how to read a paper

THE BASICS OF EVIDENCE-BASED MEDICINE

FIFTH EDITION

TRISHA GREENHALGH

WILEY Blackwell

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FIFTH EDITION

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WILEY BMJ|Books

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In November 1995, my friend Ruth Holland, book reviews editor of the *British Medical Journal*, suggested that I write a book to demystify the important but often inaccessible subject of evidence-based medicine. She provided invaluable comments on earlier drafts of the manuscript, but was tragically killed in a train crash on August 8, 1996. This book is dedicated to her memory.

Foreword to the first edition by Professor Sir David Weatherall

Not surprisingly, the wide publicity given to what is now called *evidence-based medicine* has bee greeted with mixed reactions by those who are involved in the provision of patient care. The bulk the medical profession appears to be slightly hurt by the concept, suggesting as it does that unt recently all medical practice was what Lewis Thomas has described as a frivolous and irresponsib kind of human experimentation, based on nothing but trial and error, and usually resulting in precisel that sequence. On the other hand, politicians and those who administrate our health services hav greeted the notion with enormous glee. They had suspected all along that doctors were total uncritical and now they had it on paper. Evidence-based medicine came as a gift from the goo because, at least as they perceived it, its implied efficiency must inevitably result in cost saving.

The concept of controlled clinical trials and evidence-based medicine is not new, however. It recorded that Frederick II, Emperor of the Romans and King of Sicily and Jerusalem, who lived fro 1192 to 1250 ad, and who was interested in the effects of exercise on digestion, took two knights an gave them identical meals. One was then sent out hunting and the other ordered to bed. At the end several hours, he killed both and examined the contents of their alimentary canals; digestion ha proceeded further in the stomach of the sleeping knight. In the 17th century, Jan Baptista va Helmont, a physician and philosopher, became sceptical of the practice of blood-letting. Hence h proposed what was almost certainly the first clinical trial involving large numbers, randomisation an statistical analysis. This involved taking 200–500 poor people, dividing them into two groups b casting lots, and protecting one from phlebotomy while allowing the other to be treated with as muc blood-letting as his colleagues thought appropriate. The number of funerals in each group would h used to assess the efficacy of blood-letting. History does not record why this splendid experiment wa never carried out.

If modern scientific medicine can be said to have had a beginning it was in Paris in the mid-19 century and where it had its roots in the work and teachings of Pierre Charles Alexandre Louis. Lou introduced statistical analysis to the evaluation of medical treatment and, incidentally, showed th blood-letting was a valueless form of treatment, although this did not change the habits of th physicians of the time, or for many years to come. Despite this pioneering work, few clinicians o either side of the Atlantic urged that trials of clinical outcome should be adopted, although th principles of numerically based experimental design were enunciated in the 1920s by the geneticis Ronald Fisher. The field only started to make a major impact on clinical practice after the Secon World War following the seminal work of Sir Austin Bradford Hill and the British epidemiologist who followed him, notably Richard Doll and Archie Cochrane.

But although the idea of evidence-based medicine is not new, modern disciples like David Sacke and his colleagues are doing a great service to clinical practice, not just by popularising the idea b by bringing home to clinicians the notion that it is not a dry academic subject but more a way thinking that should permeate every aspect of medical practice. While much of it is based on meg trials and meta-analyses, it should also be used to influence almost everything that a doctor doe After all, the medical profession has been brain-washed for years by examiners in medical schools an Royal Colleges to believe that there is only one way of examining a patient. Our bedside rituals cou

do with as much critical evaluation as our operations and drug regimes; the same goes for almo
every aspect of doctoring.

As clinical practice becomes busier, and time for reading and reflection becomes even mo
precious, the ability effectively to peruse the medical literature and, in the future, to become famili
with a knowledge of best practice from modern communication systems, will be essential skills f
doctors. In this lively book, Trisha Greenhalgh provides an excellent approach to how to make be
use of medical literature and the benefits of evidence-based medicine. It should have equal appeal f
first year medical students and grey-haired consultants, and deserves to be read widely.

