Creating guidelines and treating patients if there are no trials or systematic reviews

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Readers will be familiar with the tenets of evidence-based medicine. The process can be summarized in four steps. First, the clinical problem must be formulated into an answerable question. Second, the best evidence to answer the question must be located. Third, the evidence must be appraised for validity, relevance and applicability. Fourth, the results must be implemented in practice.

Within the usual ‘hierarchy of evidence,’ a systematic review of randomised controlled trials (RCTs) is said to provide the soundest foundation to support clinical decision-making, with single RCTs the next best source of evidence. Observational studies and case reports make up the lower levels of the hierarchy.

This is now well known but needs to be tempered by two caveats. First, whilst RCTs are the preferred study design for questions about the effectiveness of interventions, they not always be possible for ethical or logistical reasons and may also be quite inappropriate for the question being posed. Other designs are better suited for other types of question (Table 1).

Table 1. Research questions and appropriate study designs

<table>
<thead>
<tr>
<th>Research question</th>
<th>Study design</th>
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<tr>
<td>Hypothesis generation</td>
<td>Cross-sectional study, case series</td>
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<td>Prognosis</td>
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It is also true that the nature of patients recruited into trials, and the carefully controlled conditions under which trials are conducted, may make the results less applicable to patients in general. Secondly, the hierarchy holds true when the evidence is of high enough quality, but not necessarily in every case. A well-conducted, relatively unbiased large observational study may provide more compelling evidence than a group of small poorly conducted RCTs. Furthermore, although systematic reviews such as those produced by the Cochrane Anaesthesia Review Group have hitherto been focused on RCTs, it is now permissible for reviews to include non-randomised studies. This may be because there are no RCTs available, as in a review in progress on the relative effectiveness and safety of physician and non-physician anaesthetists. However, when the RCT is really the only admissible study design, there may be only a few eligible studies. It is uncommon for a review to be completely ‘empty’, that is, to have no RCTs at all.
Although of course no field of medicine is fully evidence-based, for a number of reasons, anaesthesia and critical care could be said to be less so than many. The research evidence itself is often lacking, not clinically relevant or of relatively poor quality; the body of literature relating to anaesthesiology is dispersed amongst multiple journals, both clinical, general medicine and subspecialties, critical care and surgery, and basic science, cell biology, shock and circulation. One might expect some difficulties in embracing evidence based medicine on an individual and organisational level.

The philosophical question is, ‘Should we continue to practice when there is no evidence, possibly risking harm to patients from unproven actions and interventions, or cease practice until there is proof of benefit?’ Of course, practically this is nonsense; our primary duty is to patients, not principles, nevertheless we must navigate our way round these problems in our day-to-day work. Paradoxically, although doctors have practised for centuries without what we today regard as research evidence, it is only recently, when such evidence has begun to emerge, that it has become possible for the prospect of practising when evidence is not available to be a problem.

Creating guidelines

Clinical guidelines are a useful tool for integrating research evidence into practice, as their production includes all four steps of the evidence-based medicine process above, for a given clinical question or set of questions. Clinical guidelines have an important role to play within the promotion of evidence-based practice. They are defined by the World Health Organisation as ‘systematically developed evidence-based statements which assist providers, recipients and other stakeholders to make informed decisions about appropriate health interventions.’

The definition implies a careful search for relevant literature, the use of approved measures for appraising the validity and applicability of the findings, and explicit procedures for forming recommendations.

The stated advantages of guidelines include the facilitation of the practice of evidence-based medicine in that they can provide a practically-orientated summary of the relevant research literature. They are suggested to reduce variations in practice, discourage outdated and inefficient practice and improve the efficiency or healthcare delivery. They can raise awareness of a subject and also be a source of practical advice – well-written guidelines can be practically useful on a day-to-day basis. Finally, protocols can be developed to help standardise clinical management and promote best practice more widely.

Disadvantages include the potential difficulty of applying a document designed for a ‘typical’ patient to others – for instance, those with co-morbidities. There may be less or no evidence for this type of patient. A further and often unacknowledged problem is that, as guideline production confers prestige and authority on the organisation which issues them, the impetus to produced them is substantial and may lead to duplication, or even recommendations which conflict despite being based on the same evidence.

All these factors mean that there is pressure to produce guidelines even when evidence is lacking. Guideline production needs evidence, but may also require expert opinion to set the research evidence into its clinical context and produce an authoritative recommendation. Both evidence and opinion have their place, but I believe that it should be possible to distinguish between them in the finished
guideline. Furthermore, if experts disagree, as is likely when the evidence is lacking, then this should also be made explicit. An important point too is that all those involved in the production process should declare their interests. It is almost inevitable that those who are well known in their field will have made a substantial personal investment in their academic career and many will have some industrial connection too. These interests should be declared. It could be argued that it is precisely when evidence is lacking that authoritative guidance is needed, though in these circumstances the potential for conflicts of interest to bias expert judgment may be greater too, so extra transparency is also necessary. A recently published guideline from the European Society of Anaesthesiology has tried to attempt exactly that – to focus on topics which are relevant to practice, but which are not well covered by the literature. 

A useful template for the guideline production process is the AGREE-II instrument. This comprises a 23-point checklist covering scope and purpose, stakeholder involvement, rigour of development, clarity and presentation, applicability and editorial independence. 

I also believe that new guidelines should state why they have been produced and what they add to existing ones. Organisations should justify why a new guideline has been produced, instead of a simple endorsement of an existing one. Furthermore, reasons for conclusions which diverge from previous guidelines on the same subject should be explored and disclosed.

