

Evidence-based Resource in Anaesthesia and Analgesia

Second edition

Edited by

Martin R Tramèr

Division of Anaesthesiology, Geneva University Hospitals,
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Introduction

This is the second edition of the first book on evidence-based anaesthesia and analgesia. Those who have read the first edition¹ know that this is not a conventional textbook. And those who are looking for authoritative opinion, eminence-based doctrine, and cookbook medicine will definitely be disappointed. This book is about best-evidence data in anaesthesia, pain treatment, and critical care, about dissemination of these data, and about implementation of data into daily clinical practice. We tried hard to provide both methodological and clinical messages, and to formulate valid guidelines whenever feasible.

This second edition is both an update and a further development of the first. Obviously, the volume of the book has increased, as many more high-quality systematic reviews that critically appraise and summarise the relevant and valid literature have been published in the past few years. Authors from Australia, Canada, Denmark, Hong Kong, the United Kingdom, the United States, and Switzerland have participated in writing this book. Little attempt was made to standardise the composition and the style of the chapters, and so each chapter reflects the author's personal style.

The book has been divided into three parts. The first part starts with Nev Goodman's critical appraisal of evidence-based medicine. Then, Paul Myles presents the strengths of large randomised trials, and Andrew Moore does the same for systematic reviews and meta-analyses.

The second part of the book is on clinical application of best-evidence data. The topics fitted the criteria for inclusion if they were related to anaesthesia, pain treatment, or critical care, and had been discussed in several published systematic reviews. This does not mean that other subjects are less important; it only indicates either that other subjects have not (yet) been studied with the same systematic scientific rigour, or that we were unable to find an author to write a relevant chapter. In the first edition, there were five clinically oriented chapters, and three of those were on postoperative pain treatment. Now, the reader will find seven chapters in that part of the book, only two of which are on postoperative pain treatment. We had long discussions about whether or not we should change the title of the book to *Evidence-based Resource in Perioperative Medicine*. We eventually decided to stay with the original title, knowing that in many countries perioperative medicine is a subheading of anaesthesia, rather than *vice versa*.

The chapters on central venous catheters (by Mehrengise Cooper and Adrienne Randolph), intravenous fluids for resuscitation (by Peter Choi), and propofol for sedation and anaesthesia (by Bernhard Walder and Martin Tramèr) indicate that the book has widened its spectrum to include evidence-based critical care. Chapters relevant to postoperative pain treatment include an overview on the usefulness of peripheral analgesia (by Steen Møiniche and Jørgen Dahl) and Henry McQuay's update on acute pain, with special reference to oral analgesics. Stephen Halpern and Barbara Leighton wrote the chapter on the role of epidurals for labour. Finally, Martin Tramèr updated the chapter on prevention and treatment of postoperative nausea and vomiting. Unfortunately, we were unable to motivate anybody to write an update on transfusions; interested readers are referred to the first edition of the book.¹

The third part of the book is about dissemination, implementation, health economy, and research agenda. Dissemination and implementation of scientific data are becoming increasingly important. Great advances have been made in designing and conducting valid clinical trials and in performing powerful systematic reviews. Evidence-based medicine, however, is not only about creating new valid scientific knowledge or about systematically searching and appraising existing contemporaneous research findings; it is also about using these data as the basis for making clinical decisions.² There is a need for innovation to make high-quality data comprehensible, to transfer the data to the clinician, and to motivate clinicians to accept a change in daily clinical practice towards improved and safer patient care. The Cochrane Collaboration plays a role in this process; Tom Pedersen, in his chapter, presents the Cochrane Anaesthesia Review Group.³ Anna Lee and Tony Gin present models to facilitate the application of the aggregate results of quantitative systematic reviews to the individual patient level.

Economic constraints are increasingly interacting with clinicians' freedom to use their favourite interventions. However, what we like most is not necessarily the best for our patients. For each intervention – prophylactic, therapeutic, or diagnostic – the gold standard – the most efficacious, the least harmful, and the cheapest – needs to be identified.⁴ Ceri Phillips' chapter is an easily understandable introduction into health economics and cost effectiveness.

Last, but not least, systematic reviews are important tools for defining rational, and thus ethical, research agendas. They tell us what we know and, as a consequence, what we don't know. Thus, research protocols that are submitted to ethical committees should ideally be accompanied by a systematic review of the relevant literature, to strengthen the rationale behind the planned scientific project and to justify the design of the study. The chapter by Kathrine

Holte and Henrik Kehlet is a powerful example of this; on the basis of data from large randomised trials and from systematic reviews, the authors explain how future clinical research in the field of epidural analgesia should be designed, and what should be avoided.

