how to

read a paper

THE BASICS OF EVIDENCE-BASED MEDICINE AND HEALTHCARE

SIXTH EDITION

TRISHA GREENHALGH

WILEY Blackwell

How to Read a Paper

How to Read a Paper

The Basics of Evidence-Based Medicine and Healthcare

SIXTH EDITION

Trisha Greenhalgh

Professor of Primary Care Health Sciences University of Oxford Oxford, UK

WILEY Blackwell

This edition first published 2019 © 2019 John Wiley & Sons Ltd

Edition History John Wiley & Sons Ltd (4e, 2010; 5e, 2014)

All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, recording or otherwise, except as permitted by law. Advice on how to obtain permission to reuse material from this title is available at http://www.wiley.com/go/permissions.

The right of Trisha Greenhalgh to be identified as the author of this work has been asserted in accordance with law.

Registered Office(s) John Wiley & Sons, Inc., 111 River Street, Hoboken, NJ 07030, USA John Wiley & Sons Ltd, The Atrium, Southern Gate, Chichester, West Sussex, PO19 8SQ, UK

Editorial Office 9600 Garsington Road, Oxford, OX4 2DQ, UK

For details of our global editorial offices, customer services, and more information about Wiley products visit us at www.wiley.com.

Wiley also publishes its books in a variety of electronic formats and by print-on-demand. Some content that appears in standard print versions of this book may not be available in other formats.

Limit of Liability/Disclaimer of Warranty

The contents of this work are intended to further general scientific research, understanding, and discussion only and are not intended and should not be relied upon as recommending or promoting scientific method, diagnosis, or treatment by physicians for any particular patient. In view of ongoing research, equipment modifications, changes in governmental regulations, and the constant flow of information relating to the use of medicines, equipment, and devices, the reader is urged to review and evaluate the information provided in the package insert or instructions for each medicine, equipment, or device for, among other things, any changes in the instructions or indication of usage and for added warnings and precautions. While the publisher and authors have used their best efforts in preparing this work, they make no representations or warranties with respect to the accuracy or completeness of the contents of this work and specifically disclaim all warranties, including without limitation any implied warranties of merchantability or fitness for a particular purpose. No warranty may be created or extended by sales representatives, written sales materials or promotional statements for this work. The fact that an organization, website, or product is referred to in this work as a citation and/or potential source of further information does not mean that the publisher and authors endorse the information or services the organization, website, or product may provide or recommendations it may make. This work is sold with the understanding that the publisher is not engaged in rendering professional services. The advice and strategies contained herein may not be suitable for your situation. You should consult with a specialist where appropriate. Further, readers should be aware that websites listed in this work may have changed or disappeared between when this work was written and when it is read. Neither the publisher nor authors shall be liable for any loss of profit or any other commercial damages, including but not limited to special, incidental, consequential, or other damages.

Library of Congress Cataloging-in-Publication Data

Names: Greenhalgh, Trisha, author.

Title: How to read a paper : the basics of evidence-based medicine and healthcare / Trisha Greenhalgh.

Description: Sixth edition. | Hoboken, NJ : John Wiley & Sons Ltd, 2019. | Includes bibliographical references and index. |

Identifiers: LCCN 2019001711 (print) | LCCN 2019002837 (ebook) | ISBN 9781119484738 (Adobe PDF) | ISBN 9781119484721 (ePub) | ISBN 9781119484745 (pbk.)

Subjects: | MESH: Evidence-Based Practice | Research | Journalism, Medical

Classification: LCC R118.6 (ebook) | LCC R118.6 (print) | NLM WB 102.5 | DDC 610.72-dc23 LC record available at https://lccn.loc.gov/2019001711

Cover image: © TECHDESIGNWORK/iStock.com Cover design by Wiley

Set in 9.5/12pt Minion by SPi Global, Pondicherry, India

Pb printing 10 9 8 7 6 5 4 3 2 1

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 the original draft of the manuscript, but was tragically killed in a train crash on 8th August 1996. This book is dedicated to her memory.

