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Introducing evidence-based anaesthesia

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Every year, more than two million new papers are published in scientific medical journals. To keep updated even in a small field or speciality takes an ever-increasing amount of time. The main purpose of evidence-based medicine (EBM) is to aid busy clinicians in making decisions based on scientific evidence. The goal of EBM is to produce systematic reviews and clinical guidelines that summarise scientific knowledge about a topic in a single publication that preferably is updated regularly.

So why should you read (and buy) this book? Because today's clinical anaesthesiologists are faced with an ever-increasing amount of work and new challenges. We have to handle our patients in both a safe and high-quality manner and at the same time adopt new scientific developments. On top of this, we have to teach our skills to those who will succeed us: the trainees. All in all, time is short and our duties are many.

The aim of this book is to meet the needs of health professionals in anaesthesiology as medicine moves to be evidence-based. Our aim is that this book should be a tool to understand the basic and advanced use of evidence-based methodology. It should integrate the results from research articles into useful, clinically orientated summaries of diagnosis, treatment and patient management in anaesthesiology and critical care medicine. Hopefully this book will become both a resource for clinical decision-making, and for decisions concerning the implementation of new technologies or interventions. This book is aimed at practising clinicians, trainees, other health professionals, medical students, teachers in evidence-based anaesthesia and EBM and, last but not least, politicians, managers and decision-makers. The chapters make clear what we know, what we think we know and what we do not know.

The book has been organised into two parts. The first 12 chapters provide the basics of EBM. They introduce EBM, critical appraisal and meta-analysis to identify and/or minimise bias. Other chapters explore clinical and statistical heterogeneity, how papers can be read and their results interpreted. Integrating the principles of EBM into daily practice is an important but often difficult task. Although we are faced with obstacles caused by lack of knowledge, skills and resources, many tools exist to

help us teach and learn EBM. This book attempts to provide, you, the reader with the highlights of educational programmes in EBM, which have been shown to change the behaviour of clinicians; improve critical appraisal skills and the implementation of EBM in the clinical workplace.

Established educational activities, such as journal clubs, can be modified in such a manner as to place EBM at their core. Strategies to disseminate evidence, such as educational programmes, clinical decision support systems and audit, can be useful tools for changing the practice of our colleagues.

The final 14 chapters of this book detail how to practise EBM in preoperative evaluation, regional and general anaesthesia, fluid therapy and the use of antiemetics; and how to use EBM in the subspecialities in anaesthesia, postoperative pain therapy, critical care and emergency medicine. These chapters deal with a selection of topics, which currently are of practical and scientific importance to clinicians.

We hope that this book will provide an exciting agenda for research and clinical work in the field of evidence-based anaesthesia.

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How to define the questions

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The practice of evidence-based medicine (EBM) begins with the formulation of a clinical question. Defining the clinical question forces you to think about what you really want to know. Clinical questions consist of three parts: the patient or population, the interventions to be compared and the clinically relevant outcomes. The clinical question can be about a single patient, or any group of patients. It can be narrow and thus specific, or it can be wide and sensitive. The intervention can be compared to nothing, to a placebo or to any other relevant intervention or interventions. The outcomes should be clinically relevant; all important outcomes should be considered. Spending time on the question helps the researcher focus on what is important. A well-defined question is a good starting point for finding relevant literature.

Introduction

In our practice, we come across clinical questions many times a day. These clinical questions may arise from several sources: the patient asking for information; your colleagues seeking advice; or from you, simply asking yourself what to do in a clinical situation. The question will often start off as open ended and poorly defined, such as: is propofol better than sevoflurane?

If you want to use an evidence-based approach to finding the answer to your question, your question needs to be well defined. The question can be about diagnosis, prognosis or management. The purpose of this chapter is to describe a strategy for formulating answerable clinical questions. That strategy can help you make conscientious, explicit and judicious use of the current best evidence for making decisions about the care of an individual patient, or a group of patients.

Formulating the question

A well-defined clinical question has three core elements:

1 The patient/population/problem

Key words: clinical question, systematic reviews, outcomes.