We abstained from again including a comprehensive list of systematic reviews that are relevant to healthcare providers in anaesthesia, pain treatment, and critical care. In the first edition of the book, that list contained almost 100 titles.¹ Today, more than 300 relevant references can be accessed through the web page of the Geneva Evidence-based Perioperative Medicine Group;⁵ the group takes due care to update the list periodically.

Martin R Tramèr

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For further information and a list of systematic reviews go to <http://www.evidbasedanaesth.com>

Part I

Evidence-based medicine, randomised trials, and systematic reviews

1: Is evidence-based medicine still an option?

NEVILLE W GOODMAN

“What is the true value of knowledge? That it makes our ignorance more precise.”

Anne Michaels. *Fugitive pieces*. London: Bloomsbury, 1998.

“The basic error of EBM is quite simple. It is that epidemiological data do not provide the information necessary to treat individual patients. The error is intractable and intrinsic to the methodological nature of epidemiology, and no amount of statistical jiggery-pokery with huge data sets can make any difference.”

Bruce Charlton¹

Patients are not all the same

About 10 years after the term “evidence-based medicine” was first used, an editorial written by enthusiasts² included this statement: “The notion that decisions may vary from circumstance to circumstance, and from patient to patient with the same circumstances, has received increasing attention. But achieving the right balance among the factors that can affect a decision is not necessarily easy”. This summarises what is wrong with evidence-based medicine. Not only is what they say true, but critics of evidence-based medicine have been saying it for the whole of the 10 years, and have been ignored. The editorialists ended by suggesting that the term “evidence-based medicine” be replaced by “research enhanced health care”, but does that imply that there is some sort of health care that is not research enhanced, and, if so, who would profess to practise it? There are some, it seems, who are unwilling to accept that medicine can be an infuriatingly complicated activity.

Medicine based on evidence is not EBM: the meaning of “evidence”

In the chapter that introduced the first edition of this book,³ I distinguished between medicine based on evidence and Evidence-Based Medicine. The capital letters were intentional, and allow the

abbreviation EBM. EBM relies mainly on randomised controlled trials (assessed explicitly and strictly), meta-analyses, and megatrials. Although we know that proper evidence is lacking in many fields of health care, nobody argues against medicine that is based on evidence. But EBM is a conceit: it appropriates the word “evidence” placing its own specific meaning on it, and thereby puts critics of EBM – who are presumed to object to the use of evidence at all – at a disadvantage. It is in the meaning of evidence that the disagreements and criticisms lie, and they have not yet been resolved: the evidence of EBM is based in clinical epidemiology, which, as Charlton (see above) drew out^{4,5} from the ideas of Feinstein^{6,7} among others,⁸ is not a sound foundation for the treatment of individual patients.

My own syntheses of these ideas, in detail and fully referenced, are in Chapter 1 of the first edition,³ and also in a subsequent essay.⁹ The arguments from that essay were then developed further,¹⁰ and they still stand. What little counter-criticism there was¹¹ suffered the problem common to many attempted refutations: getting trapped in the rhetorical bind of using the word “evidence” in the general sense, and not in the specific sense of EBM.

Analysis of EBM: critics ignored

It is instructive to ask colleagues for their views on EBM. Although there are those who are enthusiastically in favour and those who are nihilistically against, there are few who are properly aware of the considered objections to EBM, because in general the enthusiasts do not mention them, nor cite the articles that discuss them. Many medical journals acknowledge some of the difficulties of EBM – in particular, of generalising from randomised controlled trials and of a general lack of evidence – but nonetheless, most journals more or less enthusiastically endorse EBM. The only medical journal that, to my knowledge, has carried any real analysis of EBM is the *Journal of Evaluation in Clinical Practice*, which has now published six thematic issues. The editorial commentary¹² in the latest, sixth issue summarises, by reference to the editorial commentaries in the earlier issues, how the discussion has developed. The main change in EBM has been the acceptance that individual clinicians are unlikely to be able themselves to apply the classical five-step EBM technique, but are likely to have to base their practice on the systematic reviewing of others. There has also been a softening of the authority of the statistical meta-analytic number. But there has been no attempt to refute – that is, to argue logically against – the criticism that this number does not have that authority at all: that meta-analysis and megatrials, inevitably, sacrifice methodological rigour on the altar of statistical precision⁵ and cannot therefore be secure bases on which

to treat individual patients. As Miles *et al.*¹² write, “the intrinsic and extrinsic limitations of randomised controlled trials and their meta-analyses were effectively ignored”, and “doubts about the utility of EBM were treated by its protagonists ... as simply personal problems of the doubter”.