Contents

Foreword to the first edition by Professor Sir David Weatherall		
Preface to the sixth edition	xiv	
Preface to the first edition	xvi	
Acknowledgements	xviii	
Chapter 1 Why read papers at all?	1	
Does 'evidence-based medicine' simply mean 'reading papers		
in medical journals'?	1	
Why do people sometimes groan when you mention		
evidence-based healthcare?	4	
Before you start: formulate the problem	11	
Exercises based on this chapter	13	
References	14	
Chapter 2 Searching the literature	16	
What are you looking for?	17	
Levels upon levels of evidence	18	
Synthesised sources: systems, summaries and syntheses	19	
Pre-appraised sources: synopses of systematic reviews		
and primary studies	22	
Specialised resources	23	
Primary studies – tackling the jungle		
One-stop shopping: federated search engines	25	
Asking for help and asking around	26	
Online tutorials for effective searching	26	
Exercises based on this chapter	27	
References	27	
Chapter 3 Getting your bearings: what is this paper about?	29	
The science of 'trashing' papers	29	
Three preliminary questions to get your bearings	31	

viii **Contents**

Randomised controlled trials	35		
Cohort studies			
Case-control studies			
Cross-sectional surveys	41		
Case reports	41		
The traditional hierarchy of evidence	42		
Exercises based on this chapter	43		
References	43		
Chapter 4 Assessing methodological quality	45		
Was the study original?	45		
Whom is the study about?	46		
Was the design of the study sensible?	47		
Was bias avoided or minimised?	49		
Was assessment 'blind'?	53		
Were preliminary statistical questions addressed?	54		
A note on ethical considerations	57		
Summing up	58		
Exercises based on this chapter	59		
References	60		
Chapter 5 Statistics for the non-statistician	62		
How can non-statisticians evaluate statistical tests?	62		
Have the authors set the scene correctly?	64		
Paired data, tails and outliers	69		
Correlation, regression and causation	71		
Probability and confidence	73		
The bottom line	75		
Summary	77		
Exercises based on this chapter	77		
References	78		
Chapter 6 Papers that report trials of drug treatments and other simple			
interventions	79		
'Evidence' and marketing	79		
Making decisions about therapy	82		
Surrogate endpoints	82		
What information to expect in a paper describing a randomised controlled			
trial: the CONSORT statement	86		
Getting worthwhile evidence from pharmaceutical representatives			
Exercises based on this chapter 8			
References	89		

Contents ix

Chapter 7	Papers that report trials of complex interventions	92
Complex inte	erventions	92
Ten question	s to ask about a paper describing a complex intervention	94
Exercises bas	ed on this chapter	99
References		100

Chapter 8 Papers that report diagnostic or screening tests	101
Ten men in the dock	101
Validating diagnostic tests against a gold standard	102
Ten questions to ask about a paper that claims to validate	
a diagnostic or screening test	107
Likelihood ratios	111
Clinical prediction rules	113
Exercises based on this chapter	114
References	115

Chapter 9	Papers that summarise other papers (systematic reviews	
	and meta-analyses)	117
When is a re	eview systematic?	117
Evaluating s	ystematic reviews	120
Meta-analys	is for the non-statistician	125
Explaining h	neterogeneity	130
New approa	ches to systematic review	132
Exercises ba	sed on this chapter	133
References		133

Chapter 10	Papers that tell you what to do (guidelines)	137
The great gui	delines debate	137
Ten question	s to ask about a clinical guideline	141
Exercises bas	ed on this chapter	147
References		148