2 The interventions/exposures considered
3 The relevant outcomes

Formulating the clinical questions has several purposes. The process of formulating the question helps you consider what you really want to know; several choices have to be made within this process. Once the question has been formulated, it will be a great aid in the process of searching and evaluating the results (as described later in this book).

The formulation of the clinical question is the starting point; whether you intend to use EBM in the handling of an individual patient, if you are writing a clinical guideline for the department you work in, or you are preparing a systematic review.

The patient/population/problem

The patient population can be described from basic factors such as age, sex, race and educational status, or by the presence or absence of a clinical condition such as obesity, chronic heart disease or the need for a specific surgical procedure. Other factors used to describe the patient could be whether they are outpatients or inpatients; whether they live in urban or rural surroundings. The list is endless.

When choosing the patient population, one must be aware that a very narrow and well-defined population description will provide a very precise result (i.e. if a result can be found). An example of this could be: male patients aged between 50 and 70 years, with coronary heart disease scheduled for colorectal cancer surgery. This detailed description is likely to produce very specific results, but only for the narrow group in question. If the next patient is not like the first (i.e. is older, younger or a woman), problems may arise when trying to extrapolate the result.

On the contrary, choosing a wider group of patients will probably yield more results, and these results will cover a much larger group of patients. An example could be: all patients scheduled for knee arthroscopy. This group will include athletic, fit people in their 20s as well as older people with multiple co-existing diseases. With a broader group, there is always the risk that some subgroups of patients will react differently to the intervention. However, the results are much easier to extrapolate. The decision whether to use a narrow or broad question has to be placed within sound clinical judgement on the composition of the patient group.

When performing a systematic review, the approach could be to include a wide group of patients and if plausible, plan some subgroup analysis in advance if there is a suspicion that some groups will be different from the others (e.g. children, ASA3+, etc.).

The interventions/exposures considered

The intervention is something we consider "doing" to the patient. It could be a medication, surgical procedure or lifestyle counselling. An intervention could also be anaesthesia, intensive care, ventilatory support or fast tracking. The exposure could

be a toxin, tobacco smoke, or any other substance or incident that "happened" to the patient. The handling would be the same, except usually we find no randomised controlled trials (RCTs) dealing with exposure.

It is important when trying to focus our clinical question to consider which interventions we would offer the patient. If the hospital cannot offer a specific treatment, we may not need to look for it. On the other hand, if the literature search finds that a specific treatment does have a beneficial effect, we may after all wish to consider it to be introduced.

A treatment can be compared to another treatment (surgical versus medical treatment, or comparison of two different surgical methods), to placebo (mostly pharmaceutical trials) or to no treatment.

If feasible, more than two interventions can be compared. Again, this depends on the purpose of the search and how generalised or specific we wish the results to be.

A thorough description of the interventions will help the researcher find relevant papers and appraise their quality.

The relevant outcomes

The definition of, and dealing with, relevant outcomes are described elsewhere in this book (Chapter 6).

However, clinically relevant outcomes are outcomes that the patients feel, function or survive. Other relevant outcomes are for example: costs, length of stay in hospital or intensive care unit and ease of practice. When comparing different interventions it is important to take all relevant outcomes into consideration: even when information on these specific outcomes is likely not to be found.

As in the other part of the question, it is important to define the outcome measures carefully. This will often be a source of heterogeneity between trials. A straight definition will help overcome this problem.

Practice points

1 The formulation of the clinical question helps focus the question. It is the basis of literature search and helps the researcher appraise the papers critically.
2 A clinical question consists of three parts:
The patient/population/problem
The interventions/exposures considered
The relevant outcomes
3 A narrow question yields specific results that are hard to extrapolate. A broad question yields sensitive results that are easier to extrapolate, but carries the risk of overlooking differences in subgroups.

Conclusion

Spending time and energy, formulating the clinical question before undertaking the literature search, and appraisal, is likely to improve the outcome of the process. By concentrating on the problem, one can "straighten" the search and make the critical appraisal more focused.