With increasing years, the privilege of being invited to write a foreword to a book by one's e
students becomes less of a rarity. Trisha Greenhalgh was the kind of medical student who never let h
teachers get away with a loose thought and this inquiring attitude seems to have flowered over t
years; this is a splendid and timely book and I wish it all the success it deserves. After all, the conce
of evidence-based medicine is nothing more than the state of mind that every clinical teacher hopes
develop in their students; Dr Greenhalgh's sceptical but constructive approach to medical literatu
suggests that such a happy outcome is possible at least once in the lifetime of a professor of medicin

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Preface to the first edition: do you need to read this book?

This book is intended for anyone, whether medically qualified or not, who wishes to find their wa into the medical literature, assess the scientific validity and practical relevance of the articles the find, and, where appropriate, put the results into practice. These skills constitute the basics evidence-based medicine.

I hope this book will help you to read and interpret medical papers better. I hope, in addition, convey a further message, which is this. Many of the descriptions given by cynics of what evidenc based medicine is (the glorification of things that can be measured without regard for the usefulne or accuracy of what is measured, the uncritical acceptance of published numerical data, th preparation of all-encompassing guidelines by self-appointed 'experts' who are out of touch with re medicine, the debasement of clinical freedom through the imposition of rigid and dogmatic clinic protocols, and the over-reliance on simplistic, inappropriate and often incorrect economic analyse are actually criticisms of what the evidence-based medicine movement is fighting *against*, rather tha of what it represents.

Do not, however, think of me as an evangelist for the gospel according to evidence-based medicin I believe that the science of finding, evaluating and implementing the results of medical research ca and often does, make patient care more objective, more logical, and more cost-effective. If I didn believe that, I wouldn't spend so much of my time teaching it and trying, as a general practitioner, practise it. Nevertheless, I believe that when applied in a vacuum (that is, in the absence of commo sense and without regard to the individual circumstances and priorities of the person being offere treatment or to the complex nature of clinical practice and policymaking), 'evidence-based' decisio making is a reductionist process with a real potential for harm.

Finally, you should note that I am neither an epidemiologist nor a statistician, but a person wh reads papers and who has developed a pragmatic (and at times unconventional) system for testin their merits. If you wish to pursue the epidemiological or statistical themes covered in this book, would encourage you to move on to a more definitive text, references for which you will find at th end of each chapter.

Trisha Greenhalg

Preface to the fifth edition

When I wrote this book in 1996, evidence-based medicine was a bit of an unknown quantity. handful of academics (including me) were already enthusiastic and had begun running ‘training t trainers’ courses to disseminate what we saw as a highly logical and systematic approach to clinic practice. Others—certainly the majority of clinicians—were convinced that this was a passing fad th was of limited importance and would never catch on. I wrote *How to Read a Paper* for two reason First, students on my own courses were asking for a simple introduction to the principles presented what was then known as *Dave Sackett's Big Red Book* (Sackett DL, Haynes RB, Guyatt GH, Tugwell *Clinical epidemiology—a basic science for clinical medicine*. London: Little, Brown & Co., 1991)- an outstanding and inspirational volume that was already in its fourth reprint, but which some novic apparently found a hard read. Second, it was clear to me that many of the critics of evidence-base medicine didn't really understand what they were dismissing—and that until they did, serious deba on the political, ideological and pedagogical place of evidence-based medicine as a discipline cou not begin.

I am of course delighted that *How to Read a Paper* has become a standard reader in many medic and nursing schools, and that it has so far been translated into French, German, Italian, Spanis Portuguese, Chinese, Polish, Japanese, Czech and Russian. I am also delighted that what was recently a fringe subject in academia has been well and truly mainstreamed in clinical service. In t UK, for example, it is now a contractual requirement for all doctors, nurses and pharmacists practise (and for managers to manage) according to best research evidence.

In the 18 years since the first edition of this book was published, evidence-based medicine h waxed and waned in popularity. Hundreds of textbooks and tens of thousands of journal articles no offer different angles on the ‘basics of EBM’ covered briefly in the chapters that follow. A increasing number of these sources point out genuine limitations of evidence-based medicine certain contexts. Others look at evidence-based medicine as a social movement—a ‘bandwagon’ th took off at a particular time (the 1990s) and place (North America) and spread dramatically quick with all sorts of knock-on effects for particular interest groups.