Chapter 11 Papers that tell you what things cost (economic analyses)	150
What is economic analysis?	150
Measuring the costs and benefits of health interventions	152
A note on 'Choosing Wisely'	157
Ten questions to ask about an economic analysis	157
Conclusions	162
Exercises based on this chapter	162
References	162

x Contents

Chapter 12 Papers that go beyond numbers (qualitative research)	165
What is qualitative research?	165
Ten questions to ask about a qualitative research paper	169
Conclusions	176
Exercises based on this chapter	176
References	177
Chapter 13 Papers that report questionnaire research	179
The rise and rise of questionnaire research	179
Ten questions to ask about a paper describing a questionnaire study	180
Conclusions	188
Exercises based on this chapter	189
References	189
Chapter 14 Papers that report quality improvement case studies	191
What are quality improvement studies, and how should we research them?	191
Ten questions to ask about a paper describing a quality improvement initiative	193
Conclusions	200
Exercises based on this chapter	200
References	201
Chapter 15 Papers that describe genetic association studies	203
The three eras of human genetic studies (so far)	203
What is a genome-wide association study (GWAS)?	204
Clinical applications of GWAS	207
Direct-to-consumer genetic testing	209
Mendelian randomisation studies	210
Epigenetics – a space to watch	211
Ten questions to ask about a genetic association study	212
Conclusions	216
Exercises based on this chapter	216
References	216
Chapter 16 Applying evidence with patients	219
The patient perspective	219
Patient-reported outcome measures (PROMs)	221
Shared decision-making	222
Option grids	223
N of 1 trials and other individualised approaches	227
Exercises based on this chapter	228
References	229

Contents xi

Chapter 17	Criticisms of evidence-based healthcare	232
What's wrong with EBHC when it's done badly?		232
What's wrong	235	
Why is 'evide	238	
Exercises bas	239	
References	240	
Appendix 1	Checklists for finding, appraising	
	and implementing evidence	242
Appendix 2	Assessing the effects of an intervention	252
Index		253

Foreword to the first edition by Professor Sir David Weatherall

Not surprisingly, the wide publicity given to what is now called *evidencebased medicine* has been greeted with mixed reactions by those who are involved in the provision of patient care. The bulk of the medical profession appears to be slightly hurt by the concept, suggesting as it does that until recently all medical practice was what Lewis Thomas has described as a frivolous and irresponsible kind of human experimentation, based on nothing but trial and error, and usually resulting in precisely that sequence. On the other hand, politicians and those who administrate our health services have greeted the notion with enormous glee. They had suspected all along that doctors were totally uncritical and now they had it on paper. Evidence-based medicine came as a gift from the gods 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 is recorded that Frederick II, Emperor of the Romans and King of Sicily and Jerusalem, who lived from 1192 to 1250 AD, and who was interested in the effects of exercise on digestion, took two knights and gave them identical meals. One was then sent out hunting and the other ordered to bed. At the end of several hours he killed both and examined the contents of their alimentary canals; digestion had proceeded further in the stomach of the sleeping knight. In the 17th century Jan Baptista van Helmont, a physician and philosopher, became sceptical of the practice of blood-letting. Hence he proposed what was almost certainly the first clinical trial involving large numbers, randomisation and statistical analysis. This involved taking 200-500 poor people, dividing them into two groups by casting lots, and protecting one from phlebotomy while allowing the other to be treated with as much blood-letting as his colleagues thought appropriate. The number of funerals in each group would be used to assess the efficacy of bloodletting. History does not record why this splendid experiment was never carried out.

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

But although the idea of evidence-based medicine is not new, modern disciples like David Sackett and his colleagues are doing a great service to clinical practice, not just by popularising the idea, but by bringing home to clinicians the notion that it is not a dry academic subject but more a way of thinking that should permeate every aspect of medical practice. While much of it is based on mega-trials and meta-analyses, it should also be used to influence almost everything that a doctor does. After all, the medical profession has been brain-washed for years by examiners in medical schools and Royal Colleges to believe that there is only one way of examining a patient. Our bedside rituals could do with as much critical evaluation as our operations and drug regimes; the same goes for almost every aspect of doctoring.

