Medical decision making at the individual and population level: The increasing role of evidence

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Abstract

The major change in medical decision making over the last 50 years has been the realisation that treatment decisions would be improved if doctors' existing knowledge was supplemented by evidence generated systematically through health services research. This paper discusses this changing paradigm and explains the related activities of evidence-based medicine, comparative effectiveness research, and health technology assessment. The latter is particularly important for making decisions on the provision of healthcare at the population level. The key steps in undertaking health technology assessments are explained, focussing on the types of literature they generate.

Introduction

When we think of medical decision making, the image that comes to mind is that of the doctor discussing with the patient, diagnosing their health condition, and then using a lifetime of accumulated knowledge and experience to determine the most appropriate treatment. Indeed, this remains the case, but over the last 50 years the paradigm of medical decision making has been changing, involving a greater role for published evidence and an expansion of the clinician's role to include both individual-level and population-level decision making.

The objective of this paper is to examine the evolving role of medical decision making, and to explore its links with comparative effectiveness research and health technology assessment. A particular focus will be the types of literature that these activities have generated, with a view to assisting medical writers in their task of producing relevant text, thereby facilitating the publication of research papers relating to these topics.

The changing paradigm of medical decision making

When doctors use their accumulated knowledge and experience to make treatment decisions, they are mainly relying on a body of evidence that is based on what they learned during their training, and the results of their previous treatment decisions. However, this knowledge is not acquired systematically, and in the middle of the last century it became clear that treatment decisions would be improved if doctors' existing knowledge was supplemented by evidence generated systematically through clinical research.

The cornerstone of clinical research is the randomised controlled trial (RCT), where in order to assess whether a new treatment does more good than harm, patients are randomly allocated to receive either a placebo or the current standard of care (the control group), or the new treatment (the experimental group). The purpose of randomisation is to minimise any biases in the assessment of comparative treatment outcomes resulting from differences in the characteristics of the patients in the two treatment groups. The main problem with studying the outcomes resulting from a new treatment in regular practice, without randomisation, is the possibility of selection bias, whereby the new therapy is given to patients who are sicker than the average or are thought to be more likely benefit from it.

Evidence-based medicine

The notion that practising physicians should be considering evidence from the literature in their decision making has become known as evidence-based medicine (EBM). There have been many thought leaders in this field, but one worth a special mention is Archie Cochrane, a Scottish physician and epidemiologist. While practising as an army medical officer in World War II, and then later dealing with the illnesses experienced by coal miners in South Wales, he realised that randomised controlled trials were the only reliable source of evidence on whether the treatments he was giving did more good than harm.

The most important contribution of Cochrane's career was the publication of a monograph called *Effectiveness and efficiency: random reflections on health services* in 1972.[1] This book advocated the use of randomised controlled trials to make medicine more effective and efficient. Although Cochrane's main concern was with (clinical) effectiveness, he also recognised that to maximise his contribution as a physician, he also needed to consider the resources he was using. His logic was that resources, such as the doctor's own time, were limited, so that more time spent with one patient meant less time spent helping others. This raised the spectre of considering costs when making clinical decisions, which was controversial then and remains controversial today. (More on this later).

Since Cochrane's day the terminology has developed. Today we distinguish between the tthree E's (Box 1).

