How to read a paper

The basics of evidence-based healthcare

Seventh Edition

Trisha Greenhalgh and Paul Dijkstra



How to Read a Paper

How to Read a Paper

The Basics of Evidence-Based Healthcare

SEVENTH EDITION

Trisha Greenhalgh

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

Paul Dijkstra

Director of Medical Education and Consultant Sport and Exercise Medicine Physician Aspetar Orthopaedic and Sports Medicine Hospital Doha, Qatar Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences University of Oxford Oxford, UK

WILEY Blackwell

This edition first published 2025 © 2025 John Wiley & Sons Ltd

Edition History John Wiley & Sons Ltd (4e, 2010; 5e, 2014; 6e, 2019)

All rights reserved, including rights for text and data mining and training of artificial technologies or similar technologies. 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 and Paul Dijkstra to be identified as the authors of this work has been asserted in accordance with law.

Registered Offices

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

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.

Trademarks: Wiley and the Wiley logo are trademarks or registered trademarks of John Wiley & Sons, Inc. and/or its affiliates in the United States and other countries and may not be used without written permission. All other trademarks are the property of their respective owners. John Wiley & Sons, Inc. is not associated with any product or vendor mentioned in this book.

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. 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. 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. 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 Applied for

Paperback ISBN: 9781394206902

Cover Design: Wiley

Set in 9.5/12pt Minion by Straive, Pondicherry, India

In November 1995, Trisha's friend Ruth Holland, book reviews editor of the *British Medical Journal*, suggested that she 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 seventh edition	xiv	
Preface to the first edition	xvii	
Acknowledgements	xix	
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	15	
The information jungle	15	
What are you looking for?	16	
Levels upon levels of evidence	17	
Synthesised sources: systems, summaries and syntheses	18	
Pre-appraised sources: synopses of systematic reviews and primary studies		
Specialised resources	22	
Primary studies: tackling the jungle	23	
One-stop shopping: federated search engines	25	
Using artificial intelligence to search the literature	25	
Asking for help and asking around	26	
Online tutorials for effective searching	26	
Exercises based on this chapter	27	
References	28	
Chapter 3 Getting your bearings: what is this paper about?	30	
The science of 'trashing' papers	30	
Three preliminary questions to get your bearings		

viii **Contents**

What are randomised controlled trials and why do they matter?	34
What are cohort studies?	38
What are case_control studies?	40
What are cross-sectional surveys?	40
What are 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
Who is the study about?	46
Was the design of the study sensible?	47
Was bias avoided or minimised?	49
Was assessment 'blind'?	54
Were preliminary statistical questions addressed?	55
A note on ethical considerations	58
Summing up	59
Exercises based on this chapter	60
References	60
Chapter 5 Statistics for the non-statistician	63
How can non-statisticians evaluate statistical tests?	63
Have the authors set the scene correctly?	65
Paired data, tails and outliers	71
Correlation, regression and causation	72
Probability and confidence	74
The bottom line (quantifying the chance of benefit and harm)	77
Summary	79
Exercises based on this chapter	79
References	80
Chapter 6 Papers that report clinical trials of simple interventions	82
What is a clinical trial?	82
Drug trials: 'evidence' and marketing	83
Making decisions about therapy	86
Surrogate endpoints	87
What information to expect in a paper describing a randomised	
controlled trial: the CONSORT statement	91
Getting worthwhile evidence from pharmaceutical representatives	91
A note on vaccine trials	94
Exercises based on this chapter	95
References	95

