previously thought of simply as heavy drinking), suicide (previously thought of as a criminal offence, it was illegal in the UK until the 1960s so that failed suicides were prosecuted and successful suicides forfeited all their property to the State), and psychosomatic illness (previously dismissed as mere malingering).

Some new disease categories have arisen simply because new tests and investigations allow important differences to be recognised among what were previously thought of as single diseases. For example people died in past times of what was believed to be the single disease of dropsy (peripheral oedema), which we now know to be a feature of a wide range of diseases ranging across primary heart disease, lung disease, kidney disease and venous disease of the legs. There are still disagreements in modern medicine about the classification of disease states. For example, controversy remains around the underlying pathophysiology of chronic fatigue syndrome (myalgic encephalomyelitis) and Gulf War syndrome.

The sociocultural context of health, illness and the determinants of health-care-seeking behaviour as well as the potential adverse effects of labelling and stigma are main topics of interest for medical sociologists and health psychologists and the interested reader may wish to read further in other texts (see Further reading at the end of this chapter).

Abnormal as unusual (statistical)

In clinical medicine – especially in laboratory testing – it is common to label values that are unusual as being abnormal. If, for example, a blood sample is sent to a hospital haematology laboratory for measurement of haemoglobin concentration the result form that is returned may contain the following guidance (the absolute values will differ for different laboratories and units will differ by country):

Male reference range	Female reference range
130–170 g/L	115–155 g/L

This **reference range** is derived as follows: a large number (several hundred) of **samples** from people believed to be free of disease (usually blood donors) are measured and the reference range is defined as that central part of the range which contains 95% of the values. By definition, this approach will result in 5% of individuals who may be completely well, being classified as having an **abnormal** test result.

Normal (Gaussian) distributions

In practice, as with haemoglobin concentration above, many distributions in medical statistics may be described by the **Normal**, also known as **Gaussian distribution**. It is worth noting that the statistical term for 'Normal' bears no relation to the general use of the term 'normal' by clinicians. In statistics, the term simply relates to the name of a particular form of frequency distribution. The curve of the Normal distribution is symmetrical about the **mean** (see Chapter 2) and bell-shaped.

The theoretical Normal distribution is continuous. Even when the variable is not measured precisely, its distribution may be a good approximation to the Normal distribution. For example in Figure 1.1, heights of men in South Wales were measured to the nearest cm, but are approximately Normal.

Abnormal as increased risk of future disease (prognostic)

An alternative definition of abnormality is one based on an increased risk of future disease. A biochemical measure in an asymptomatic (undiagnosed) individual may or may not be associated with future disease in a **causal** way (see Chapter 7). For example, a raised C-reactive protein level in the blood indicates infection or inflammation. Whilst noncausally related, epidemiological studies demonstrate that C-reactive protein can also predict those at an increased future risk of coronary heart disease (CHD). Treatments focused on lowering C-reactive protein will not necessarily reduce the risk of CHD.

In a man of 50 years a systolic blood pressure of 150 mm Hg is well within the usual range and may not produce any clinical symptoms. However, his risk of a fatal myocardial infarction (heart attack) is about twice that of someone with a low blood pressure.

- Does he have a disease, and should he be treated?
- What factors might influence this decision?

These are important questions to consider when we come to think of disease in terms of increased risk of future adverse health outcomes.