As clinical practice becomes busier, and time for reading and reflection becomes even more precious, the ability effectively to peruse the medical literature and, in the future, to become familiar with a knowledge of best practice from modern communication systems, will be essential skills for doctors. In this lively book, Trisha Greenhalgh provides an excellent approach to how to make best use of medical literature and the benefits of evidencebased medicine. It should have equal appeal for 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 ex-students becomes less of a rarity. Trisha Greenhalgh was the kind of medical student who never let her teachers get away with a loose thought and this inquiring attitude seems to have flowered over the years; this is a splendid and timely book and I wish it all the success it deserves. After all, the concept of evidence-based medicine is nothing more than the state of mind that every clinical teacher hopes to develop in their students; Dr Greenhalgh's sceptical but constructive approach to medical literature suggests that such a happy outcome is possible at least once in the lifetime of a professor of medicine.

DJ Weatherall Oxford September 1996

Preface to the sixth edition

When I wrote this book in 1996, evidence-based medicine was a bit of an unknown quantity. A handful of academics (including me) were already enthusiastic and had begun running 'training the trainers' courses to disseminate what we saw as a highly logical and systematic approach to clinical practice. Others - certainly the majority of clinicians - were convinced that this was a passing fad that was of limited importance and would never catch on. I wrote How to Read a Paper for two reasons. First, students on my own courses were asking for a simple introduction to the principles presented in what was then known as 'Dave Sackett's big red book' (Sackett DL, Haynes RB, Guyatt GH, Tugwell P. 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 novices apparently found a hard read. Second, it was clear to me that many of the critics of evidence-based medicine didn't really understand what they were dismissing - and that until they did, serious debate on the clinical, pedagogical and even political place of evidence-based medicine as a discipline could not begin.

I am of course delighted that *How to Read a Paper* has become a standard reader in many medical and nursing schools, and that so far it has been translated into 20 languages including French, German, Italian, Spanish, Portuguese, Chinese, Polish, Japanese, Czech and Russian. I am also delighted that what was so recently a fringe subject in academia has been well and truly mainstreamed in clinical service. In the UK, for example, it is now a contractual requirement for all doctors, nurses and pharmacists to practise (and for managers to manage) according to best research evidence.

In the 23 years since the first edition of this book was published, evidencebased medicine (and, more broadly, evidence-based healthcare) has waxed and waned in popularity. Hundreds of textbooks and tens of thousands of journal articles now offer different angles on the 'basics of EBM' covered briefly in the chapters that follow. An increasing number of these sources point out genuine limitations of evidence-based healthcare in certain contexts. Others look at evidence-based medicine and healthcare as a social movement – a 'bandwagon' that took off at a particular time (the 1990s) and place (North America) and spread quickly with all sorts of knock-on effects for particular interest groups.

When preparing this sixth edition, I began with no fewer than 11 reviews of the previous edition, mostly from students who are the book's main target audience. They wanted updated references, more worked examples, more (and better) pictures and some questions to aid reflection at the end of each chapter. I've added all these, along with a new chapter on population genetics and big data. I did not change much else, because there is clearly still room on the bookshelves for a no-frills introductory text. Since the publication of the fifth edition, I have written a new book on *How to Implement Evidence-Based Healthcare*, so I have removed the (now somewhat outdated) chapter on implementation that was included in the fourth and fifth editions.

As ever, I would welcome any feedback that will help make the text more accurate, readable and practical.

Trisha Greenhalgh November 2018

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 way into the medical and healthcare literature, assess the scientific validity and practical relevance of the articles they find, and, where appropriate, put the results into practice. These skills constitute the basics of evidence-based medicine (if you're thinking about what doctors do) or evidence-based healthcare (if you're looking at the care of patients more widely).

I hope this book will improve your confidence in reading and interpreting papers relating to clinical decision-making. I hope, in addition, to convey a further message, which is this. Many of the descriptions given by cynics of what evidence-based healthcare is (the glorification of things that can be measured without regard for the usefulness or accuracy of what is measured, the uncritical acceptance of published numerical data, the preparation of allencompassing guidelines by self-appointed 'experts' who are out of touch with real medicine, the debasement of clinical freedom through the imposition of rigid and dogmatic clinical protocols, and the over-reliance on simplistic, inappropriate and often incorrect economic analyses) are actually criticisms of what the evidence-based healthcare movement is fighting *against*, rather than of what it represents.