SUGGESTED READING

1 Sackett DL, Straus SE, Glasziou P, Richardson WS, Rosenberg W, Haynes RB. *Evidence Based Medicine*. Churchill Livingstone: London, 2005.
2 Chalmers I (ed.) et al. *Systematic Reviews*. *BMJ Publishing Group,* London 2002.
3 Higgins J, Green S. (eds). *Cochrane Handbook for Systematic Reviews of Interventions 4.2.5*. The Cochrane Library. Chichester, UK: John Wiley & Sons Ltd, 2005.

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Developing a search strategy, locating studies and electronic databases

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This chapter shows how to conduct a comprehensive, objective and reproducible search for studies. It can be the most time-consuming and challenging task in preparing a clinical question for a project or a systematic review. Yet it is also one of the most important. Identifying all relevant studies, and documenting the search for studies with sufficient detail so that it can be reproduced, is after all, largely what distinguishes a systematic review from a traditional narrative review in evidence-based medicine. This chapter explains how, and where, the reviewers should look for studies that may be eligible for inclusion in *The Cochrane Library*, MEDLINE, EMBASE and other relevant databases that identify appropriate MeSH terms (Medical Subjects Headings). Although currently it is necessary to search multiple sources to identify relevant published studies, it is envisioned that the *Cochrane Central Register of Controlled Trials* (CENTRAL) in *The Cochrane Library* will become a comprehensive source for published studies, thus reducing the searching burden for authors. Identifying ongoing studies, however, will continue to remain a challenge until a comprehensive, searchable, ongoing trial register is produced to track, organise, and disseminate reports for ongoing studies, as CENTRAL in *The Cochrane Library* does for reports of studies that have been published.

Introduction

How do you find studies that meet your review's inclusion criteria?

You could do a very quick search of one electronic database and find a couple of relevant articles that meet your review's inclusion criteria. At the other extreme you could try to find every single study that has ever been done which addresses your review's question. As you might expect, there are problems with both these approaches. If you do not look very hard, the studies you do find are unlikely to

Key words: Search Strategy, *The Cochrane Library*, MEDLINE, EMBASE, CENTRAL.

be representative of all the studies done on the subject. The reasons for this are explained in detail in Chapter 8 (section "Publication bias"). For the moment, you just need to know that studies with dramatic results are much easier to find than studies that do not have dramatic findings. Another problem with only looking for a few studies is that you end up with less information. This can limit the precision of the results of your review, and restrict the conclusions you can make. However, is it feasible to find absolutely every relevant study that has ever been done? It is certainly not easy and might not be possible in most reviews. Many studies are never published, and those that are, may not be indexed in places, such as MEDLINE, that you would normally look. At some point, the effort required to find more studies becomes too much, but there is relatively little evidence on exactly when we need to stop searching. So, for now, most people adopt a pragmatic approach: look as far and as wide as possible, taking care to look in such a way that we take account of what we know about the biases in finding studies.

Search strategy for the identification of studies

Databases should include: *The Cochrane Library*, MEDLINE, EMBASE and all other relevant databases that identify appropriate MeSH terms and include the optimally sensitive. A common problem with search terms is inadequate indexing in MEDLINE and other databases. For example, random allocation was first introduced as a descriptor term in 1978; randomised controlled trial (RCT) was not introduced as a descriptor term until 1990 and did not appear as a publication type until 1991. All efforts should be made to search conference proceedings of important meetings and abstracts and contact experts in the field in order to identify unpublished research and trials still underway. Any speciality journals that have been hand searched should be identified and referenced. The name of the journal should be entered in full. Your search strategy must be reproducible, and not limited by language or publication status.

How to develop a search strategy?

It is always necessary to strike a balance between comprehensiveness and precision when developing a search strategy. Increasingly the comprehensiveness of a search entails reducing its precision and retrieving more non-relevant articles. Developing a search strategy is an iterative process in which the terms that are used are modified, based on what has already been retrieved. There are diminishing returns for search efforts; after a certain stage, each additional unit of time invested in searching returns fewer references that are relevant to the review. Consequently there comes a point when the rewards of further searching may not be worth the effort required to identify the additional references. The decision as to how much time and effort to invest

in the search process depends on the question the review addresses, and the resources that are available to the reviewer.