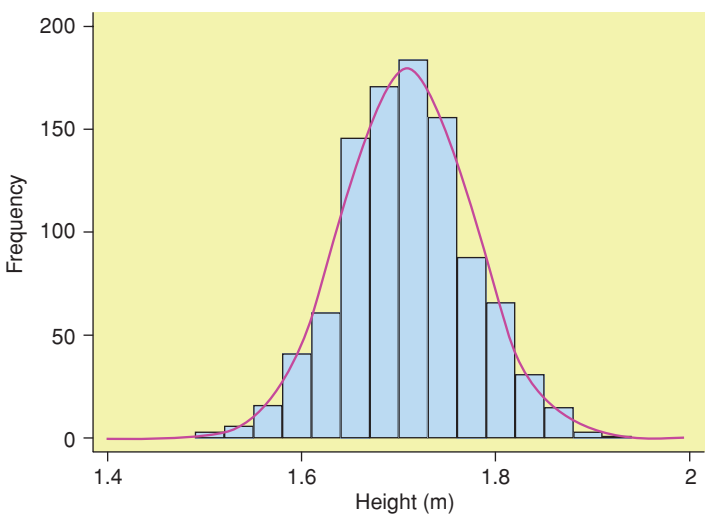

Figure 1.1 Heights of 1,000 men in South Wales.
Note: This figure is known as a **histogram** and is used for displaying grouped numerical data (see Chapter 2) in which the relative frequencies are represented by the areas of the bars (as opposed to a **bar chart** used to display categorical data, where frequencies are represented by the heights of the bars).
The superimposed continuous curve denotes the theoretical Normal distribution.

Thresholds for introducing treatment for blood pressure have changed over the years, generally drifting downwards. This is due to two main factors:

(1) researchers have gradually extended their limits of interest as they have become more confident that blood pressure well within usual limits may have adverse effects in the future.

(2) newer drugs have tended to have fewer and less dangerous side effects, making it reasonable to consider extending treatment to lower levels of blood pressure, where the benefits – though present – are less striking.

Blood glucose levels provide similar problems to blood pressure levels – specifically, for type II diabetes which is treated with diet control, tablets and occasionally insulin (rather than type I which requires insulin as a life-saving measure). At what blood glucose level should one attach the label 'diabetic' and consider starting treatment? To address these questions large prospective studies (called **cohort studies**) are required. In such studies, subjects have a potential risk factor such as blood glucose levels measured at the beginning of the study. They are then followed up, sometimes for many years, to examine whether rates of disease differ according to levels of blood glucose at the start of the study.

Does a fasting glucose in a healthy individual have any implication for their future health?

The glucose tolerance test is commonly used as a diagnostic aid for diabetes. In one of the very early epidemiological studies, conducted in Bedford UK (Keen *et al.*, 1979), 552 subjects had their blood glucose measured when fasting and again two hours after a 50 g glucose drink. On the basis of this they were classified as having high, medium or low glucose levels. The cohort was then followed for ten years, at which point the pattern of deaths that had occurred was as illustrated in Table 1.1.

Amongst both men and women, those with high levels of glucose following the glucose tolerance test had an increased risk of all causes and cardiovascular death. In addition, the female medium glucose group had an increased risk compared to the low glucose group. This additional risk is far less dramatic amongst the men in this study. Basing a definition of abnormality on future 10-year risk of death, treatment might be considered for women with a medium glucose level in addition to those with a high glucose level.

Based on studies such as this, the World Health Organisation (WHO) recommends levels of blood glucose, which should be regarded as indicating diabetes and therefore considered for treatment (fasting glucose $\geq$7.0 mmol/L (126 mg/dl) and/or 2 hour post-load glucose $\geq$11.1 mmol/L (200 md/dl). It also identifies an intermediate risk group who are said to have Impaired Glucose Tolerance or borderline diabetes (fasting glucose $<$7.0 mmol/L and 2 hour post-load glucose $\geq$7.8 mmol/L but $<$11.1 mmol/L). Such individuals are not generally treated but may legitimately be kept under increased surveillance. However, the increased risk of cardiovascular disease appears to show a linear relationship with fasting glucose with no obvious threshold. A recent WHO report concluded 'there are insufficient data to accurately define normal glucose levels, the term normoglycaemia should be used for glucose levels associated with low risk of developing diabetes or cardiovascular disease' (WHO/IDF, 2006).