Do not, however, think of me as an evangelist for the gospel according to evidence-based healthcare. I believe that the science of finding, evaluating and implementing the results of clinical research can, and often does, make patient care more objective, more logical and more cost-effective. If I didn't believe that, I wouldn't spend so much of my time teaching it and trying, as a doctor, to practise it. Nevertheless, I believe that when applied in a vacuum (that is, in the absence of common sense and without regard to the individual circumstances and priorities of the person being offered treatment or to the complex nature of clinical practice and policy-making), 'evidence-based' decision-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 who reads papers and who has developed a pragmatic

Preface to the first edition xvii

(and at times unconventional) system for testing their merits. If you wish to pursue the epidemiological or statistical themes covered in this book, I would encourage you to move on to a more definitive text, references for which you will find at the end of each chapter.

> Trisha Greenhalgh November 1996

Acknowledgements

I am not by any standards an expert on all of the subjects covered in this book (in particular, I am very bad at sums), and I am grateful to the people listed here for help along the way. I am, however, the 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. In particular, ten people (five experts in genetic studies and five novices in that topic) gave feedback on the new Chapter 15.
- 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 on @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 work and writing. Our sons Rob and Al had not long been born when the first edition of this book was being written. It is a source of great pride to me that both are now pursuing scientific careers (Rob in marine biology, Al in medicine) and have begun to publish their own scientific papers.

Chapter 1 Why read papers at all?

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

Evidence-based medicine (EBM), which is part of the broader field of evidence-based healthcare (EBHC), is much more than just reading papers. According to what is still (more than 20 years after it was written) the most widely quoted definition, it is 'the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients' [1]. I find this definition very useful but it misses out what for me is a very important aspect of the subject – and that is the use of mathematics. Even if you know almost nothing about EBHC, you probably know it talks a lot about numbers and ratios! Anna Donald and I decided to be upfront about this in our own teaching, and proposed this 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 EBHC, then, is the use of figures derived from research on *populations* to inform decisions about *individuals*. This, of course, begs the question 'What is research?' – for which a reasonably accurate answer might be 'Focused, systematic enquiry aimed at generating new knowledge.' In later chapters, I explain how this definition can help you distinguish genuine research (which should inform your practice) from the poor-quality endeavours of well-meaning amateurs (which you should politely ignore).

If you follow an evidence-based approach to clinical decision-making, therefore, all sorts of issues relating to your patients (or, if you work in public

How to Read a Paper: The Basics of Evidence-Based Medicine and Healthcare, Sixth Edition. Trisha Greenhalgh.

© 2019 John Wiley & Sons Ltd. Published 2019 by John Wiley & Sons Ltd.

2 How to read a paper

health medicine, issues relating to groups of people) will prompt you to ask questions about scientific evidence, seek answers to those questions in a 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 left-sided chest pain, what is the probability that there is a serious heart problem, and, if there is, will it show up on a resting ECG?'), about physical or diagnostic signs ('In an otherwise uncomplicated labour, does the presence of meconium [indicating fetal bowel movement] in the amniotic fluid indicate significant deterioration in the physiological state of the fetus?'), about the prognosis of an illness ('If a previously well 2-year-old has a short fit associated with a high temperature, what is the chance that she will subsequently develop epilepsy?'), about therapy ('In patients with an acute coronary syndrome [heart attack], are the risks associated with thrombolytic drugs [clot busters] outweighed by the benefits, whatever the patient's age, sex and ethnic origin?'), about cost-effectiveness ('Is the cost of this new anti-cancer drug justified, compared with other ways of spending limited healthcare resources?'), about patients' preferences ('In an 87-yearold woman with intermittent atrial fibrillation and a recent transient ischaemic attack, do the potential harms and inconvenience of warfarin therapy outweigh the risks of not taking it?') and about a host of other aspects of health and health services.