When preparing this fifth edition, I was once again minded not to change too much apart fro updating the examples and the reference lists, as there is clearly still room on the bookshelves for no-frills introductory text. In the last (fourth edition), I also added two new chapters (on quali improvement and complex interventions), and in this latest edition I have added two more—one applying evidence-based medicine with patients (the science of shared decision making) and anoth on common criticisms of EBM and responses to those. As ever, I would welcome any feedback th will help make the text more accurate, readable and practical.

Trisha Greenhalg
January 201

Acknowledgements

I am not by any standards an expert on all of the subjects covered in this book (in particular, I am ver bad at sums), and I am grateful to the people listed here for help along the way. I am, however, th final author of every chapter, and responsibility for any inaccuracies is mine alone.

1. To Professor Sir Andy Haines and Professor Dave Sackett who introduced me to the subject of evidence-based medicine and encouraged me to write about it.

2. To the late Dr Anna Donald, who broadened my outlook through valuable discussions on the implications and uncertainties of this evolving discipline.

3. To Jeanette Buckingham of the University of Alberta, Canada, for invaluable input to Chapter 2.

4. To various expert advisers and proofreaders who had direct input to this new edition or who advised me on previous editions.

5. To the many readers, too numerous to mention individually, who took time to write in and point out both typographical and factual errors in previous editions. As a result of their contributions, I have learnt a great deal (especially about statistics) and the book has been improved in many ways. Some of the earliest critics of *How to Read a Paper* have subsequently worked with me on my teaching courses in evidence-based practice; several have co-authored other papers or book chapters with me, and one or two have become personal friends.

6. To the authors and publishers of articles who gave permission for me to reproduce figures or tables. Details are given in the text.

7. To my followers on Twitter who proposed numerous ideas, constructive criticisms and responses to my suggestions when I was preparing the fifth edition of this book. By the way, you should try Twitter as a source of evidence-based information. Follow me on @trishgreenhalgh - and while you're at it you could try the Cochrane Collaboration on @cochrancollab, Ben Goldacre o n @bengoldacre, Carl Heneghan from the Oxford Centre for Evidence Based Medicine on @cebmblog and the UK National Institute for Health and Care Excellence on @nicecomms.

Thanks also to my husband, Dr Fraser Macfarlane, for his unfailing support for my academic wor and writing. My sons Rob and Al had not long been born when the first edition of this book was bein written. It is a source of great pride to me that they have now read the book, applied its messages to their own developing scientific careers (one in medicine) and made suggestions on how to improve it

Chapter 1

Why read papers at all?

Does ‘evidence-based medicine’ simply mean ‘reading papers in medical journals’?

Evidence-based medicine (EBM) is much more than just reading papers. According to the most wide quoted definition, it is ‘the conscientious, explicit and judicious use of current best evidence making decisions about the care of individual patients’ [1]. I find this definition very useful but misses out what for me is a very important aspect of the subject—and that is the use of mathematic Even if you know almost nothing about EBM, you probably know it talks a lot about numbers ar ratios! Anna Donald and I decided to be upfront about this in our own teaching, and proposed th alternative definition:

> *Evidence-based medicine is the use of mathematical estimates of the risk of benefit and harm derived from high-quality research on population samples, to inform clinical decision-making in the diagnosis, investigation or management of individual patients*.

The defining feature of EBM, then, is the use of figures derived from research on *populations* inform decisions about *individuals*. This, of course, begs the question ‘What is research?’—for whic a reasonably accurate answer might be ‘Focused, systematic enquiry aimed at generating ne knowledge’. In later chapters, I will explain how this definition can help you distinguish genuin research (which should inform your practice) from the poor-quality endeavours of well-meanin amateurs (which you should politely ignore).

If you follow an evidence-based approach to clinical decision-making, therefore, all sorts of issu relating to your patients (or, if you work in public health medicine, issues relating to groups of peopl will prompt you to ask questions about scientific evidence, seek answers to those questions in systematic way and alter your practice accordingly.