Box 1. Types of assessment of health care interventions

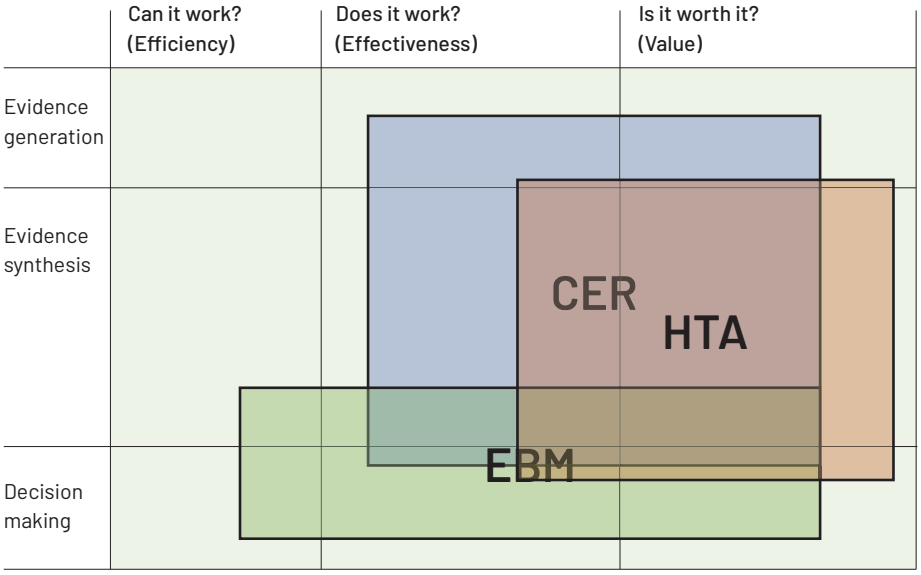
Efficacy: Can the therapy work under ideal conditions?
Effectiveness: Does therapy work in practice?
Efficiency: Is the therapy worth the cost?

The three E's are each associated with their own set of literature. Efficacy studies are characterised by the clinical studies (normally randomised controlled trials) that are considered by regulatory health agencies such as the European Medicines Agency (EMA) or the Food and Drug Administration (FDA) in the US. In these studies, the new treatment (such as a drug, medical device, surgical procedure, or any "health technology") is studied under ideal conditions. For example, the study may be conducted in a specialised clinical centre, the patients admitted to the study will not have any complicating co-existing health conditions other than the one for which the treatment is being given, patients and physicians will be "blinded" to the therapy to which individual patients have been assigned, and care will be taken to ensure full adherence to the therapy.

Efficacy studies are used to investigate whether the therapy does more good than harm as bodies like the EMA assess the trade-offs between the benefit the therapy offers and its risks (i.e., the possibility of adverse events). Recent examples are the judgements made by these agencies on the suitability of the vaccines for COVID-19. However, while efficacy is important to the health agencies, practising physicians and those funding healthcare are more interested in effectiveness studies because they want to know whether the therapy works in real life settings. There are several reasons why effectiveness might not reflect efficacy: the delivery of the treatment might require expertise or resources that are not widely available, the treatment might not work as well in patients with comorbidities (which were excluded from the efficacy studies), or the nature of the treatment (e.g. complicated dosing) may cause patients not to adhere closely to the treatment regimen.

Therefore, effectiveness studies are conducted under conditions resembling regular practice. They are often randomised studies, termed "pragmatic" clinical trials, following the terminology developed by Schwartz and Lellouch.[2] In fact, the distinction between efficacy and effectiveness is somewhat blurred, in that clinical trials may have differing levels of pragmatism (on a spectrum from efficacy to effectiveness) depending on the setting in which they are conducted, the breadth of the patient population enrolled, the level of patient monitoring, and so on.

Many effectiveness studies are not randomised, however, because randomisation may not be possible when studying real life. Therefore, series of patients receiving different treatments may be compared in observational studies. A classic example would be the analysis of a large registry such as the National Joint Registry in the United Kingdom,[3] which has enrolled thousands of patients receiving different types of joint replacements; another would be analysis of data from administrative claims databases in the US.[4] The issue here is that since potential biases are not controlled by randomisation, it is necessary to control for potential differences between patients through the data analysis. This can involve matching approaches, such as propensity scoring, or statistical approaches involving different types of multivariate regression.[5]



Notes:
- EBM = evidence based medicine
- CER = comparative effectiveness research
- HTA = health technology assessment

Figure 1. Current confusion over the relationship between EBM, CER, and HTA.
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The success of all these analytic methods depends on the extent of information on the characteristics of patients that might independently affect the effectiveness of the therapy (e.g. age, previous treatment history, seriousness of disease, existence of other health conditions). Of course, it is only possible to account for patient differences that one is aware of, not those one is unaware of. Therefore, randomisation is in theory superior because it can minimise all possibilities of bias, although some approaches, such as the use of instrumental variables in multivariate analyses, can mimic randomised studies.[6] For some health technologies, such as medical devices, randomised studies are rarely conducted because they may not be feasible or are not universally mandated by regulatory bodies such as the FDA. In these situations, it becomes necessary to rely on observational studies.