Abnormal as clinical disease

It is better to define values of a particular test as abnormal if they are clearly associated with the presence of a disease state – rather than simply being unusual. However this is often less than straightforward.

The range of values describing diseased individuals is rarely clearly and completely separated from that for healthy individuals. The nice bell shaped curve described above may actually be bimodal with a second superimposed distribution either at the top (see Figure 1.2) or bottom end or both. This overlap means that there will be healthy people with 'abnormal' results and people with disease with apparently 'normal' results (see Chapter 9 on diagnostic tests for more details).

For example, it is widely believed by many doctors that chronic (i.e. of long duration) mildly reduced haemoglobin (Hb) levels (of 100–110 g/L) or anaemia, such as might be seen in menstruating females, may account for fatigue and tiredness. In a study of 295 subjects in South Wales no association was found between Hb level and fatigue until the Hb level fell to well below 100 g/L (Wood

Table 1.1 Glucose tolerance [a] and mortality in the Bedfordshire cohort.

	Men			Women		
Glucose group	Number	All deaths	Cardiovascular deaths	Number	All deaths	Cardiovascular deaths
High glucose	51	19 (37.2%)	15 (29.4%)	63	25 (39.7%)	18 (28.5%)
Medium glucose	130	29 (22.3%)	19 (14.6%)	119	35 (29.4%)	25 (21.0%)
Low glucose	104	20 (19.2%)	12 (11.5%)	85	9 (10.6%)	4 (4.7%)

[a] Oral glucose tolerance test: After an overnight fast the participant is asked to drink a solution containing 1.75 g/kg body weight (maximum 75 g) of glucose dissolved in 250 ml of water within 2–3 minutes. Blood samples are taken just before and two hours after ingestion of the glucose solution.

and Elwood, 1966). Fatigue is common in the population generally for a wide range of reasons and is only strongly associated with Hb level among severely anaemic individuals. A longstanding Hb of between 100 and 115 g/L (which it should be noted is outside the laboratory reference range, whose lower limit is 115 in women and 130 in men) in an otherwise healthy person who is complaining only of fatigue shouldn't therefore generally be considered as responsible for this symptom.

In general, the definition of abnormality as clinical abnormality is both logical and clear. It is nevertheless an approach that usually involves thinking in terms of the probability of disease being present, rather than the certainty.

Defining a case in epidemiological studies

Before an epidemiologist is able to study any disease s/he needs to develop and agree upon a case definition: a definition of disease that is as free as possible of ambiguity. This should enable researchers to apply this definition reliably on a large number of subjects, without access to sophisticated investigations. Because epidemiological case definitions are not used as a guide to the treatment of individuals they may differ from the sorts of definitions used in routine clinical practice.

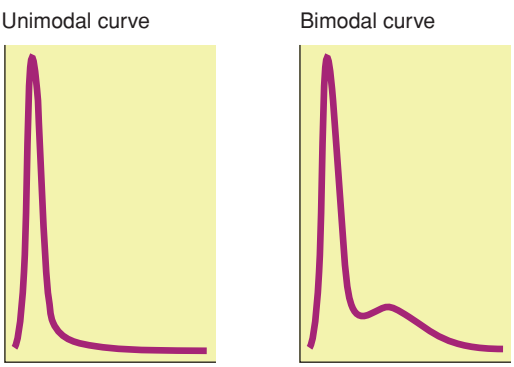

Figure 1.2 Potential distributions (taken from WHO report (2006) Definition and diagnosis of diabetes mellitus and intermediate hyperglycaemia).

Chronic Fatigue Syndrome provides a good example of the problems of agreeing on a case definition for a rather ill-defined condition. At a meeting in Oxford in 1990, 28 UK experts met to agree a case definition for Chronic Fatigue Syndrome (Sharpe *et al.*, 1991). They came up with the following:

- Fatigue must be the principal symptom.
- There must be a definite point of onset (fatigue must not have been lifelong).
- Fatigue must have been present for at least 6 months and present for at least 50% of that time.
- Other symptoms may be present – e.g. myalgia (muscle pain), mood and sleep disturbance.
- Certain patients should be excluded: those with medical conditions known to produce chronic fatigue (such as severe anaemia); patients with a current diagnosis of schizophrenia, manic-depressive illness, substance abuse, eating disorder.