You might ask questions, for example, about a patient's symptoms (‘In a 34-year-old man with lef sided chest pain, what is the probability that there is a serious heart problem, and, if there is, will show up on a resting ECG?’), about physical or diagnostic signs (‘In an otherwise uncomplicate childbirth, does the presence of meconium [indicating fetal bowel movement] in the amniotic flu indicate significant deterioration in the physiological state of the fetus?’), about the prognosis of a illness (‘If a previously well two-year-old has a short fit associated with a high temperature, what the chance that she will subsequently develop epilepsy?’), about therapy (‘In patients with an acu coronary syndrome [heart attack], are the risks associated with thrombolytic drugs [clot buster outweighed by the benefits, whatever the patient’s age, sex and ethnic origin?'), about cos effectiveness (‘Is the cost of this new anti-cancer drug justified, compared with other ways spending limited healthcare resources?’), about patients' preferences (‘In an 87-year-old woman wi intermittent atrial fibrillation and a recent transient ischaemic attack, does the inconvenience

warfarin therapy outweigh the risks of not taking it?'), and about a host of other aspects of health a health services.

Professor Sackett, in the opening editorial of the very first issue of the journal *Evidence-Base Medicine* summarised the essential steps in the emerging science of EBM [2]:

1. To convert our information needs into answerable questions (i.e. to formulate the problem);

2. To track down, with maximum efficiency, the best evidence with which to answer these questions—which may come from the clinical examination, the diagnostic laboratory, the published literature or other sources;

3. To appraise the evidence critically (i.e. weigh it up) to assess its validity (closeness to the truth) and usefulness (clinical applicability);

4. To implement the results of this appraisal in our clinical practice;

5. To evaluate our performance.

Hence, EBM requires you not only to read papers but to read the *right* papers at the right time, a then to alter your behaviour (and, what is often more difficult, influence the behaviour of oth people) in the light of what you have found. I am concerned that how-to-do-it courses in EBM t often concentrate on the third of these five steps (critical appraisal) to the exclusion of all the other Yet if you have asked the wrong question or sought answers from the wrong sources, you might a well not read any papers at all. Equally, all your training in search techniques and critical apprais will go to waste if you do not put at least as much effort into implementing valid evidence a measuring progress towards your goals as you do into reading the paper. A few years ago, I adde three more stages to Sackett's five-stage model to incorporate the patient's perspective: the resultin eight stages, which I have called a *context-sensitive checklist for evidence-based practice*, are shov in Appendix 1 [3].

Box 1.1 Web-based resources for Evidence-based medicine

Oxford Centre for Evidence-Based Medicine: A well-kept website from Oxford, UK, containing a wealth of resources and links for EBM. http://cebm.net.

National Institute for Health and Care Excellence: This UK-based website, which is also popular outside the UK, links to evidence-based guidelines and topic reviews. http://www.nice.org.uk/.

National Health Service (NHS) Centre for Reviews and Dissemination: The site for downloading the high-quality evidence-based reviews is part of the UK National Institute for Health Research—a good starting point for looking for evidence on complex questions such as 'what should we do about obesity?' http://www.york.ac.uk/inst/crd/.

Clinical Evidence: An online handbook of best evidence for clinical decisions such as 'what's the best current treatment for atrial fibrillation?' Produced by BMJ Publishing Group. http://clinicalevidence.bmj.com.

If I were to be pedantic about the title of this book, these broader aspects of EBM should not ev get a mention here. But I hope you would have demanded your money back if I had omitted the fin section of this chapter (Before you start: formulate the problem), Chapter 2 (Searching the literature Chapter 15 (Implementing evidence-based practice) and Chapter 16 (Applying evidence wi patients). Chapters 3–14 describe step three of the EBM process: critical appraisal—that is, what yo should do when you actually have the paper in front of you. Chapter 16 deals with common criticism

of EBM.

Incidentally, if you are computer literate and want to explore the subject of EBM on the Interne you could try the websites listed in Box 1.1. If you're not, don't worry at this stage, but do p learning/use web-based resources to on your to-do list. Don't worry either when you discover th there are over 1000 websites dedicated to EBM—they all offer very similar material and you certain don't need to visit them all.

Why do people sometimes groan when you mention evidence-based medicine?

Critics of EBM might define it as 'the tendency of a group of young, confident and highly numera medical academics to belittle the performance of experienced clinicians using a combination epidemiological jargon and statistical sleight-of-hand' or 'the argument, usually presented with nea evangelistic zeal, that no health-related action should ever be taken by a doctor, a nurse, a purchaser health services, or a policymaker, unless and until the results of several large and expensive researc trials have appeared in print and approved by a committee of experts'.