It follows that synthesising the results of several similarly conducted clinical trials would give more overall confidence in the result obtained and enable a more precise estimate of the relative clinical effect.

Finally, *efficiency studies* assess whether a therapy is "worth it" by comparing the benefits with the costs. As mentioned earlier, the logic for including costs is that, under conditions of limited resources, the costs represent the benefits forgone to other patients. Some clinicians find this a difficult concept and struggle with it ethically. They are used to rationing care in emergency situations, such as triage on the battlefield or dealing with the allocation of intensive care beds during a pandemic, but it is not so easy to identify the resource constraints when working in a modern, well-resourced health care system. Also, it expects the doctor to consider not only the person currently being treated but a broader population of patients, most of whom are "not in the room".[7] However, as will be discussed later, doctors are increasingly becoming involved in medical decision making at the population level as well as at the individual patient level.

Efficiency studies are collectively called "economic evaluations" but generally go under the name of the particular form of economic evaluation, such as "cost-effectiveness analysis", "cost-utility analysis", or "cost-benefit analysis".[8] All the methods follow the same general methodological approach but differ in the way the benefits are measured and valued. Cost-effectiveness analysis (CEA) leaves the benefits in the clinical units of measurement, such as years of life gained, cases prevented, or disability avoided. Cost-utility analysis (CUA), also called CEA in the US literature, converts the clinical effects into a generic measure of health gain, the most well-known of which is the quality-adjusted life-year (QALY). Cost-benefit analysis (CBA) converts all the costs and benefits into monetary terms but is not very common in the health literature, owing to mixed feelings about placing a monetary value on improved health or life-years gained.

The other major development following the Cochrane era was the realisation that although a single RCT is a reliable source of evidence about the efficacy or effectiveness of a treatment, it is ultimately specific to the precise circumstances in which it was conducted. It would be even more convincing if the same finding was reproduced in several similar clinical studies. Also, the precision by which a given relative clinical effect can be estimated depends on the sample size of the clinical trial. It follows that synthesising the results of several similarly conducted clinical trials would give more overall confidence in the result obtained and enable a more precise estimate of the relative clinical effect.

This has been the motivation for conducting systematic reviews of clinical trials, or of the available clinical evidence more generally. The most important organisation that promotes the conduct and use of systematic reviews is appropriately named the Cochrane Collaboration. This has developed into a major international movement with the mission "to promote evidence-informed health decision-making by producing high-quality, relevant, accessible systematic reviews and other synthesised research evidence". The organisation's vision is "a world of improved health where decisions about health and healthcare are informed by high-quality, relevant, and up-to-date synthesised research evidence".[9]

Comparative effectiveness research

Finally, "comparative effectiveness research" (CER) is a term that is now in common usage in the US. It refers to any type of effectiveness study, including pragmatic clinical trials, analysis of registries, and administrative databases. A committee of the Institute of Medicine in the US has defined CER as "the generation and synthesis of evidence that compares the benefits and harms of alternative methods to prevent, diagnose, treat, and monitor a clinical condition or to improve the delivery of care. The purpose of CER is to assist consumers, clinicians, purchasers, and policy makers to make informed decisions that will improve healthcare at both the individual and population levels".[10]

However, despite the intention to assist purchasers and policy makers, in most cases CER excludes consideration of costs. Indeed, the organisation established to fund these studies in the US, the Patient-Centred Outcomes Research Institute (PCORI), is explicitly barred from using measures such as the QALY under the terms of the Patient Protection and Affordable Care Act (also known as "Obamacare") and does not generally fund economic evaluations.[11]

