Pricing and economic value

Early economic modelling to optimise clinical development

The need for early economic models

Predicting the economic consequences of research and development (R&D) decisions has become a critical part of the drug development process. Crucially, understanding the likelihood of achieving patient access at a price that allows meaningful returns on investment is central to making decisions which can optimise the drug development path.

Decision makers' willingness to pay (WTP) can and should be explored using a variety of analytical techniques including conjoint analysis and discrete choice experiments (DCEs) which are particularly useful for investigating technologies with a range of well understood attributes. However, perhaps the most informative approach, in terms of understanding the drivers of value and gaps in evidence, is to carry out early economic modelling at a stage of development prior to conducting pivotal clinical trials.

Early economic models can help in three ways:

- Establishing a view of the potential price band that is supported by the assumed clinical benefits and therefore allowing an understanding of product financial viability;
- Understanding the critical drivers of economic value and uncertainty;
- Understanding the most critical evidence gaps that will need to be addressed.

Potential price band: the economically justifiable price

Whereas the intended drug price has normally been decided at the stage of health technology assessment (HTA) appraisal, the question to be addressed by an early model is the price, or range of prices, at which the product is likely to be cost-effective: the economically justifiable price (EJP).

For a given improvement in clinical outcome, the incremental benefit of the product can be assessed as the cost savings which the technology might generate plus the value of quality-adjusted life year (QALY) gains, the monetary value of a QALY being equal to the decision maker's WTP. For National Institute for Health and Care Excellence (NICE) appraisals, this is given by the stated 'threshold' of between £20,000 and £30,000 (this can be higher depending on the nature of the technology) or, in other contexts, the oft-quoted figure of $50,000. It should be remembered that QALY value can lie in short term effects (e.g. time spent in hospital) as well as long term survival.

Using commonly applied decision criteria, the potential value on average per patient of a technology which may generate cost offsets is equal to:

(QALYs per patient x WTP per QALY) + cost savings per patient

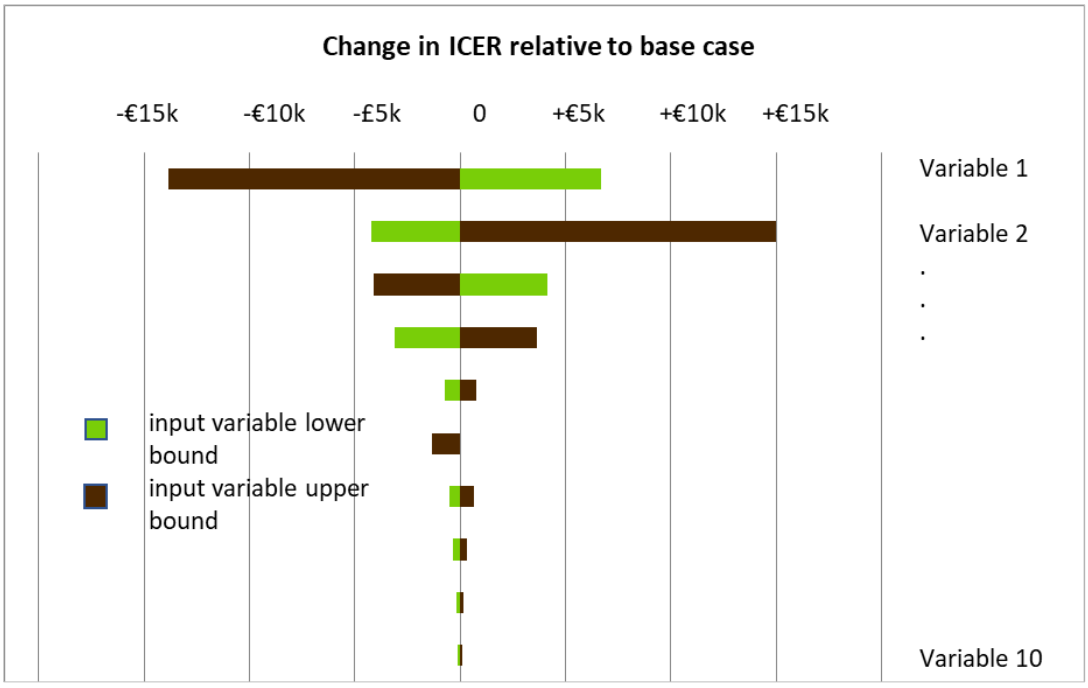
Expressing this value per course of treatment or per dose gives a limit on the price which is likely to be accepted by a health care purchaser. The EJP can be used to explore the viability of the intended list price in relation to the QALYs and cost savings generated and the WTP of interest.

Uncertainty and value: the gaps in evidence

Whereas late stage HTA focussed models should be built to best illustrate the data and limit the uncertainty in the outcomes, early economic models should embrace uncertainty and identify uncertainty gaps whose closure might improve the final economic case.