The resentment amongst some health professionals towards the EBM movement is mostly a reactio to the implication that doctors (and nurses, midwives, physiotherapists and other health professional were functionally illiterate until they were shown the light, and that the few who weren't illitera wilfully ignored published medical evidence. Anyone who works face-to-face with patients know how often it is necessary to seek new information before making a clinical decision. Doctors hav spent time in libraries since libraries were invented. In general, we don't put a patient on a new dru without evidence that it is likely to work. Apart from anything else, such off-licence use of medicatio is, strictly speaking, illegal. Surely we have all been practising EBM for years, except when we we deliberately bluffing (using the 'placebo' effect for good medical reasons), or when we were il overstressed or consciously being lazy?

Well, no, we haven't. There have been a number of surveys on the behaviour of doctors, nurses an related professionals. It was estimated in the 1970s in the USA that only around 10–20% of all healt technologies then available (i.e. drugs, procedures, operations, etc.) were evidence-based; that figu improved to 21% in 1990, according to official US statistics [4]. Studies of the interventions offere to consecutive series of patients suggested that 60–90% of clinical decisions, depending on th specialty, were 'evidence-based' [5]. But as I have argued elsewhere, such studies had methodologic limitations [3]. Apart from anything else, they were undertaken in specialised units and looked at th practice of world experts in EBM; hence, the figures arrived at can hardly be generalised beyond the immediate setting (see section 'Whom is the study about?'). In all probability, we are still selling ou patients short quite most of the time.

A recent large survey by an Australian team looked at 1000 patients treated for the 22 mo commonly seen conditions in a primary care setting. The researchers found that whilst 90% of patien received evidence-based care for coronary heart disease, only 13% did so for alcohol dependence [6 Furthermore, the extent to which any individual practitioner provided evidence-based care varied the sample from 32% of the time to 86% of the time. These findings suggest room for improveme all round.

Let's take a look at the various approaches that health professionals use to reach their decisions

reality—all of which are examples of what EBM *isn't*.

Decision-making by anecdote

When I was a medical student, I occasionally joined the retinue of a distinguished professor as h made his daily ward rounds. On seeing a new patient, he would enquire about the patient's symptom turn to the massed ranks of juniors around the bed, and relate the story of a similar patie encountered a few years previously. ‘Ah, yes. I remember we gave her such-and-such, and she wa fine after that’. He was cynical, often rightly, about new drugs and technologies and his clinic acumen was second to none. Nevertheless, it had taken him 40 years to accumulate his expertise, an the largest medical textbook of all—the collection of cases that were outside his personal experienc —was forever closed to him.

Anecdote (storytelling) has an important place in clinical practice [7]. Psychologists have show that students acquire the skills of medicine, nursing and so on by memorising what was wrong wi particular patients, and what happened to them, in the form of stories or ‘illness scripts’. Stories abo patients are the unit of analysis (i.e. the thing we study) in grand rounds and teaching session Clinicians glean crucial information from patients' illness narratives—most crucially, perhaps, wh being ill *means* to the patient. And experienced doctors and nurses rightly take account of th accumulated ‘illness scripts’ of all their previous patients when managing subsequent patients. B that doesn't mean simply doing the same for patient B as you did for patient A if your treatme worked, and doing precisely the opposite if it didn't!

The dangers of decision-making by anecdote are well illustrated by considering the risk–benef ratio of drugs and medicines. In my first pregnancy, I developed severe vomiting and was given th anti-sickness drug prochlorperazine (Stemetil). Within minutes, I went into an uncontrollable and ve distressing neurological spasm. Two days later, I had recovered fully from this idiosyncratic reactio but I have never prescribed the drug since, even though the estimated prevalence of neurologic reactions to prochlorperazine is only one in several thousand cases. Conversely, it is tempting dismiss the possibility of rare but potentially serious adverse effects from familiar drugs—such thrombosis on the contraceptive pill—when one has never encountered such problems in oneself one's patients.

We clinicians would not be human if we ignored our personal clinical experiences, but we would b better to base our decisions on the collective experience of thousands of clinicians treating millions patients, rather than on what we as individuals have seen and felt. Chapter 5 (Statistics for the no statistician) describes some more objective methods, such as the number needed to treat (NNT), f deciding whether a particular drug (or other intervention) is likely to do a patient significant good harm.