Making better health care decisions: the rise of health technology assessment

The discussion above indicates that both evidence-based medicine and comparative effectiveness research seek to improve medical and healthcare decision-making at the individual and population level. This is also the claim of health technology assessment (HTA), an approach that is increasingly popular in Europe and has been the subject of a major European Union (EU) joint action, the EUNetHTA project.[12] HTA has been defined as "a multidisciplinary process that uses explicit methods to determine the value of a health technology at different points in its lifecycle. The purpose is to inform decision-making in order to promote an equitable, efficient, and high-quality health system".[13] Technology" in this case is defined very broadly and can mean a drug, a medical device, a surgical procedure, a prevention programme, or a system of organising healthcare.

Luce et al.[14] have explained the relationship between the three activities of EBM, CER, and HTA by categorising them according to two dimensions:

i. the question being asked (can it work, does it work, is it worth it?) and
ii. the main focus of the activity (evidence generation, evidence synthesis, decision making).

Figure 1 illustrates that the three activities clearly overlap although they have slightly different emphasis in respect of the two dimensions. Figure 2 presents a more definitive

distinction between the three activities and illustrates the role of many of the analytical approaches described, along with the relationships between them.

Health technology assessment is best viewed as the most over-arching activity of the three activities. It encompasses both clinical and economic assessments and although it is mostly relevant to population level decisions, it can be used at the individual patient level through a "shared decision making" approach in which the doctor discusses both the clinical and economic evidence with the patient. (See the paper by Finderup and Stacey in this issue.[15]) The explicit consideration of cost in shared decision making is particularly relevant in those settings, such as the US, where the patient may face a co-payment for their treatment.

The key steps in the HTA process are outlined in Box 2.

Box 2. Key steps in the HTA process

- Identifying topics for assessment
- Specifying the decision problem
- Searching for evidence
- Systematic review of the clinical evidence
- Economic evaluation
- Assessing social, legal, and ethical implications
- Formulating recommendations and implementation of policies
- Monitoring impact

Adapted from Goodman[16]

A full overview of HTA is given in the paper by Wendy Babidge in this issue,[17] so only a brief description is given here, focusing on the studies that might be produced at each step. Topics for assessment are typically identified by several routes, e.g. recommendations for future research made by previous research studies, requests by government or other healthcare decision making bodies, or horizon scanning. Horizon scanning involves searching databases of ongoing clinical trials, the websites of technology manufacturers, and the general literature. The results of horizon scanning exercises are occasionally submitted for publication.

Since it is not possible to assess every new technology given the resources available for HTA, priorities need to be set. The criteria most often used by HTA agencies are the anticipated clinical or economic impact of the new technology and the availability of evidence to conduct an assessment.[18]

The specification of the decision problem is a very important step, which is often conducted through a scoping exercise. A common framework used is called PICO. (Box 3).

*Box 3. The PICO framework**

Patients/population: Which patients or populations are of interest?
Intervention: What is the new intervention or technology to be studied?
Comparison: What is/are the current alternative(s) to be compared with the new intervention (e.g. current standard of care)
Outcome: What is/are the main outcome(s) of interest?

*In some versions of the PICO framework, an "S" is added to PICO, representing study design.

In the HTA step on "searching for evidence", the most important feature is to have an effective search strategy to help identify the published and grey literature. The search strategy is normally presented in publications of systematic reviews, along with the outcome of the search. This is typically published in the form of a Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) diagram, showing the number of records/abstracts identified, the number and reasons for exclusions, and the final number of abstracts selected for full review.[19]

The systematic review of the clinical evidence is one of the most important steps in the whole process and is almost always published, either as a free-standing paper or as part of the HTA report. The main objective is usually to produce a summary estimate of the relative clinical effect of the intervention as compared with the comparator, through a process called meta-analysis. However, some studies only present a narrative review if it is considered that producing a summary estimate will be misleading or unhelpful. There are several important considerations in systematic review such as checking for publication bias, assessing the quality of the included studies, and checking for heterogeneity in the studies. A good guide to undertaking systematic reviews has been produced by the Centre for Reviews and Dissemination at the University of York.[20]