What is being attempted here is to produce a reasonably reliable definition (one that will classify the same person in the same way when used repeatedly by different observers) that can be applied without recourse to sophisticated tests, that excludes already well recognised causes of fatigue such as anaemia but which encompasses relevant patients.

This has now been updated in the UK by NICE guidelines (2007) that state a diagnosis should be

made after other possible diagnoses have been excluded and the symptoms have persisted for 4 months in an adult and 3 months in a child or young person (a shorter duration than previously stated). They suggest guidelines based on expert consensus opinion (see Box 1.1).

The use by both UK and American epidemiologists of the descriptive term 'Chronic Fatigue Syndrome' rather than 'Post-viral Fatigue Syndrome' is deliberate. The term implies no particular aetiology (cause) unlike 'Post-viral Fatigue Syndrome', which presupposes that a viral cause is established and which may therefore inhibit exploration of other possible causes.

The NICE definition is intended to be used by clinicians and often 'research case definitions' are stricter so that some true cases are missed but you are less likely to include any false positive cases. So for example the USA Centre for Disease Control and Prevention case definition still has a requirement for a 6-month minimum period of symptoms.

Box 1.1 Symptoms that may indicate CFS/ME.

Consider the possibility of CFS/ME if a person has:

- fatigue with all of the following features:
  - new or a specific onset (i.e. not lifelong)
  - persistent and/or recurrent
  - unexplained by other conditions
  - has resulted in a substantial reduction in *activity* level characterised by post-exertional malaise and/or fatigue (typically delayed, e.g. by at least 24 hours, with slow recovery over several days)

and

- one or more of the following symptoms:
  - difficulty with sleeping, such as insomnia, hypersomnia, unrefreshing sleep, a disturbed sleep–wake cycle
  - muscle and/or joint pain that is multi-site and without evidence of inflammation
  - headaches
  - painful lymph nodes without pathological enlargement
  - sore throat
  - cognitive dysfunction, such as difficulty thinking, inability to concentrate, impairment of short-term memory, and difficulties with word-finding, planning/organising thoughts and information processing
  - physical or mental exertion makes symptoms worse
  - general malaise or 'flu-like' symptoms
  - dizziness and/or nausea
  - palpitations in the absence of identified cardiac pathology

The symptoms of CFS/ME fluctuate in severity and may change in nature over time.
Source: NICE (2007) *NICE Quick Reference Guide – Chronic Fatigue Syndrome/myalgic Encephalomyelitis (or Encephalopathy*. NICE, UK).

KEY LEARNING POINTS

- Epidemiology is the study of the population determinants and distribution of disease in order to understand its causes and prevention
- Epidemiology studies populations of either healthy individuals (before disease onset) or patients with symptoms or established disease
- The acceptance of what is a disease changes over time with some disease disappearing e.g. homosexuality, and others appearing, e.g. Attention Deficit Hyperactivity Disorder
- Sociocultural factors can influence whether some societies label different phenomena as disease
- Doctors often define abnormality as lying outside the normal range which reflects a statistical definition but may not be due to disease
- Screening can identify risk factors, not associated with symptoms, which predict future disease (prognostic) and may be amenable to intervention thereby preventing disease
- Doctors usually have to diagnose disease from patients, symptomatic complaints and/or physical abnormalities
- Epidemiological studies have to specify clear objective criteria, usually more rigorous than that used by doctors in everyday practice, that they use to identify cases in research

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2

Measuring and summarising data

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Learning objectives

In this chapter you will learn:

- ✓ how we classify different types of variables;
- ✓ to recognise and define measures of central tendency, variability and range;
- ✓ four measures of disease frequency: prevalence, risk, incidence rate and odds;
- ✓ to identify exposure and outcome variables;
- ✓ to define and calculate absolute and relative measures of association between an exposure and outcome.

