Decision analysis and the implementation of evidence-based medicine

F.P. SARASIN
From the Department of Internal Medicine, Hôpital Cantonal, University of Geneva Medical School, Geneva, Switzerland

Summary
The evidence-based medicine movement has received enthusiastic endorsement from editors of major medical journals. Hardly anyone can disagree with the aim of helping clinicians to make judicious use of the best scientific evidence for decisions in patient care. Evidence-based medicine, however, because of its dependence on randomized trials, cannot be applied to all individuals seen in daily practice. Specifically, patients may differ in age, severity of illness, presence of comorbidity and myriad of other clinical nuances. In response to these limitations, decision analysis, a technique which allows to consider multiple health outcomes, provides a rational means of allowing health professionals to move from finding evidence to implementing it. Such formal approach may reconcile evidence-based medicine with ‘real life’ and patient’s preference. It should therefore be considered complementary to evidence-based medicine.

Applying evidence-based medicine to individual patients
There is increasing pressure on health-care professionals to ensure that their practice is based on evidence from good quality research, such as randomized controlled trials, or systematic reviews of randomized controlled trials (e.g. meta-analyses). Consequently, the ‘evidence-based medicine’ (EBM) movement, which encourages the use of current best evidence in making decisions about the care of individual patients, has established its own journal and received enthusiastic endorsement from editors of major medical journals.1,2 Hardly anyone can disagree with the aim of helping clinicians to make judicious use of the best scientific evidence for decisions in patient care.

An almost exclusive focus on randomized clinical trials and meta-analyses is evident in the material currently published in the EBM journals. To determine the efficacy of treatments, results are usually expressed as the odds or risk of outcome events in the experimental group compared with a control group, e.g. the relative reduction in odds or risk. It is then generally considered that the relative treatment effect is generalizable to all patients in the trial and all similar future patients.3 This assumption, which is convenient, simplifies a complex problem encountered by all physicians in their daily activities, which is that of applying average group-derived data (e.g. ‘on average’ treatment estimate) to a unique patient.4,5 EBM, however, because of its dependence on randomized controlled trials and meta-analyses, cannot be simply applied to all individuals seen in clinical practice. Derived from a non-representative,
carefully selected population that is confined to patients expected to be highly responsive to treatment, overall results may not be always pertinent for patients seen in everyday practice. Specifically, patients may differ in age, severity of illness, presence of comorbidity and myriad other clinical nuances.

**Approaches to individualizing decision-making**

Glasziou et al. have proposed criteria for applying average group-derived data to individual patients: (i) stratification of findings according to patients characteristics, (ii) assessment of whether the intervention can be approximated in a non-study setting, (iii) quantification of benefits and harm, and (iv) incorporation of individual preferences. Although such a formal approach may be helpful, we would like to emphasize the usefulness of clinical decision analysis in relating the average results from a trial to a particular patient. Formal decision analysis uses probabilities together with values assigned to different outcomes to determine the best course of action. Specifically, for a therapeutic choice involving substantial change in absolute benefit or risk compared with predicted results, it can examine the tradeoffs between these risks and benefits. In addition, this technique allows to consider multiple attributes of health outcomes, such as the patient’s preferences for different states of health, and to measure the consequences of many strategies for which randomized trials are not feasible.

**An example of decision analysis**

A 70-year-old hypertensive diabetic woman has heart disease and asymptomatic chronic atrial fibrillation (> 3 months). Echocardiography shows enlarged left atrium and normal left ventricular function. She is at risk for thromboembolic events. If the patient is given oral anticoagulants, the risk of major haemorrhage is increased, while the risk of systemic embolism is decreased. Either event can lead to one of three consequences: death, permanent morbidity, and/or short-term morbidity. Should oral anticoagulants be given? We used a standard computer program (Decision Maker) to construct a decision analysis model representing recurrent events such as bleeding and/or embolism and their related consequences (morbidity), in addition to parameters such as patient’s age, and mortality due to underlying cardiac disease, and we applied it to explore the consequences of giving or withholding anticoagulation in the setting of chronic atrial fibrillation. Such models, enabling projections about life expectancy, quality-adjusted life expectancy and the number of adverse events associated with each strategy have been detailed elsewhere.