The final component of the assessment phase of the HTA process is economic evaluation. Not all HTAs contain an economic evaluation component, but this is more often the case now as issues of resource allocation and the efficient provision of healthcare are becoming increasingly important. The economic evaluation may be published as part of the HTA report and as a free-standing paper. Issues in the reporting of economic evaluations are explored in the paper by Husereau et al. in this issue.[21]

The social, legal, and ethical implications need to be considered as adoption of some technologies may require changes in legislation or may infringe upon certain religious, social, or political principles. These issues may be discussed in the HTA report but do not often generate free-standing publications.

Finally, the formulation of recommendations and implementation of policies suggested by the HTA are important steps as the whole purpose of HTA is to improve health care provision. Studies of the implementation of HTA findings and monitoring of the impact are sometimes undertaken and published as free-standing papers.[22,23]

HTA in practice

Health technology assessment has a history stretching back to the 1970s and is now practised in a wide range of countries. Experience with HTA in various countries is discussed in other papers in this issue.[17,24] Given the broad application of HTA, it is possible to compare the approaches used and to specify principles of good practice.

The practice of HTA varies between countries, both in the extent of its use and the methods used. For example, the UK and Canada are high users, but the US is a low user. The reasons for this are not entirely clear, but HTA seems to be more widely used in countries with a national health service or a national health insurance system. In countries like the US, with upwards of 1000 private health insurers, it is less clear that a single, centrally conducted HTA would be equally relevant in a wide range of diverse settings.