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

- 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, EBHC requires you not only to read papers, but to read the *right* papers at the right time and then to alter your behaviour (and, what is often more difficult, influence the behaviour of other people) in the light of what you have found. I am concerned that how-to-do-it courses in EBHC too often concentrate on the third of these five steps (critical appraisal) to the exclusion of all the others. Yet if you have asked the wrong question or sought answers from the wrong sources, you might as well not read any papers at all.

Why read papers at all? 3

Equally, all your training in search techniques and critical appraisal will go to waste if you do not put at least as much effort into implementing valid evidence and measuring progress towards your goals as you do into reading the paper. A few years ago, I added three more stages to Sackett's five-stage model to incorporate the patient's perspective: the resulting eight stages, which I have called a *context-sensitive checklist for evidence-based practice*, are shown in Appendix 1.

If I were to be pedantic about the title of this book, these broader aspects of EBHC should not even get a mention here. But I hope you would have demanded your money back if I had omitted the final section of this chapter ('Before you start: formulate the problem'), Chapter 2 (Searching the literature) and Chapter 16 (Applying evidence with patients). Chapters 3–15 describe step three of the EBHC process: critical appraisal – that is, what you should do when you actually have the paper in front of you. Chapter 16 deals with common criticisms of EBHC. I have written a separate book on the challenges of implementation, *How to Implement Evidence-Based Healthcare* [3].

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

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. www.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. 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 policy questions such as 'what should we do about obesity?' https://www.york.ac.uk/inst/crd/
- *BMJ Best Practice*: 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. https://bestpractice.bmj.com/info/evidence-information

4 How to read a paper

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

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

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

Well, no, we haven't. There have been a number of surveys on the behaviour of doctors, nurses and related professionals. It was estimated in the 1970s in the USA that only around 10–20% of all health technologies then available (i.e. drugs, procedures, operations, etc.) were evidence-based; that estimate improved to 21% in 1990. Studies of the interventions offered to consecutive series of patients suggested that 60–90% of clinical decisions, depending on the specialty, were 'evidence-based' [4]. But such studies had major methodological limitations (in particular, they did not take a particularly nuanced look at whether the patient would have been better off on a different drug or no drug at all). In addition, they were undertaken in specialised units and looked at the practice of world experts in EBHC; hence, the figures arrived at can hardly be generalised beyond their immediate setting (see Chapter 4 'Whom is the study about?'). In all probability, we are still selling our patients short most of the time.

A large survey by an Australian team looked at 1000 patients treated for the 22 most commonly seen conditions in a primary care setting. The researchers found that while 90% of patients received evidence-based care for coronary heart disease, only 13% did so for alcohol dependence [5].

Why read papers at all? 5

Furthermore, the extent to which any individual practitioner provided evidence-based care varied in the sample from 32% of the time to 86% of the time. More recently, a review in *BMJ Evidence-Based Medicine* cited studies of the proportion of doctors' clinical decisions that were based on strong research evidence; the figure varied from 14% (in thoracic surgery) to 65% (in psychiatry); this paper also reported new data on primary health care, in which around 18% of decisions were based on 'patient-oriented high-quality evidence' [6]. Perhaps what is most striking about all these findings is the very wide variation in performance, which ranges from terrible to middling.

Let's take a look at the various approaches that health professionals use to reach their decisions in reality – all of which are examples of what EBHC *isn't*.

Decision-making by anecdote

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

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

The dangers of decision-making by anecdote are well illustrated by considering the risk-benefit ratio of drugs and medicines. In my first pregnancy, I developed severe vomiting and was given the anti-sickness drug prochlorperazine (Stemetil). Within minutes, I went into an uncontrollable and very distressing neurological spasm. Two days later, I had recovered fully from

6 How to read a paper

this idiosyncratic reaction, but I have never prescribed the drug since, even though the estimated prevalence of neurological reactions to prochlorperazine is only one in several thousand cases. Conversely, it is tempting to dismiss the possibility of rare but potentially serious adverse effects from familiar drugs – such as thrombosis on the contraceptive pill – when one has never encountered such problems in oneself or one's patients.