Any early economic model should be able to disaggregate the impact of key parameters on the EJP and establish the relative sensitivity of output to input parameters or modelling assumptions (Figure 1). At an early stage of development, it can indicate where the economic case is most vulnerable (whether in long term extrapolation, quality of life impacts or wider societal benefits) and therefore the risks involved in proceeding with clinical development.

Figure 1: One way sensitivity analysis



Abbreviation: ICER, incremental cost-effectiveness ratio

Developing an early model

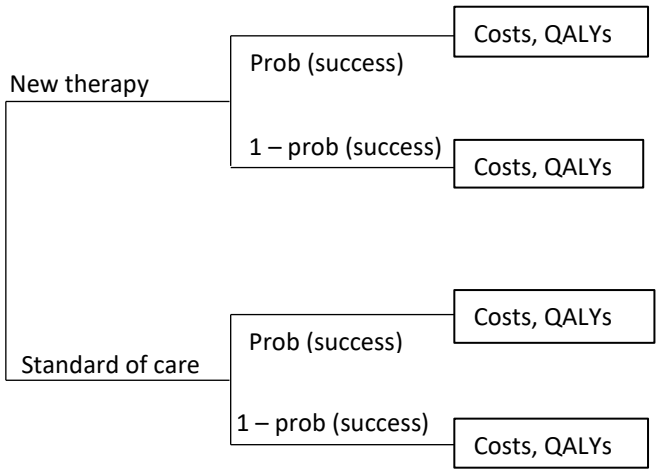
An early model approach needs to be clear, transparent and flexible to allow a full understanding of the drivers of value and of those variables. The value of the model will depend on key decisions about model structure and inputs.

Choosing a structure

Selection of model structure should seek to achieve an appropriate trade-off between being comprehensive and transparent. The model structure should reflect the nature of the disease, the potential mode of action of the product and the critical questions and data gaps.

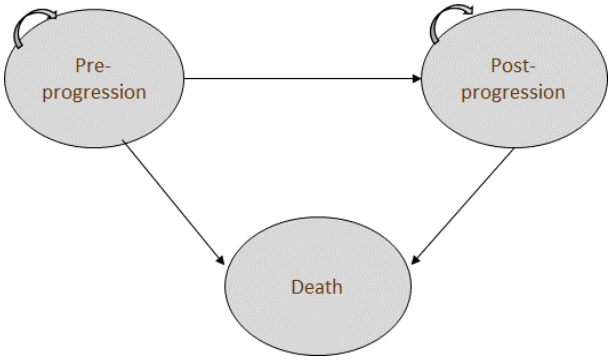
Given the uncertainties at an early stage of development and a lack of data for key variables, care needs to be taken not to over-engineer the model – the model needs to allow these uncertainties to be understood and the value of reducing the uncertainty, through data collection, to be captured.

Figure 2: Decision tree



Abbreviation: QALY, quality-adjusted life year

Figure 3: Markov model



While there is no one size fits all answer to issues of model structure, creating an overly complex model may result in spurious precision about disease pathways. Simplicity provides for transparency and ease of exploring model responses to different assumptions.

A simpler more aggregated structure such as a decision tree (Figure 2) may be preferable in many cases to guide decision making compared with a more complex structure such as a Markov model, for example the three-state model frequently used in oncology (Figure 3). Models should, however, have the flexibility to incorporate a broader range of inputs where required.

Inputs and assumptions

At the stage of HTA appraisal, it is relevant to tease out the multidimensional facets of a product's impacts in clinical practice. In contrast, given the hypothetical nature of clinical benefits at the stage of early modelling and the degree of uncertainty around them at early stages of development, the ability to characterise the detail of a product's effects is limited.

It should be borne in mind that a target product profile (TPP), often the only source of information on a product's effects at such an early stage of development, is a best guess normally with an element of optimism and based on hypothetical benefits.

Strengths and limitations of early modelling

Decision analytic techniques can provide a useful way of structuring the decisions which companies need to make about investment in their product pipelines. At the same time, it should be remembered that early models may rely on strong assumptions. Therefore early models should not be used as the sole determinant of pricing strategy or clinical development approach but as one component of the wider picture that contributes to knowledge and challenges thinking.

Conclusion

With R&D costs continuing to escalate and HTA processes becoming more closely aligned with the regulatory process, the pressure has increased on manufacturers to plan evidence generation activities earlier in the development process. As experience with HTA bodies around the world grows, manufacturers have been able to gain a clearer picture of HTA bodies' decision making criteria and WTP for the benefits of new therapy. This has provided valuable information about the incremental benefits R&D programmes must provide in order to achieve the desired returns on investment.

Early economic models can help to inform companies' R&D go/no go decisions by providing an illustrative estimate of the incremental benefits required to achieve the desired revenues and indicating in which geographies and for which patients the product is likely to be most cost-effective. However, in gaining an understanding of the true value of a technology, early modelling's role in identifying key areas of uncertainty, is perhaps more significant by informing the choice of clinical trial endpoints and the collection of real world evidence. The trend for earlier HTA suggests that there is a greater role for early modelling for companies and HTA bodies in highlighting and establishing a common understanding of the key drivers of value.

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