The role of modelling in prioritising and planning clinical trials

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Executive summary

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Executive summary

Background

Most decision-analytic models in health technology assessment describe pathways through health states and events in a population. Mathematical models of the natural history of a disease are used to estimate health outcomes, resource usage and costs, and to compare the clinical and economic effectiveness of the technologies under assessment. The most common mathematical techniques used are decision analysis, state transition models and discrete event simulation. The appropriate technique depends on the characteristics of the treatment under evaluation.

Objectives

- To assess modelling methods used in the construction of disease models to support health technology assessment, and methods for their analysis and interpretation.
- To identify the role of mathematical modelling in planning and prioritising trials. ‘Trials’ is defined as all forms of primary research supporting health technology assessment of the clinical and economic consequence of alternative interventions.

Methods

Systematic reviews of the methodological and case study literature were undertaken. Search strategies focused on the intersection between modelling, health technology assessment, and priorities and prioritisation.

Results and conclusions

Five central questions were addressed.

(1) In what ways can modelling extend the validity of trials?

By:

- extending analysis to relevant rather than trial comparators
- adjusting for prognostic factors in trials
- synthesising primary research results

These conclusions are drawn from the review of methodological and case studies of economic models from the general health technology assessment literature that claims some value in research planning and design. In undertaking modelling or interpreting the results of modelling studies, the degree of reliance that can be placed on these studies is important, so close attention must be paid to guidelines for good practice.

(2) What characteristics of the trial/technology affect the success of modelling?

The review does not highlight specific success factors within the trials or technologies; given analytical expertise, there are no theoretical distinctions between alternative disease areas. Modelling may offer greater benefits as an evaluative tool for certain forms of health technology, such as diagnostics and screening, which may have an impact over a long period and where key disease/technology characteristics may not be directly observable. It may also provide more substantial benefits for technologies with long lead times in research, or for rapidly changing technologies.

A limited evidence base will reduce the ‘success’ of modelling, if the criterion is usefulness of a model in deciding on the adoption of the technology in practice. However, if the criterion for a model’s success is its usefulness in helping to decide on further research, then a limited evidence base is inevitable, and provides the key source material to describe the current uncertainty.

(3) What aspects of trial design can modelling feasibly inform?

Cost-effectiveness modelling and sensitivity analysis can inform research design by: identifying key parameters requiring further investigation, specifying the minimum clinical difference needed for sample size calculations for a proposed trial, and defining the duration and population characteristics of a proposed trial.
Some methodological discussion and case studies
use standard methods of sensitivity analysis in
informing these aspects, but these methods have
weaknesses. Analytical methods focusing on trial
design and prioritisation are required. Two
methods identified in the literature are payback
methods and expected value of information (EVI)
analysis.

- Payback methodology presupposes a specific
  trial design and therefore does not explicitly
  address this issue. Specific applications have
  focused on its role in informing the sample size
  of trials.
- EVI analysis of economics models has been
  applied in practice and can address all these
  issues.

(4) How feasible, costly and beneficial
might modelling be as part of the
prioritisation process?

Although the payback approach has not always
been implemented successfully, it has potential
feasibility. There are no published results on its
implementation costs. The benefits are unproven
but are often conceived as increased explicitness of
the prioritisation process and improved decision-
making. The main requirement for research into
payback methods is the implementation of
stochastic sensitivity analysis within exemplar case
studies.

EVI analyses have been shown to be possible
within the financial, resource and time constraints
of the NHS HTA R&D Programme. The potential
benefits of EVI are:

- The value of further research relates directly to
  its impact on technology commissioning
decisions and the consequential health and
economic benefits, and is demonstrated in real
and absolute rather than relative terms.
- It avoids the misleading rankings of
  uncertainties that may result from conventional
  sensitivity analyses.
- It does not start from a prespecified research
design, but identifies key uncertainties and
  allows the technical efficiency of many different
types of research to be assessed. Further research
  is required to establish the benefits in practice.

(5) How far can modelling substitute
for low-priority trials?

Modelling is not a substitute for data collection.
By identifying the absolute and relative value of
further research on specific parameters, EVI
analysis directly identifies trial designs of low
priority in informing technology commissioning
decisions.

Recommendations for further
research

- To report issues of good practice in
  undertaking and reporting economic
  modelling. Areas for development include
  model validation, stochastic sensitivity analyses,
  and specifically the cost-effectiveness
  acceptability curve presentation of uncertainty
  and the explicit reporting of assumptions. The
  guidelines identified here should be
  recommended to journals that publish
  economic evaluations to provide a structure for
  peer review.
- To develop case studies using stochastic
  sensitivity analyses within the payback
  approach to prioritisation of research.
- To encourage the calculation of the overall
  expected value of perfect information for a
decision problem in modelling studies seeking
to inform the prioritisation and planning of
health technology assessment.
- To identify the potential benefits of EVI
  analysis and assess whether they can be realised
  in R&D prioritisation and planning in
  practice.
- To define an objective function that captures
  the issues of importance to decision-makers in
  health technology assessment planning and
  prioritisation, and includes quantifiable aspects
to incorporate into a process that supports the
  arbitration of subjective judgement.
- To develop approximation methods to allow the
  general application of EVI methods.
- To develop a general method to estimate
  expected value and expected net benefit of
  sample information, through methodological
  research into updating of prior probability
distributions. These methods should be
demonstrated in case studies.

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