Contents ix

Chapter 7	Papers that report trials of complex interventions	99	
Complex int	erventions	99	
Ten questions to ask about a paper describing a complex intervention			
Exercises based on this chapter			
References		107	
Chapter 8	Papers that report diagnostic or screening tests	109	
Ten suspects	in the dock	109	
Validating diagnostic tests against a gold standard			
Ten questior	is to ask about a paper that claims to validate		
a diagnost	tic or screening test	115	
Likelihood r	atios	119	
Clinical prec	liction models	122	
Exercises ba	sed on this chapter	124	
References		125	
Chapter 9	Papers that summarise other papers		
	(systematic reviews and meta-analyses)	128	
When is a re	view systematic?	128	
Evaluating s	ystematic reviews: five questions to ask	131	
Meta-analys	is for the non-statistician	137	
Explaining h	leterogeneity	142	
New approa	ches to systematic review	145	
Exercises ba	sed on this chapter	146	
References		146	
Chapter 10	Papers that advise you what to do (guidelines)	151	
The great gu	idelines debate	151	
Ten questior	ns to ask about a clinical guideline	155	
Exercises ba	sed on this chapter	162	
References		162	
Chapter 11	Papers that estimate what things cost		
	(health economic evaluations)	164	
What is an e	conomic evaluation?	164	
Health econ	omics studies: two key approaches	166	
Costs and be	enefits of health interventions	167	
Measuring t	he value of health states	168	
Quality-adjusted life-years			
Low-value health: choosing wisely			
Twelve quest	tions to ask about a health economic evaluation	172	
Conclusion			
Exercises based on this chapter			
References			

x Contents

Chapter 12 Papers that go beyond numbers (qualitative research)	179		
What is qualitative research?			
Summarising and synthesising qualitative research Nine questions to ask about a qualitative research paper			
Exercises based on this chapter			
References	192		
Chapter 13 Papers that report questionnaire research	195		
The rise and rise of questionnaire research	195		
Ten questions to ask about a paper describing a questionnaire study			
Exercises based on this chapter	205		
References	206		
Chapter 14 Papers that report quality improvement case studies What are quality improvement studies and how should	208		
we research them?	208		
Ten questions to ask about a paper describing a quality			
improvement initiative	210		
Conclusion	217		
Exercises based on this chapter	217		
References	218		
Chapter 15 Papers that describe genetic association studies	220		
The three eras of human genetic studies (so far)	220		
What is a genome-wide association study?	222		
Clinical applications of genome-wide association studies	225		
Direct-to-consumer genetic testing	226		
Mendelian randomisation studies	227		
Epigenetics: a space to watch	228		
Ten questions to ask about a genetic association study	230		
Exercises based on this chapter	234		
References	234		
Chapter 16 Applying evidence with patients	237		
The patient perspective	237		
Patient-reported outcome measures	239		
Shared decision-making	240		
Option grids	243		
n-of-1 trials and other individualised approaches	244		
Exercises based on this chapter	246		
References	247		

Contents xi

Chapter 17	Papers on artificial intelligence in healthcare	249	
Introduction		249	
Artificial inte	elligence	251	
Big data		253	
Machine lear	ming	254	
Generative artificial intelligence: large language and multimodal models Ethical principles for the use of artificial intelligence for health			
Ten question	s to ask about a paper that reports AI studies in healthcare	260	
Summary		264	
Exercises bas	eed on this chapter	264	
References		265	
Chapter 18	EBM+: the importance of mechanistic evidence	268	
What is mecl	hanistic evidence? An example	268	
The many ty	pes of mechanistic evidence and a preliminary hierarchy	269	
EBM+ mean	s 'both and', not 'either or'	270	
Mechanistic	evidence in the COVID-19 pandemic	272	
Exercises bas	sed on this chapter	275	
References		276	
Chapter 19	Papers that report consensus exercises	278	
Why are con	sensus method papers important?	279	
How do expe	erts choose and reach consensus on a specific topic?	279	
Consensus m	nethods	281	
Ten question	s to ask about a paper that reports a consensus statement	285	
Exercises bas	eed on this chapter	290	
References		291	
Chapter 20	Criticisms of evidence-based healthcare	293	
What's wrong	g with evidence-based healthcare when it's done badly?	293	
What's wron	g with evidence-based healthcare when it's done well?	296	
Why is 'evide	ence-based policymaking' so hard to achieve?	299	
Exercises bas	sed on this chapter	301	
References		301	
Appendix 1	Checklists for finding, appraising		
	and implementing evidence	304	
Appendix 2	Assessing the effects of an intervention	316	
Index		317	