Epidemiology is a **quantitative** discipline. It involves the collection of data within a **study sample** and analyses using statistical methods to summarise, examine associations and test specific hypotheses from which it infers generalisable conclusions about **aetiology** (causes of disease) and **health care evaluation** in the **target population**. In order to be able to understand epidemiological research, one must have a basic understanding of the statistical tools that are used for data analysis both in epidemiological and basic science research.

Types of variables

A **variable** is a quantity that varies; for example, between people, occasions or different parts of the body. A variable can take any one of a specified set of values. Medical data may include the following types of variables.

Numerical variables

There are two types of **numerical variables**. **Continuous variables** are measurements made on a continuous scale; for example, height, haemoglobin or systolic blood pressure. **Discrete variables** are counts, such as the number of children in a family, or the number of asthma attacks in a week.

Categorical variables

There are two basic types of **categorical variable**, which are variables that take nonnumeric values

Epidemiology, Evidence-based Medicine and Public Health Lecture Notes, Sixth Edition. Yoav Ben-Shlomo, Sara T. Brookes and Matthew Hickman.

and refer to categories of data. Firstly, **unordered categorical variables** are used to class observations into a number of named groups; for example, ethnic group, marital status (single, married, widowed, other), or disease categories. A special case of the unordered categorical variable is one which classes observations into two groups. Such variables are known as **dichotomous** or **binary** and generally indicate the presence or absence of a particular characteristic. Presence versus absence of chest pain, smoker versus nonsmoker, and vaccinated versus unvaccinated are examples of dichotomous or binary variables.

Secondly, **ordered categorical variables** are used to rank observations according to an ordered classification, such as social class, severity of disease (mild, moderate, severe), or stages in the development of a cancer. Often in epidemiological studies a variable may be measured as numerical and then subsequently categorised. For example height may be measured in feet and inches and then categorised as: <5ft, 5ft–5ft 5in, 5ft 5in–6ft, >6ft.

The type of variable will determine how that variable is displayed and what subsequent analyses are carried out. In general, continuous and discrete variables are treated in the same way.

Descriptive statistics for numerical variables

Most medical, biological, social, physical and natural phenomena display variability. Frequency distributions express this variability and are summarised by measures of **central tendency** ('location') and of **variability** ('spread'). We will explore these measures using the following hypothetical data on the number of days spent in hospital by 19 patients following admission with a diagnosis of an acute exacerbation of chronic obstructive airways disease.

3 4 4 6 7 8 8 8 10 10 12 14 14 17 20 25 27 37 42

Measures of central tendency

There are three important measures of central tendency or location.

(1) Mean

The mean is the most commonly used 'average'. It is the sum of all the values in a set of observations divided by the number of observations in that set.

So the mean number of days spent in hospital by the 19 patients is

$$(3+4+4+6+7+8+8+8+10+10+12+14+14+17+20+25+27+37+42)/19 = 276/19 = 14.53 \text{ days.}$$

The algebraic formula for this calculation is given in Table 2.1.

(2) Median

The median is the middle value when the values in a set are arranged in order. If there is an even number of values the median is defined as the mean of the two middle values.

Thus, the median number of days spent in hospital is 10 days (see Figure 2.1).

(3) Mode

The mode is the most frequently occurring value in a set. It is rarely used in epidemiological practice.

The modal number of days spent in hospital is 8 days.

For data presented in grouped form, e.g. if hospital stay were grouped as 0–10, 11–20, 21–30 and 30+ days, we can identify the modal class in this instance as 0–10 days. Thought of in this way, it is a peak on a frequency distribution or histogram. When there is a single mode, the distribution is known as **unimodal**. If there is more than one peak the distribution is said to be **bimodal** (two peaks) or **multimodal**.