The ignoring of limitations continues in the latest issue. Ghali and Sargious¹³ attempt a justification of the development of EBM into providing clinical care pathways for busy physicians. (They title their paper *The evolving paradigm of evidence-based medicine*, despite Couto's¹⁴ scathing ridiculing of the use of the word “paradigm”. Couto pointed out that EBM is not a new paradigm; it is a new way of approaching particular clinical problems, which, in its “belief in the supremacy of the results of clinical trials over pathophysiology is irrational”. But at least Ghali and Sargious have contributed to the dialogue.) The editorial comment is that “Very disappointingly for us, there is no evidence whatsoever in their article of an explicit appreciation of the scientific and clinical limitations of EBM discussed in outline earlier” – which means earlier in the sixth editorial comment – “and in detail elsewhere” – which is referenced to the five previous issues. The editorialists still see evidence of the “familiar ‘we know best’ pseudoauthority” and are especially upset by Ghali and Sargious' conclusion that “this new and improved brand of EBM ... will ultimately be central to the maintenance of professionalism in medicine”.

The *Journal of Evaluation in Clinical Practice* has carried analysis of EBM, but there has been no real debate about EBM. Debate implies two sides and, as Buetow¹⁵ points out, with a few exceptions the protagonists have “isolated their critics by effectively avoiding them”. A good example of this is the Cochrane review of the use of albumin (Chapter 7).¹⁶ Horsey¹⁷ documents the difficulties he had trying to challenge the validity of the review. Swales¹⁸ lamented the complete denial by the review's authors of any “evidence” from the critics because it was not the reviewers' sort of evidence. Horsey worried that the real harm was being done to the Cochrane Collaboration itself by the stubborn refusal of the reviewers to accept they may have been wrong and he comments that it calls into question all the other meta-analyses.

But now we have come full circle: it did not need the albumin review to define the problems of meta-analysis. Feinstein, Charlton, and others have repeatedly (and to me persuasively) explained how meta-analysis is a limited technique, used largely by non-clinical epidemiologists and statisticians. It is another factor of which to take account when treating individual patients, but it cannot be – by virtue of its methodology – the one and most secure basis for treatment.

I have previously commented⁹ that the most widely known handbook of EBM cited no critical references at all. Its second edition¹⁹ does ask, “does providing evidence-based care improve

outcome for patients?” and “what are the limitations of EBM?”. In answer to the first question, they write that population outcome studies show that patients do better if they receive evidence-based (by which they mean EBM-based) therapies, and they give examples from treatments for heart attacks and strokes. But their comparison is of patients who receive these therapies and patients who don't. That is not the question. The true question is whether the process of EBM, as opposed to some other process of drawing conclusions from properly considered available evidence, was necessary to the patients receiving those therapies. Also, it must be true that some meta-analyses will provide a secure clinical answer, because the patients are sufficiently alike in their disease and their response to treatment that generalisation is robust. Given the methodology of meta-analysis and the usual lack of clinical experience of many of the meta-analysts, this is likely to be a matter of luck rather than of scientific consideration. But even if a meta-analytic result is shown to be clinically robust, one cannot then draw conclusions about the robustness of meta-analysis in all circumstances.

The main reference they cite to their second question is a report of a literature search for criticisms of EBM.²⁰ The authors write that they contacted “experts in the field” (without irony), but although they thank many people well known in EBM circles for comments on earlier versions of the paper, they do not say whether they contacted critical experts as well as supportive experts. They do cite a number of critical papers, although not Feinstein,⁶ which many would consider the pivotal one. Their comment on the “basic error” (they cite Charlton⁴) is that biological variability hampers all attempts to extrapolate evidence from basic or applied research to individual patients, and thus the problem is not limited to EBM. However, EBM claims that it *can* be applied to patients, and the problem of variability is no less – in fact it is necessarily more – in a meta-analysis. Straus and McAlister's strongest argument is the circular one – that patients do better if they have been given efficacious treatment. Their counter to EBM being “anti-science” is that there are problems if one uses basic science as a sole basis for treatment.²⁰

(Without going into too much detail, the best example of how EBM is anti-science is the application of EBM to alternative medicine.²¹ This elevates the idea that clinical trial evidence is the highest form of evidence to ludicrous heights and shows what happens when observations are made outside contextual scientific knowledge. This activity can be done only by people who do not have that knowledge, or who are unable to understand its implications. There are indeed problems if basic science alone is used to treat patients, but from the knowledge of basic science one can formulate properly grounded and clinically testable hypotheses. Unfortunately, the methods of EBM are now being used to provide answers to questions in science.^{22,23}