We clinicians would not be human if we ignored our personal clinical experiences, but we would be better to base our decisions on the collective experience of thousands of clinicians treating millions of patients, rather than on what we as individuals have seen and felt. Chapter 5 (Statistics for the non-statistician) describes some more objective methods, such as the number needed to treat (NNT), for deciding whether a particular drug (or other intervention) is likely to do a patient significant good or harm.

When the EBM movement was still in its infancy, Sackett emphasised that evidence-based practice was no threat to old-fashioned clinical experience or judgement [1]. The question of *how* clinicians can manage to be both 'evidence-based' (i.e. systematically informing their decisions by research evidence) and 'narrative-based' (i.e. embodying all the richness of their accumulated clinical anecdotes and treating each patient's problem as a unique illness story rather than as a 'case of X') is a difficult one to address philosophically, and beyond the scope of this book. The interested reader 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 my medical weeklies before binning the less interesting parts. If an article or editorial seemed to have something new to say, I consciously altered my clinical practice in line with its conclusions. All children with suspected urinary tract infections should be sent for scans of the kidneys to exclude congenital abnormalities, said one article, so I began referring anyone under the age of 16 with urinary symptoms for specialist investigations. The advice was in print, and it was recent, so it must surely replace what had been standard practice – in this case, referring only the small minority of such children who display 'atypical' features.

This approach to clinical decision-making is still very common. How many clinicians do you know who justify their approach to a particular clinical problem by citing the results section of a single published study, even though they could not tell you anything at all about the methods used to obtain those results? Was the trial randomised and controlled (see Chapter 3 'Cross-sectional surveys')? How many patients, of what age, sex and disease severity, were involved (see Chapter 4 'Whom is the study about?')? How many withdrew from ('dropped out of') the study, and why (see Chapter 4

Why read papers at all?

'Were preliminary statistical questions addressed?')? By what criteria were patients judged cured (see Chapter 6 'Surrogate endpoints')? If the findings of the study appeared to contradict those of other researchers, what attempt was made to validate (confirm) and replicate (repeat) them (see Chapter 8 'Ten questions to ask about a paper that claims to validate a diagnostic or screening test')? Were the statistical tests that allegedly proved the authors' point appropriately chosen and correctly performed (see Chapter 5)? Has the patient's perspective been systematically sought and incorporated via a shared decision-making tool (see Chapter 16)? Doctors (and nurses, midwives, medical managers, psychologists, medical students and consumer activists) who like to cite the results of medical research studies have a responsibility to ensure that they first go through a checklist of questions like 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 most common sort of guideline was what was known as a *consensus statement* – the fruits of a weekend's hard work by a dozen or so eminent experts who had been shut in a luxury hotel, usually at the expense of a drug company. Such 'GOBSAT (good old boys sat around a table) guidelines' often fell out of the medical freebies (free medical journals and other 'information sheets' sponsored directly or indirectly by the pharmaceutical industry) as pocket-sized booklets replete with potted recommendations and at-a-glance management guides. But who says the advice given in a set of guidelines, a punchy editorial or an amply referenced overview is correct?

Cindy Mulrow [10], 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 objective review of all the available evidence than a non-expert who approaches the literature with unbiased eyes. In extreme cases, an 'expert opinion' may consist simply of the lifelong bad habits and personal press cuttings of an ageing clinician, and a gaggle of such experts would simply multiply the misguided views of any one of them. Table 1.1 gives examples of practices that were at one time widely accepted as good clinical practice (and which would have made it into the GOBSAT guideline of the day), but which have subsequently been discredited by high-quality clinical trials. Indeed, one growth area in EBHC is using evidence to inform disinvestment in practices that were once believed to be evidence-based [11].

Chapter 9 takes you through a checklist for assessing whether a 'systematic review of the evidence' produced to support recommendations for practice or policymaking really merits the description, and Chapter 10 discusses the harm that can be done by applying guidelines that are not evidence-based.