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 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 CE, 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 blood-letting. 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 evidence-based 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 seventh edition

From Trisha

When I published the first edition of this book in 1996, I was a young physician in family medicine and a junior lecturer in a university; evidencebased medicine was still somewhat of an unknown quantity. It's now 2024, I am now approaching retirement (no longer practising clinical medicine but still working as a full-time professor) and evidence-based healthcare (no longer 'medicine' alone) is a major force in science and clinical practice. This seventh edition is co-written with new blood in the shape of Paul Dijkstra, a consultant physician and academic who has applied evidence-based healthcare in rigorous and imaginative ways in his own clinical field (sports medicine).

Back in 1995, when the idea for this book emerged, 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 - 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; 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 did not 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 it so far been translated into over 20 languages, including French, German, Italian, Spanish, Portuguese, Chinese, Polish, Japanese, Czech and Russian. I am also delighted

Preface to the seventh edition xv

that what was initially dismissed as 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 28 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.

It has been a delight working with Paul on this latest edition of what has become a classic introductory textbook. I think the new jointly authored text is more vibrant and varied than the previous single-author editions, and I hope you agree! As ever, we would welcome any feedback that will help make the text more accurate, readable and practical.

From Paul

When my wife Andrea and I bought our first copy of How to Read a Paper (at the time, I was a young sports medicine doctor and Andrea a masters student in experimental therapeutics at Oxford), I never thought I would one day have the privilege to co-author edition seven with Trisha Greenhalgh! While Andrea introduced Oxford and the Centre for Evidence-Based Medicine to me, Trisha opened my eyes to the new world (for me) of evidence-based healthcare: How to Read a Paper spotlighted shortcomings in my own undergraduate and early graduate training and changed how I practised sports medicine. The book inspired me to think and practice in a more 'evidence-based' way, to embrace patients' expertise more, to listen and question more, and to read healthcare (and other) papers more critically. Working with Trisha on the seventh edition (and to have had Trisha as one of my five DPhil in Evidence-Based Health Care mentors), was far more than an enlightening experience; it continues to be a joyous and humbling learning journey for which I'm eternally grateful! I am keen to share the lessons from this journey with you too.

When preparing this seventh edition, Trisha and I began with some formal reviews of the previous edition, and also a social media call for suggestions on how to improve it (including ones from students, who are the book's main target audience). They wanted a wider variety of chapters, updated examples

xvi Preface to the seventh edition

and – the most significant suggestion perhaps – coverage of how the artificial intelligence (AI) revolution changes EBM and EBHC. After all, in these days of ChatGPT, maybe you don't need to read a paper at all, since your digital assistant could read it for you! We've included more examples of big data studies and other AI-supported research (see, in particular, Chapter 17). We added two more chapters, one on mechanistic evidence (Chapter 18) and another on papers reporting consensus exercises (Chapter 19).

Trisha Greenhalgh Paul Dijkstra September 2024

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 policymaking), '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

xviii Preface to the first edition

(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

We are grateful to the people listed below for help and advice in preparing this book, though we take full responsibility for any inaccuracies.

To the people who, long ago, inspired and supported Trisha to write the first edition of *How to Read a Paper*, including Ruth Holland, Professor Sir Andy Haines, Professor Dave Sackett and Dr Anna Donald.

To people who have contributed ideas, references, feedback or suggestions to particular chapters for the current edition (those contributing to previous editions are mentioned in the text of the relevant chapter). We mention them in the relevant chapters. In sum, they are:

- Drs Jason Oke and Mohammed Farooq (chapter 5)
- Professor Mike Clarke (chapter 9)
- Professor Stavros Petrou (chapter 11)
- Dr Lennard Lee (chapter 15);
- Ms Yosra Mekki (chapter 17)

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

To various additional advisers and proofreaders who had direct input to this new edition or who advised Trisha on previous editions.

To the many readers, too numerous to mention individually, who took time to write in and point out ambiguities and typographical and factual errors in previous editions.