Based on randomized controlled trials, our patient’s presumed rate of systemic embolism without anticoagulation therapy is about 5%/year, that of major haemorrhage 1.3%/year, while anticoagulation therapy provides a relative risk reduction for embolism of 68%. Thus, the expected outcome of therapeutic abstention expressed in quality-adjusted-life-years (QALYs) is 8.6 QALYs, while that of anticoagulation therapy is 9.3 QALYs, a gain of 8%. In population-based studies of patients receiving anticoagulant therapy outside of trials, however, the excess risk for bleeding was higher, around 3%/year.

Should anticoagulation still be given? To what extent can this change modify the preferred option and eventually lead to withhold therapy? The process of examining the clinical implications of variations in the baseline scenario is called sensitivity analysis. By varying probabilities, it is possible to see how a decision would change, that is, how robust it is. Our model shows that anticoagulation is preferable as long as the rate of bleeding remains below 12%/year (‘threshold’ value), a value well above most estimates. However, the gain in QALYs decreased from 10% to 6% (rate of bleeding 3%/year), a useful piece of information. The patient says that she is terrified of having a haemorrhagic stroke. What should be done? A utility represents a patient’s preference for one outcome over others and is given a numerical value which is then used in the decision analysis. Values are usually quantified on a scale from zero to one. Thus, even if you assume a strong desire to avoid the disability associated with haemorrhagic stroke, giving it a utility of 0.1, our model suggests that the choice of anticoagulant therapy remains the preferred strategy.

Decision analysis enables us to make multiple projection. For example, what would be the optimal strategy in an elderly patient with a limited life expectancy due to severe comorbid conditions? And if anticoagulation still remains the preferred strategy, what would be the magnitude of the gain yielded by this option? Only a few days? Similarly, what would be the effect of adding a third strategy with intermediate efficacy (aspirin), assuming that if patients suffer a thromboembolic event while receiving antiplatelet drugs, their therapy is switched to oral anticoagulants? For patients with chronic atrial fibrillation, there is a wide range of risks for embolism and for bleeding, in addition to individual variables such as age or patient’s preference, making uniform recommendations very difficult, if not dangerous. Decision analysis allows us to explore each combination of these features, resulting in a unique patient-tailored decision.
Discussion

The scope of randomized trials is limited by direct applicability only to non-representative ‘average’ patients. In response to these limitations, clinical decision analysis allows us to create models that can be applied to many different individuals encompassing a wide variety of clinical scenarios (sensitivity analyses). In these models, a single decision tree is used, while patient-to-patient variability is captured through a number of internal parameters. These variables may include demographic data, such as age-, sex-, and ethnicity-associated mortality rates; excess mortality attributable to coincident disease processes; or excess risks of treatment, to name a few. Also, the information provided by randomized controlled trials is often limited by the short duration of follow-up and the restricted choice of interventions. Since long-term outcomes such as life expectancy (LE) are often important to the patient, these should be modelled by decision analysis, in addition to the many strategies for which randomized trials are not feasible.

In addition to crude risk-benefit ratios as yielded by randomized trials, decision analysis expresses outcomes in terms of gain in LE. Although this unit should not be used simplistically in clinical decision-making, it is a rich measure of the effectiveness of medical interventions. The great advantage of the gain in LE as a measure of outcome is that it is a direct measure of the shift of the survival curve caused by the intervention. Outcome measurements in terms of number of cases prevented does not tell us how premature the avoided adverse events would have been. For example, preventing death from stroke among middle-age patients would be regarded differently from preventing a death from an elderly patient with severe comorbid disease(s). One great strength of decision analysis, however, is to consider the quality of a patient’s life as a major factor in clinical decision-making by adjusting LE for the loss of quality experienced by the patient (QALYs). It therefore represents a unique method for synthesizing both medical facts (probabilities) and human values (utilities) in order to determine the best course of action. Although many physicians (and patients) are still uncomfortable with quantitative expression of quality of life, and despite the current debate about the best way to obtain these utilities, decision analysis allows us to link EBM with the patient’s preferences. Finally, given the economic climate, by examining the outcomes of each strategy both in terms of effectiveness (QALYs) and costs, it provides a basis for specifying what additional gain can be achieved for what additional resource use (i.e. cost-effectiveness analysis).

In conclusion, the laudable purpose of making clinical decisions based on evidence can be impaired by the difficulty in applying randomized trials-derived data to a patient with his/her unique clinical features and personal preferences. Decision analysis, by allowing us to incorporate a patient’s particular clinical features, provides a useful mean of helping health professionals to move from scientific evidence to individualized decision making. It should therefore be considered complementary to EBM.

References