When the EBM movement was still in its infancy, Sackett emphasised that evidence-based practic was no threat to old-fashioned clinical experience or judgement [1]. The question of *how* clinicia can manage to be both ‘evidence-based’ (i.e. systematically informing their decisions by researc evidence) and ‘narrative-based’ (i.e. embodying all the richness of their accumulated clinic anecdotes and treating each patient's problem as a unique illness story rather than as a ‘case of X’) is difficult one to address philosophically, and beyond the scope of this book. The interested read might like to look up two articles I've written on this topic [8] [9].

Decision-making by press cutting

For the first 10 years after I qualified, I kept an expanding file of papers that I had ripped out of m medical weeklies before binning the less interesting parts. If an article or editorial seemed to hav something new to say, I consciously altered my clinical practice in line with its conclusions. A children with suspected urinary tract infections should be sent for scans of the kidneys to exclu congenital abnormalities, said one article, so I began referring anyone under the age of 16 with urina symptoms for specialist investigations. The advice was in print, and it was recent, so it must sure replace what had been standard practice—in this case, referring only the small minority of suc children who display 'atypical' features [10].

This approach to clinical decision-making is still very common. How many doctors do you kno who justify their approach to a particular clinical problem by citing the results section of a sing published study, even though they could not tell you anything at all about the methods used to obta those results? Was the trial randomised and controlled (see section 'Cross-sectional surveys')? Ho many patients, of what age, sex and disease severity, were involved (see section 'Whom is the stuc about?')? How many withdrew from ('dropped out of') the study, and why (see section 'Wer preliminary statistical questions addressed?')? By what criteria were patients judged cured (s section 'Surrogate endpoints')? If the findings of the study appeared to contradict those of oth researchers, what attempt was made to validate (confirm) and replicate (repeat) them (see sectio 'Ten questions to ask about a paper that claims to validate a diagnostic or screening test')? Were th statistical tests that allegedly proved the authors' point appropriately chosen and correctly performe (see Chapter 5)? Has the patient's perspective been systematically sought and incorporated via shared decision-making tool (see Chapter 16)? Doctors (and nurses, midwifes, medical manager psychologists, medical students and consumer activists) who like to cite the results of medic research studies have a responsibility to ensure that they first go through a checklist of questions lik these (more of which are listed in Appendix 1).

Decision-making by GOBSAT (good old boys sat around a table)

When I wrote the first edition of this book in the mid-1990s, the commonest sort of guideline w what was known as a *consensus statement*—the fruits of a weekend's hard work by a dozen or s eminent experts who had been shut in a luxury hotel, usually at the expense of a drug company. Suc 'GOBSAT (good old boys sat around a table) guidelines' often fell out of the medical freebies (fre medical journals and other 'information sheets' sponsored directly or indirectly by the pharmaceutic industry) as pocket-sized booklets replete with potted recommendations and at-a-glance manageme guides. But who says the advice given in a set of guidelines, a punchy editorial or an amply reference overview is correct?

Professor Mulrow [11], one of the founders of the science of systematic review (see Chapter 9 showed a few years ago that experts in a particular clinical field are *less* likely to provide an objectiv review of all the available evidence than a non-expert who approaches the literature with unbiase eyes. In extreme cases, an 'expert opinion' may consist simply of the lifelong bad habits and person press cuttings of an ageing clinician, and a gaggle of such experts would simply multiply th misguided views of any one of them. Table 1.1 gives examples of practices that were at one tim

widely accepted as good clinical practice (and which would have made it into the GOBSAT guidelin of the day), but which have subsequently been discredited by high-quality clinical trials.

Table 1.1 Examples of harmful practices once strongly supported by 'expert opinion'