Let us assume in the above example that the patient with the longest length of stay actually spent 120 days rather than 42 days in hospital because they could not be sent back home but required placement in a nursing home. This 'unusual' observation (outlier) would have a large effect on the mean value (now 18.6 days) whilst having no effect on the median and could make the performance of one hospital look worse than another depending on which summary statistic was being used for the comparison.

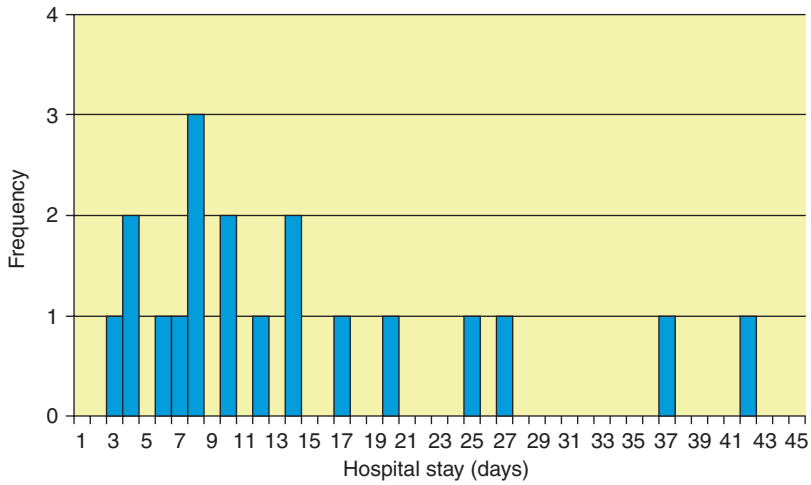

Figure 2.1 Distribution of hospital stay in sample of 19 patients.

Measures of variability

The extent to which the values of a variable in a distribution are spread out a long way or a short way from the centre indicates their variability or spread. There are several useful measures of variability.

(1) Range

The range is simply the difference between the largest and the smallest values.

The range of the number of days spent in hospital following operation for the 19 patients is:

$$42 - 3 = 39 \text{ days.}$$

As a measure of variability, the range suffers from the fact that it depends solely on the two extreme values which may give a quite unrepresentative view of the spread of the whole set of values.

(2) Interquartile range

Quantiles are divisions of a set of values into equal, ordered subgroups. The median, as defined above, delimits the lower and upper halves of the data. Tertiles divide the data into three equal groups, quartiles into four, quintiles into five, deciles into ten, and centiles into 100 subgroups. Measures of variability may thus be the interquartile range (from the first to the third quartile), the 2.5th to 97.5th centile range (containing the 'central' 95% of observations, and so on).

For example, the quartiles for the data on days spent in hospital are 7, 10 and 20 days, so the interquartile range is: 7 days to 20 days

(3) Standard deviation

The standard deviation (SD) is a measure of spread of the observations about the mean. It is based on the deviations (differences) of each observation from the mean value: these deviations are squared to remove the effect of their sign. The SD is then calculated as the square root of the sum of these squared deviations divided by the number of observations minus 1.

The SD of the data on days spent in hospital is calculated as:

$$\sqrt{\frac{(3-14.53)^2+(4-14.53)^2+\ldots+(42-14.53)^2}{19-1}}$$
$$=\sqrt{\frac{2220.7}{18}}=11.11 \text{ days.}$$

The algebraic formula for this calculation is given in Table 2.1. The square of the SD (that is, SD $\times$ SD) is known as the **variance**.

The **Normal** (or **Gaussian**) **distribution** (introduced in Chapter 1) is described entirely by its mean and standard deviation (SD). The mean, median and mode of the distribution are identical and define the location of the curve. The SD determines the shape of the curve, which is tall and