CENTRAL serves as the most comprehensive source of records related to controlled trials. As of January 2006, the register contained 463 763 citations to reports of trials and other studies potentially relevant to Cochrane Reviews. CENTRAL includes citations to reports of controlled trials that might not indexed in MEDLINE, EMBASE or other bibliographic databases; citations published in many languages; and citations that are available only in conference proceedings or other sources that are difficult to access [1].

Boolean operators: "OR" and "AND"

An electronic search strategy should generally have three sets of terms: (1) terms to search for the health condition of interest; (2) terms to search for the intervention(s) evaluated and (3) terms to search for the types of study design to be included (typically randomised trials). The exception to this is CENTRAL, which aims to contain only reports with study designs possibly relevant for inclusion in Cochrane Reviews, so searches of CENTRAL should be based on health condition and intervention only. A good approach to developing an electronic search strategy is to begin with multiple terms that describe the health condition of interest and join these together with the Boolean "OR" operator. This means you will retrieve articles containing at least one of these search terms. You can do likewise for a second set of terms related to the intervention(s) and for a third set of terms related to the appropriate study design.

These three sets of terms can then be joined together with the "AND" operator. This final step of joining the three sets with the "AND" operator limits the retrieved set to articles of the appropriate study design that address both the health condition of interest and the intervention(s) to be evaluated. A note of caution about this approach is warranted however: if an article does not contain at least one term from each of the three sets, it will not be identified. For example, if an index term has not been added to the record for the intervention or the intervention is not mentioned in the title and abstract, the article would be missed. A possible remedy is to omit one of the three sets of terms and decide which records to check on the basis of the number retrieved and the time available to check them. An example of Boolean operators is given in Table 3.1.

In the pulse oximetry review [2] the objective was to assess the effect of perioperative monitoring with pulse oximetry and to clearly identify the adverse outcomes that might be prevented or improved by the use of pulse oximetry. We searched MEDLINE (1966 to January 2005) using the following search strategy (Table 3.2).

It is helpful to approach an information specialist for help in suggesting suitable terms for the health condition and intervention. (We consulted the Cochrane Anaesthesia Review Group's Trials Search Co-ordinator.) In general, both controlled

Table 3.1. Example of search strategy for identifying reports of studies about propofol and sevoflurane in relation to postoperative nausea and vomiting (PONV) and complications in *The Cochrane Library*

Search strategy in text words
#1 propofol
#2 sevoflurane
#3 #1 OR #2
#4 PONV
#5 Complications
#6 #4 AND #5
#7 #3 AND #6

Search results: 1 Cochrane Review and 54 records in CENTRAL. For more information see: http://www.mrw.interscience.wiley.com/cochrane/cochrane_search_fs.html

Table 3.2. Search History in MEDLINE to identify perioperative adverse outcomes using pulse oximetry

#23 #6 and #13 and #20 and #21 and #22 (184 records)
#22 #14 or #15 or #16 or #17 (16 572 records)
#21 #7 or #8 or #9 or #10 or #11 or #12 (3 063 655 records)
#20 #18 or #19 (1 584 938 records)
#19 #1 or #2 or #3 or #4 or #5 (1 582 123 records)
#18 explode "Postoperative-Complications" in MIME, MJME (94 776 records)
#17 spo2 (900 records)
#16 desaturation* (4116 records)
#15 anox?em* (6408 records)
#14 hypox?em* (9665 records)
#13 an?esth* (279 578 records)
#12 blind* (132 561 records)
#11 mask* (28 347 records)
#10 control* (1 670 827 records)
#9 trial* (306 176 records)
#8 compar* (1 583 124 records)
#7 random* (290 202 records)
#6 pulse near ox?met* (3161 records)
#5 surg* (1 484 592 records)
#4 intra?op* (60 436 records)
#3 post?op* (350 479 records)
#2 peri?op* (26 679 records)
#1 operation (133 660 records)