Approximate time period	Clinical practice accepted by experts of the day	Practice shown to be harmful in	Impact on clinical practice
From 500 BC	Bloodletting (for just about any acute illness)	1820[a]	Bloodletting ceased around 1910
1957	Thalidomide for 'morning sickness' in early pregnancy, which led to the birth of over 8000 severely malformed babies worldwide	1960	The teratogenic effects of this drug were so dramati that thalidomide was rapidly withdrawn when the first case report appeared
From at least 1900	Bed rest for acute low back pain	1986	Many doctors still advise people with back pain to 'rest up'
1960s	Benzodiazepines (e.g. diazepam) for mild anxiety and insomnia, initially marketed as 'non-addictive' but subsequently shown to cause severe dependence and withdrawal symptoms	1975	Benzodiazepine prescribing for these indications fell the 1990s
1970s	Intravenous lignocaine in acute myocardial infarction, with a view to preventing arrhythmias, subsequently shown to have no overall benefit and in some cases to *cause* fatal arrhythmias	1974	Lignocaine continued to be given routinely until the mid-1980s
Late 1990s	Cox-2 inhibitors (a new class of non-steroidal anti-inflammatory drug), introduced for the treatment of arthritis, were later shown to increase the risk of heart attack and stroke	2004	Cox-2 inhibitors for pain were quickly withdrawn following some high-profile legal cases in the USA although new uses for cancer treatment (where risks may be outweighed by benefits) are now being explored

[a]Interestingly, bloodletting was probably the first practice for which a randomised controlled trial was suggested. The physician van Helmont issu this challenge to his colleagues as early as 1662: '*Let us take 200 or 500 poor people that have fevers. Let us cast lots, that one half of them may fall my share, and the others to yours. I will cure them without blood-letting, but you do as you know – and we shall see how many funerals both of us sh have*' [12]. I am grateful to Matthias Egger for drawing my attention to this example.

Chapter 9 takes you through a checklist for assessing whether a 'systematic review of the evidenc produced to support recommendations for practice or policymaking really merits the description, a Chapter 10 discusses the harm that can be done by applying guidelines that are not evidence-based. is a major achievement of the EBM movement that almost no guideline these days is produced b GOBSAT!

Decision-making by cost-minimisation

The popular press tends to be horrified when they learn that a treatment has been withheld from patient for reasons of cost. Managers, politicians and, increasingly, doctors can count on bein pilloried when a child with a rare cancer is not sent to a specialist unit in America or a frail old lady denied a drug to stop her visual loss from macular degeneration. Yet in the real world, all healthcare provided from a limited budget and it is increasingly recognised that clinical decisions must take in account the economic costs of a given intervention. As Chapter 11 argues, clinical decision-makin *purely* on the grounds of cost ('cost-minimisation'—purchasing the cheapest option with no regard how effective it is) is generally ethically unjustified, and we are right to object vocally when th occurs.

Expensive interventions should not, however, be justified simply because they are new, or becaus they ought to work in theory, or because the only alternative is to do nothing—but because they a very likely to save life or significantly improve its quality. How, though, can the benefits of a hi

replacement in a 75-year-old be meaningfully compared with that of cholesterol-lowering drugs in middle-aged man or infertility investigations for a couple in their twenties? Somewhat counte intuitively, there is no self-evident set of ethical principles or analytical tools that we can use to mat limited resources to unlimited demand. As you will see in Chapter 11, the much-derided quality adjusted life year (QALY), and similar utility-based units are simply attempts to lend som objectivity to the illogical but unavoidable comparison of apples with oranges in the field of huma suffering. In the United Kingdom, the National Institute for Health and Care Excellence (s www.nice.org.uk) seeks to develop both evidence-based guidelines and fair allocation of NH resources.

There is one more reason why some people find the term *evidence-based medicine* unpalatable. Th chapter has argued that EBM is about coping with change, not about knowing all the answers befo you start. In other words, it is not so much about what you have read in the past but about how you g about identifying and meeting your ongoing learning needs and applying your knowledg appropriately and consistently in new clinical situations. Doctors who were brought up in the o school style of never admitting ignorance may find it hard to accept that a major element of scientif uncertainty exists in practically every clinical encounter, although in most cases, the clinician fails identify the uncertainty or to articulate it in terms of an answerable question (see next section). If yo are interested in the research evidence on doctors' [lack of] questioning behaviour, see an excelle review by Swinglehurst [13].

The fact that none of us—not even the cleverest or most experienced—can answer all the questio that arise in the average clinical encounter means that the 'expert' is more fallible than he or she wa traditionally cracked up to be. An evidence-based approach to ward rounds may turn the tradition medical hierarchy on its head when the staff nurse or junior doctor produces new evidence th challenges what the consultant taught everyone last week. For some senior clinicians, learning th skills of critical appraisal is the least of their problems in adjusting to an evidence-based teachin style!