Treating patients

When we begin to learn clinical anaesthesia, we first learn a sequence of practical activities, developing proficiency in each as time goes on. It is only later that we begin to acquire the ‘evidence’, the underlying knowledge that supports these actions. But what form does this ‘evidence’ take? It may be based on argument from first principles in physiology or pharmacology, or the unequivocal support of our own senses, or a large analysis of past problems drawing lessons for practice. More rarely, there is a published research study of some description to guide us; more rarely still, a randomised controlled trial or systematic review.

So what do we draw on when we treat patients day-to-day in the operating theatre or intensive care unit? Knowledge theorists postulate two types of knowledge: tacit and explicit. Expertise in anaesthesia, in common with other fields, rests on the successful relationship between these two forms of knowledge. ‘Explicit’ knowledge, which can be readily written down, codified, and communicated in textbooks and journals and set out in examination syllabuses. ‘Tacit’ knowledge, defined as ‘knowledge that has not been, and perhaps cannot be, formulated explicitly and therefore cannot be stored or transferred entirely by impersonal means.’ It is typically acquired by demonstration followed by practice. Note, however that the tacit / explicit division may be artificial. Firstly, each relies on the other to make it work in practice and secondly, there are ways of transmitting tacit knowledge, e.g. by making and distributing a video recording of an expert performing a regional anaesthetic block. Thus, where syllabuses for anaesthesia education are set out in terms of knowledge, skills, and attitudes, within each aspect there are both tacit and explicit elements.

To take regional anaesthesia as an example, there are to my knowledge no randomised controlled trials dealing with different methods of performing ‘difficult’ spinal anaesthetics. This is such a commonly performed procedure that one might find this lack of scrutiny surprising. However, this does not mean that there is no knowledge to guide our practice, but rather that the knowledge must come from other
sources than RCTs. Our observational study of regional anaesthesia uncovered a number of elements which have no research backing but undoubtedly contribute to the effectiveness and safety of expert practice. For instance, when trainees working alone have difficulty inserting a spinal needle, they call for help. What was notable was that the consultant who came to help asked the patient to confirm that he was pressing on the spinous processes of her back as he palpated to identify the correct interspace. Whether it was this simple trick, or some unspoken aspect of experience, he succeeded on the first attempt at inserting the spinal. We suggested that experts acquire a whole repertoire of such techniques and are able to draw on these as required, selecting those that apply to a particular patient. In a similar way, we ‘individualise’ the results of a randomised controlled trial to a particular patient.

Once one is aware of tacit knowledge, one sees it everywhere. It lurks behind the apparently objective findings of research and plays a key part in what we do. A further example illustrates this. In 2002, a hospital in the United Kingdom dealt with the largest outbreak of legionnaires’ disease in the United Kingdom to date. An ‘early warning scoring’ system for identifying deteriorating patients had, by chance, just been introduced into the hospital. Retrospectively we were able to retrieve both the vital sign observations and the scoring charts and calculate the error rates in scoring. Not only was the error rate higher in patients with confirmed legionnaires’ disease than in patients with similar symptoms but negative serology (17% vs. 12%, p=0.02), but legionnaires’ positive patients were consistently overscored, making them appear sicker than they were actually. This led us to surmise that information over and above that derived from patients’ vital signs was subconsciously influencing the allocation of scores. The methodology of the study did not allow us to explore this further, though we speculated that experienced staff ‘manipulated’ scores to support their clinical impression and trigger critical care referral for the patient. The use of the word ‘manipulate’ is not meant to suggest that this was dishonest, or even intentional. A study of prediction of the risk of mortality in the intensive care unit also found that physicians’ judgements were better than those resulting from an objective scoring system, leading us to wonder what other ‘tacit’ factors are operating in risk prediction.

Conclusion

There are a number of ways of unifying the apparently polarised and conflicting message implicit in the title. Firstly, it is not only possible but also desirable to treat patients without recourse to randomised controlled trials. Even when trials are available, there are reasons why it is not appropriate to apply their results to a particular patient. In fact, in knowledge terms, we proceed in a very similar way whether there is a randomised controlled trial available or not. What differs is the type of knowledge we draw on in making our decision about the patient. Secondly, guidelines can and should be produced when there is no ‘high-level’ evidence, subject to the caveats above. Transparency of process and better methods for harnessing expert opinions within groups will help with this and as such guidelines can become high-quality, practical ‘descriptions’ of what works in practice as much as ‘prescriptions’ for what ought to happen based on research evidence.

Finally, although Archie Cochrane, the pioneer of evidence-based medicine who gave his name to the Cochrane Collaboration, is best known for his scientific approach to health care, even he knew that when there is no scientifically-based treatment available, that kindness, compassion, communication and humanity are irreplaceable in medical practice. It must be impossible to excel in anaesthesiology without aspiring to bring these elements to one’s professional life and work.
Key learning points

- Evidence-based practice has much to offer medicine and should be incorporated into medical work.
- However, many activities and interventions in anaesthesia and critical care are supported by poor quality or even no evidence.
- Useful clinical guidelines can still be formulated in such circumstances, but expert opinion should be distinguished from scientific fact.
- An alternative is to formalise existing agreed current best practice into a guideline even if it is not backed by research.
- The non-evidence based elements of experience, compassion and humanity are a vital part of patient care even when the underlying science is available.
References

17. Smith AF. In search of excellence in anaesthesiology. *Anaesthesiology* 2009; **110**: 4-5.