To our followers on social media who proposed numerous ideas and constructive criticisms. We are @trishgreenhalgh and @drpauldijkstra on X and can also be found on other platforms.

To our partners and families for their unfailing support for our academic work and writing. Shout out to Trisha's husband Dr Fraser Macfarlane and their sons Rob and Al Macfarlane. Our sons had not long been born when the first edition of this book was being written and are now pursuing

xx Acknowledgements

their own scientific careers (Rob in marine biology, Al in medicine). Another shout out to Paul's wife Andrea Dijkstra and their daughters Elisabet and Anne – Elisabet pursuing doctoral studies in music at Guildhall School of Music and Drama in London and Anne well on her way to becoming an architect.

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 25 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]. This definition is useful up to a point, but it misses out 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! A few years ago, Trisha and Anna Donald 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 *numbers* derived from research on *population samples* 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, we 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). (As an aside, it has become fashionable to include qualitative research

How to Read a Paper: The Basics of Evidence-Based Healthcare, Seventh Edition. Trisha Greenhalgh and Paul Dijkstra.

© 2025 John Wiley & Sons Ltd. Published 2025 by John Wiley & Sons Ltd.

2 How to read a paper

within EBHC, and we do cover this in chapter 12, but *most* people talking about EBM and EBHC are referring to research that generates *numbers*).

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 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 two-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 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-year-old woman with intermittent atrial fibrillation and a recent transient ischaemic attack, do the potential harms and inconvenience of thrombolytic therapy outweigh the risks of not taking it?') and about a host of other aspects of health and health services.

Professor 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]:

- Convert our information needs into answerable questions (i.e. to formulate the problem).
- 2. Track down 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. Appraise the evidence critically (i.e. weigh it up) to assess its validity (closeness to the truth) and usefulness (clinical applicability).
- 4. Implement the results of this appraisal in our clinical practice.
- 5. 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. Sometimes, how-to-do-it courses in EBHC concentrate too

Why read papers at all? 3

heavily 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. And 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, Trisha added three more stages to Sackett's five-stage model to incorporate the patient's perspective: the resulting eight stages, producing a *context-sensitive checklist for evidence-based practice*, which (like the other checklists in this book) is given in Appendix 1.

If we were to be pedantic about the title of this book, these broader aspects of EBHC should not even get a mention here. But we hope you understand that the book would be incomplete without 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 20 deals with common criticisms of EBHC. The challenges of implementation are so complex that they needed a book of their own, *How to Implement Evidence-Based Healthcare* [3].

If you want to explore the subject of EBHC on the Internet, you could try the websites listed in Box 1.1 (these were the top suggestions when we asked our X [formerly Twitter] followers which ones they found most useful). If you're not ready for that yet, don't worry at this stage, but do put learning to use web-based resources 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

- BMJ Evidence-Based Medicine Toolkit: a resource site maintained by this leading UK medical journal containing a wealth of resources and links for EBM, including links to critical appraisal checklists and statistical tools. https://best practice.bmj.com/info/toolkit
- 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
- The A–Z List of Evidence-Based Medicine Resources: A one-stop shop for various databases maintained by Dartmouth Libraries at Dartmouth College, Hanover, NH, USA, including PubMed, the Cochrane Database of Systematic Reviews and the Database of Abstracts of Reviews of Effectiveness (DARE): https://www.dartmouth.edu/library/biomed/guides/research/ebm-az-list.html

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 nearevangelistic 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'.

Anyone who works face to face with patients knows how often it is necessary to seek new information before making a clinical decision. In general, we don't put a patient on a 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?

Well, no, we haven't. There have been a number of surveys on the behaviour of doctors, nurses and related professionals and, while things seem to be improving, performance still falls short. It was estimated in the 1970s in the United States 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 were done in international centres of excellence and 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).

Evidence-based decision-making is more common in some specialties than others. A large survey by an Australian team, for example, looked at 1000 patients treated for the 22 most commonly seen conditions in a primarycare 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]. 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 healthcare, in which around 18% of decisions were based on 'patient-oriented high-quality evidence' [6].