Having defended EBM against all the standard arguments put forward by clinicians, I should confe to being sympathetic to many of the more sophisticated arguments put forward by philosophers an social scientists. Such arguments, summarised in Chapter 17 (new for this edition), address the natu of knowledge and the question of how much medicine really rests on decisions at all. But please don turn to that chapter (which is, philosophically speaking, a 'hard read') until you have fully grasped th basic arguments in the first few chapters of this book—or you risk becoming confused!

Before you start: formulate the problem

When I ask my medical students to write me an essay about high blood pressure, they often produc long, scholarly and essentially correct statements on what high blood pressure is, what causes it an what the different treatment options are. On the day they hand their essays in, most of them know f more about high blood pressure than I do. They are certainly aware that high blood pressure is th single most common cause of stroke, and that detecting and treating everyone's high blood pressu would cut the incidence of stroke by almost half. Most of them are aware that stroke, althoug devastating when it happens, is a fairly rare event, and that blood pressure tablets have side effec such as tiredness, dizziness, impotence and getting 'caught short' when a long way from the lavatory

But when I ask my students a practical question such as 'Mrs Jones has developed light-headedne

on these blood pressure tablets and she wants to stop all medication; what would you advise her do?', they are often foxed. They sympathise with Mrs Jones' predicament, but they cannot distil fro their pages of close-written text the one thing that Mrs Jones needs to know. As Smith (paraphrasir TS Eliot) asked a few years ago in a BMJ editorial: 'Where is the wisdom we have lost in knowledg and the knowledge we have lost in information?'[14].

Experienced clinicians might think they can answer Mrs Jones' question from their own person experience. As I argued in the previous section, few of them would be right. And even if they wer right on this occasion, they would still need an overall system for converting the rag-bag information about a patient (an ill-defined set of symptoms, physical signs, test results and knowledg of what happened to this patient or a similar patient last time), the particular values and preferenc (utilities) of the patient and other things that could be relevant (a hunch, a half-remembered articl the opinion of a more experienced colleague or a paragraph discovered by chance while flickir through a textbook) into a succinct summary of what the problem is and what specific additional iten of information we need to solve that problem.

Sackett and colleagues, in a book subsequently revised by Straus [15], have helped us by dissectir the parts of a good clinical question:

- First, define precisely *whom* the question is about (i.e. ask 'How would I describe a group of patients similar to this one?').
- Next, define *which* manoeuvre you are considering in this patient or population (e.g. a drug treatment), and, if necessary, a comparison manoeuvre (e.g. placebo or current standard therapy)
- Finally, define the desired (or undesired) *outcome* (e.g. reduced mortality, better quality of life, and overall cost savings to the health service).

The second step may not concern a drug treatment, surgical operation or other intervention. Th manoeuvre could, for example, be the exposure to a putative carcinogen (something that might cau cancer) or the detection of a particular surrogate endpoint in a blood test or other investigation. (surrogate endpoint, as section 'Surrogate endpoints' explains, is something that predicts, or is said predict, the later development or progression of disease. In reality, there are very few tests th reliably act as crystal balls for patients' medical future. The statement 'The doctor looked at the te results and told me I had six months to live' usually reflects either poor memory or irresponsib doctoring!) In both these cases, the 'outcome' would be the development of cancer (or some oth disease) several years later. In most clinical problems with individual patients, however, th 'manoeuvre' consists of a specific intervention initiated by a health professional.

Thus, in Mrs Jones's case, we might ask, 'In a 68-year-old white woman with essential (i.e. commo or garden) hypertension (high blood pressure), no coexisting illness, and no significant past medic history, whose blood pressure is currently X/Y, do the benefits of continuing therapy wit bendroflumethiazide (chiefly, reduced risk of stroke) outweigh the inconvenience?'. Note that framing the specific question, we have already established that Mrs Jones has never had a heart attac stroke or early warning signs such as transient paralysis or loss of vision. If she had, her risk subsequent stroke would be much higher and we would, rightly, load the risk–benefit equation reflect this.

In order to answer the question we have posed, we must determine not just the risk of stroke untreated hypertension but also the likely reduction in that risk which we can expect with dru treatment. This is, in fact, a rephrasing of a more general question (do the benefits of treatment in th case outweigh the risks?) which we should have asked before we prescribed bendroflumethiazide