INTERPRETING DECISION-ANALYTIC MODELLING-BASED ECONOMIC EVALUATIONS IN ORTHOPAEDICS

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Economic evaluation provides a framework for assessing the costs and consequences of alternative programmes or interventions. Within the health care context, it aims to identify the combination of human and material inputs that maximise health benefits or other measures of social welfare. It is increasingly used to inform reimbursement, regulatory and pricing decisions around orthopaedic surgery and allied branches of surgery by health care decision-makers in several countries.

One common vehicle for economic evaluations in the health care context is the decision-analytic model, which synthesises information on parameter inputs (for example, probabilities or costs of clinical events or health states) from multiple sources and requires application of mathematical techniques, usually within a software programme.[1] A plethora of decision-analytic modelling based economic evaluations of orthopaedic interventions have been published in recent years.[2-8] Economists claim that these decision-analytic models complement evidence provided by single study based economic evaluations, such as trial-based economic evaluations, that analyse individual patient data.[9] Importantly, they permit the estimation of economic outcomes over a longer time horizon than typically observed in a randomised controlled trial. They also provide a framework for incorporating and synthesising evidence from multiple and disparate sources, including trials, meta-analyses and observational studies. In contexts where randomised controlled trials are not possible or difficult to conduct,[10] decision-analytic modelling-based economic evaluations offer a practical approach towards estimating cost-effectiveness.

Although reporting guidelines can help readers, reviewers, and decision-makers interpret evidence from health economic evaluations,[11,12] there remains a ‘black box’ feel to many decision-analytic modelling-based studies. It can be difficult to assess what, if any, assumptions were made, how the data were combined, and how to interpret the outputs. This difficulty is compounded by the pace of methods development, which has led analysts to apply ever more complex methods. For journal editors and peer reviewers, it can be difficult to assess the quality of such work, whether sufficient evidence is provided, and what authors should be expected to report.

The key consideration when assessing a decision-analytic modelling-based economic evaluation is whether the study reports three core quantities: the additional cost of a new intervention compared to an existing alternative, its additional health benefits, and its incremental cost-effectiveness. It is crucial that economic evaluations generate estimates of *incremental* change from a comparator, which is usually the current practice. The cost-effectiveness of the new intervention is generally presented as an incremental cost-effectiveness ratio (ICER), which is defined as the difference in mean costs between the comparators divided by the difference in mean effects. Importantly, the ICER in isolation does not provide sufficient information to determine whether or not the intervention is cost-effective. Instead, reference should be made to an externally determined decision rule around the maximum acceptable ICER, i.e. the maximum willingness to pay by the decision-maker for the unit of health gain. Typically, the incremental cost-effectiveness of orthopaedic interventions is expressed in terms of incremental cost per quality-adjusted life year (QALY) gained, and pricing and reimbursement authorities in several countries have explicit thresholds for maximum willingness to pay for each additional QALY, which is currently £20,000 to £30,000 in England and Wales.[13] Occasionally, however, the incremental cost-effectiveness of orthopaedic interventions is expressed in terms of incremental cost per unit change in a biomedical measure.[14] This might be because data that allow QALY estimation are not available in a particular clinical context. In such cases, it is important that authors provide sufficient information to allow decision-makers to interpret the ICER estimate. For example, reference to the broader literature on willingness to pay for the clinical or health outcome of interest could aid interpretation. If this evidence does not exist, authors should be encouraged to present probabilities of cost-effectiveness across a range of hypothetical willingness to pay values for the clinical or health outcome of interest.

The design of a decision-analytic modelling-based economic evaluation should be fully described in a health economic analysis plan that is developed and publicly deposited before the analysis begins.[12] Although statistical analysis plans are increasingly published in advance, very few decision-analytic modelling based economic evaluations of orthopaedic interventions reference pre-specified health economics analysis plans.[2-8] Failure to pre-specify such a plan exposes the literature to risk of selective reporting of results or analyses.

Assessments of decision-analytic modelling-based economic evaluations should consider whether the modelling framework was fit for purpose. Some studies rely on decision trees to address the decision problem,[2] but this framework can quickly result in a large number of potentially complex pathways. Markov models, in which patients are assumed to reside in one of a finite number of health states at any point in time and make transitions between those health states over a series of discrete time intervals or cycles, may be preferable when modelling recurring outcomes through time. Patient-level simulation models and discrete event simulations, which track the progression of potentially heterogeneous individuals with the accumulating history of each individual determining outcomes, are used less commonly in the evaluation of orthopaedic interventions. Judging whether an appropriate modelling framework was applied requires close scrutiny from methodologists with sufficient knowledge of the decision problem being addressed. Generic methodological guidance for decision-analytic modelling,[15] as well as jurisdiction-specific methods guidance from HTA agencies, can help the appraisal process.