The fashion to analyse what proportion of clinical decisions are evidencebased seems to have waned in recent years. But an online survey of UK general practitioners published by our team in 2020 showed that their knowledge of the quantitative benefits and harms of different treatments for long-term conditions such as diabetes or heart disease was very poor, and that most of them were aware that they were ignorant in this regard [7].

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 Trisha was a medical student, she 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 [8]. 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. When Trisha was in her first pregnancy, she developed severe vomiting and was given the anti-sickness drug prochlorperazine, and developed a very distressing neurological spasm. Two days later, she had recovered fully from this idiosyncratic reaction, but she 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.

6 How to read a paper

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, 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 by Trisha on this topic [9, 10].

Decision-making by press cutting

Trisha qualified as a doctor back in 1983, when medical journals were mostly still in paper form. She used to keep a file of papers ripped out of her medical weeklies before binning the less interesting parts. If an article or editorial seemed to have something new to say, she consciously altered her clinical practice in line with its conclusions. One paper, for example, said that all children with suspected urinary tract infections should be sent for scans of the kidneys, so she 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 common, although the file of paper cuttings has usually been replaced by online articles that the clinician has bookmarked. 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 section 'What are randomised controlled trials and why do they matter?' in Chapter 3)? How many patients, of what age, sex and disease severity, were involved (see section 'Who is the study about?' in Chapter 4)? How many withdrew from ('dropped out of') the study and why (see section 'Were preliminary statistical questions addressed?' in Chapter 4)? By what criteria were patients judged cured (see section 'Surrogate endpoints' in Chapter 6)? If the findings of the study appeared to contradict those of

Why read papers at all?

other researchers, what attempt was made to validate (confirm) and replicate (repeat) them (see section 'Ten questions to ask about a paper that claims to validate a diagnostic or screening test' in Chapter 8)? 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, midwifes, allied health professionals, 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 Trisha wrote the first edition of this book in the mid-1990s, she was critical of the so-called 'GOBSAT (good old boys sat around a table) method for producing guidelines. Professor Cindy 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 objective review of all the available evidence than a non-expert who approaches the literature with unbiased eyes, partly because non-evidence-based habits may get passed on unquestioningly from seniors to juniors in a specialty. 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 [12].

While you should be wary of the 'GOBSAT' approach, there is increasing evidence that ignoring the views of subject experts entirely when constructing guidelines is not a sensible approach, for two reasons. Firstly, the embodied wisdom of people who have managed hundreds of patients with a condition can add great value to a thorough review of the published literature. And secondly, because evidence-based information is now much more readily available than it used to be, many subject experts these days have *both* clinical wisdom *and* up-to-date knowledge of the evidence base. Another growth area in EBHC is the science of how to use consensus processes in a systematic and objective manner rather than an opportunistic and partisan one. Chapter 19, new for this edition, explains a relatively new methodology for combining reviews of the evidence with tapping into experts' clinical wisdom.

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.

8 How to read a paper

 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	Impact on clinical practice
From 500 BCE	Bloodletting (for just about any acute illness)	1820ª	Bloodletting ceased around 1910
1957	Thalidomide for 'morning sickness' in early pregnancy led to the birth of over 8000 severely malformed babies worldwide	1960	The teratogenic effects of this drug were so dramatic 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 were initially marketed as 'non-addictive' but subsequently shown to cause severe dependence and withdrawal symptoms	1975	Benzodiazepine prescribing for these indications fell in the 1990s
1970s	Intravenous lignocaine in acute myocardial infarction, with a view to preventing arrhythmias, was subsequently shown to have no overall benefit and in some cases to <i>cause</i> fatal arrhythmias	1974	Lignocaine continued to be given routinely until the mid-1980s
Late 1990s	Rofecoxib (one of a new class of non-steroidal anti-inflammatory drug introduced for the treatment of arthritis) was later shown to increase the risk of heart attack and stroke	2004	Rofecoxib was 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