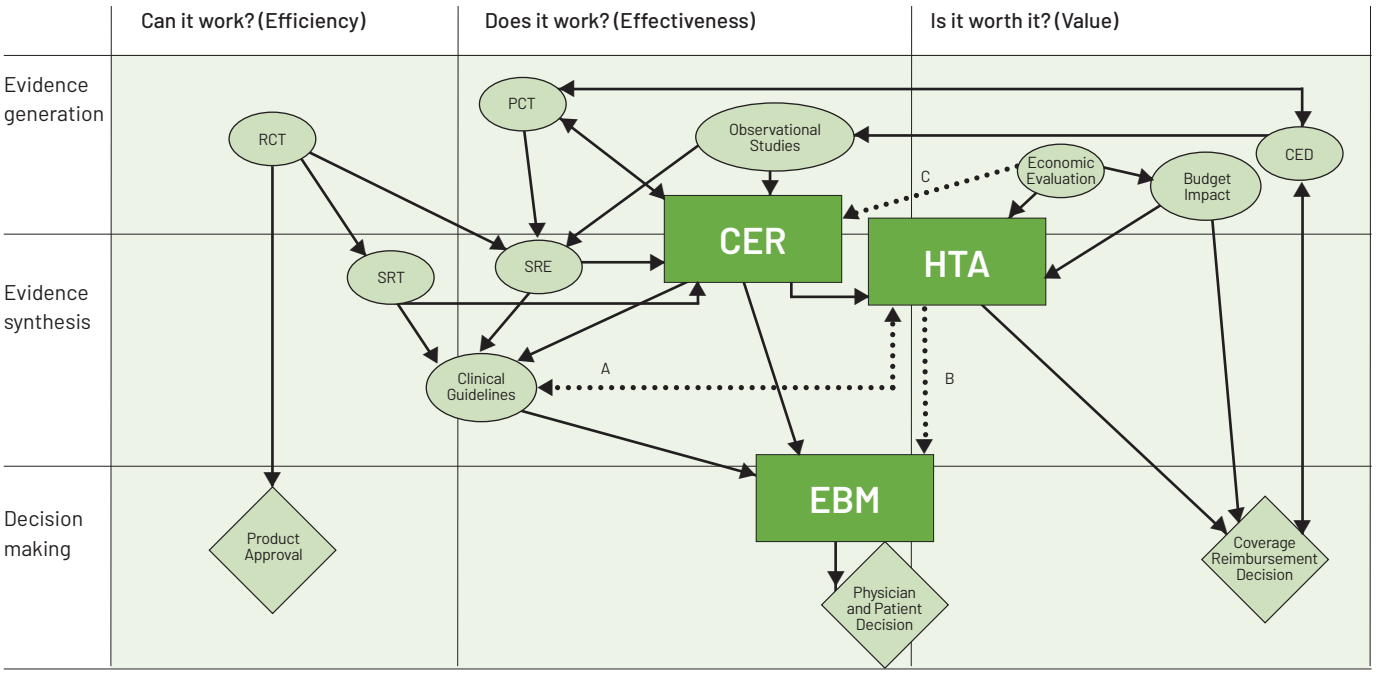

Figure 2. Redefined relationships between evidence processes and analytical approaches.

Solid lines indicate clear relationships, and dotted lines indicate disputed relationships. Diamonds represent decision processes, and circles and ovals represent all other evidence activities, except for the rectangles, which are reserved for EBM, HTA, and CER.

Abbreviations: CED, coverage with evidence development; CER, comparative effectiveness research; EBM, evidence-based medicine; HTA, health technology assessment; PCT, pragmatic clinical trial; RCT, randomised controlled trial; SRE, systematic review of evidence; SRT, systematic review of trials.

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The difference in the methods used can be illustrated by the HTA of pharmaceuticals, which has become a formal part of the approval process for reimbursement (i.e. payment by the healthcare system) in several countries. In some Northern European countries, such as the Netherlands, Sweden, and the UK, the pharmaceutical manufacturer has to produce an economic evaluation containing an estimation of the incremental cost per QALY gained from using the new drug compared with the existing standard of care. By contrast, HTA in France and Germany focuses on the "added clinical value" of the new drug, which is then used as a guide in the price negotiations between the healthcare payer and the manufacturer. Torbica et al.[25,26] have explored whether these differences in approach can be attributed to differences in culture and values in the countries concerned or in their administrative tradition and the organisation of healthcare.

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There have been several attempts to specify good practice principles for HTA. For example, Drummond et al.[27] specified 15 key principles for the improved conduct of HTAs for resource allocation decisions in healthcare. These were grouped according to issues in

i. the *structure* of HTA programmes (e.g. their independence and remit),
ii. the *methods* used (e.g. the range of costs and benefits considered),
iii. the *processes* followed (e.g. engagement of stakeholder groups), and
iv. the *use in decision making* (e.g. transparency in the link between HTA results and the decisions made).

The same group of researchers then applied these principles to a range of existing HTA programmes worldwide and developed a set of questions for benchmarking that those involved in HTA could use for self-evaluation.[28,29] They concluded that the relevance of the various principles may vary according to the local setting and the stage of development of HTA in different countries.

Future trends

The increasing role of evidence in medical decision making is clear, both at the individual patient level (primarily through EBM) and at the population level (primarily through CER and HTA). This increase in the use of evidence has

fuelled a large increase in the published literature, primarily in the areas of systematic reviews of clinical evidence and economic evaluation. This trend is likely to continue, given the shared interests of patients, healthcare policy makers, and the general public in improving the quality of healthcare decision making. In addition, we can expect to see a geographical spread of these approaches, which are already well-established in some middle-income countries. One priority area is to make the analyses conducted as useful as possible for the decision makers concerned, which is a particular challenge in multi-payer healthcare systems such as those in the US and in several middle-income countries in Latin America and Asia.

Concluding remarks

Given the increasing role of evidence in medical decision making, the interest in published studies in this field will be from a wide range of users of this evidence, including clinical practitioners, health policy makers, and patient organisations. Therefore, this literature is not exclusively aimed at researchers who are very familiar with the key concepts and terminology used. An important role of medical writing in this field is to help authors produce work that is accessible to this wide range of users with differing backgrounds and interests.

Conflicts of interest

The author has no conflicts to declare.

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