Regardless of the modelling framework, decision-analytic modelling-based economic evaluations should report all parameter inputs, including their values, estimates of uncertainty surrounding those values, their underpinning distributional assumptions, and the accompanying sources of evidence. Evidence for parameter inputs can be drawn from randomised controlled trials, observational studies or national registry data. For example, in their economic evaluation of dual-mobility components in patients with displaced femoral neck fractures**,** Montgomery and colleagues estimated key model parameter inputs in the form of revision rates for single-bearing total hip arthroplasty using data from the Australian Orthopaedic Association National Joint Replacement Registry.[16] However, researchers developing decision-analytic models often do not have access to patient-level data. In these circumstances, parameter inputs may be drawn from the literature or expert opinion when sufficient published evidence is unavailable.[2-8] Even when patient-level data are available, an argument can be made for drawing upon broader evidence where it is available. In this sense, decision-analytic modelling becomes a form of evidence synthesis. However, there is a lack of consensus about whether systematic reviews of the evidence are required for all parameter inputs.[17] Cost estimates, for example, will depend on jurisdiction-specific health care practices and jurisdiction-specific relative prices of resource inputs. Health utilities (the values placed on the health-related quality of life components of the QALY) will be driven, in part, by population-specific preference structures for health states. The over-riding principle, however, is that sufficient information should be provided for researchers wishing to replicate the analysis, and for stakeholders to appraise the evidence. Once the parameter inputs are derived, correlations between parameters in decision models can be accounted for using multi-parameter evidence synthesis techniques.[18]

It is crucial that those reporting decision-analytic modelling-based economic evaluations describe their methods for analysing or statistically transforming their data. This should include a description of methods that characterise any sources of uncertainty in the analysis, such as uncertainty surrounding the value of model parameters. Probabilistic sensitivity analysis, in which all parameters are varied simultaneously using probability distributions, has become a preferred mechanism for assessing the joint uncertainty surrounding all model parameters. This is often accompanied by graphical presentational tools such cost-effectiveness acceptability curves. However, many economic evaluations of orthopaedic interventions continue to rely on deterministic sensitivity analysis, where the effects of uncertainty surrounding individual parameters are assessed in isolation,[2,5] or completely ignore the effects of parameter uncertainty.[4] The danger of this is that cost-effectiveness results are presented with a spurious form of precision. Another form of analysis that might be relevant includes assessments for different types of heterogeneity in a study's results, which might be driven by variations between subgroups of patients, either in terms of baseline characteristics such as age, risk level or disease severity, or in terms of both baseline characteristics and relative treatment effects. Recently, health economists have also developed techniques for weighting efficiency and equity concerns within a framework of distributional cost-effectiveness analysis,[19] but we are not aware of any attempts to apply these techniques to economic evaluations of orthopaedic interventions.

In order for the results of decision-analytic modelling-based economic evaluations to gain credence amongst decision-makers, it will become increasingly important that they are subject to tests of validation. In their economic evaluations of orthopaedic interventions, Hansson et al.[6] and Montgomery et al.[16] performed tests of face or descriptive validation. The former study included verification of all data with the original sources, a series of diagnostic tests to confirm that the model had correctly applied all formulae, and a review of the calculations and programming.[6] The latter study involved validation of the model by an independent health economist checking on formulae and any other errors.[16] In other fields, there has been a move towards tests of internal validation (in which a replicate of the model, either by an independent researcher or using a different software platform, is used to assess whether consistent results are produced**)** and external validation (in which model predictions are compared to external data generated from randomised controlled trials and other external studies). However, these approaches have not yet been implemented within economic evaluations of orthopaedic interventions.[20] Another under-applied tool is the use of the decision-analytic model as a framework for assessing the value of future research through value of information analysis techniques. For example, Losina and colleagues used value of information techniques to identify the preferred treatment of meniscal tear in the presence of knee osteoarthritis on the basis of a patient-level simulation model.[21] However, no study, to our knowledge, has used the decision-analytic model as a framework for informing the design features of future orthopaedic research studies, such as determining the optimal sample size of a randomised controlled trial on economic grounds.

In summary, decision-analytic modelling represents a very useful tool for estimating the cost-effectiveness of orthopaedic interventions. It complements, and arguably enhances, the trial-based or single study based economic evaluation framework that relies on individual patient data from a single study. However, these evaluations are likely to influence commissioners of health services and so it is beholden on reviewers, editors, and readers to insist on the highest standards of methodological rigour and transparent reporting. As decision-analytic modelling methods continue to develop, these studies are likely to become an increasingly prominent feature of the orthopaedic landscape over the coming years.

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