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Reviewing the evidence used in cost-effectiveness models in health technology assessment: a qualitative investigation of current concerns and future research priorities

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Abstract

Objectives

Health technology assessments typically include a systematic review of clinical efficacy evidence and a cost-effectiveness model. The development of the model always requires additional information beyond clinical efficacy. Depending on the timing, size and number of information requirements, the researcher faces considerable difficulties ensuring that reviewing activity to inform model development is both timely and systematic. There is a tension in terms of the need to ensure that this process is transparent and reproducible. This paper uses qualitative methods to identify these issues and to explore options for their resolution.

Methods

A focus group was held with 17 experienced systematic reviewers, information specialists and health economic modellers. Framework analysis was used to analyse themes within the qualitative data.

Results

Six key themes were identified including: 1) problem structuring, 2) current practice, 3) adequate information, 4) timing, 5) ideal practice and 6) areas for further research. Reviewing, searching and modelling were seen as integrated tasks and the respondents felt that the whole team should be involved in structuring the decision problem. Good communication was deemed to be essential with more time spent on the most important information requirements. Assessments of the quality and relevance of information were also considered important by the focus group members. Future research needs include training for focussed searching, problem structuring, quality assessment and the validation of parameter estimates.

Conclusions

This preliminary investigation highlights numerous concerns and potential deficiencies in the process of identifying, selecting and using evidence to inform models. Further guidance is required to ensure that such research activity is transparent, timely and rigorous.

Introduction

Health technology assessment (HTA) reports, such as those used to inform evidence based decisions on the effectiveness of healthcare interventions, typically involve the development of a cost-effectiveness model in addition to a systematic review of the clinical efficacy evidence. The review is usually structured according to a focussed question which defines the populations, interventions, comparators and outcomes (PICO) of interest. The cost-effectiveness model addresses the same question but within an analytical framework that takes into account broader issues relating to the decision problem. The purpose of modelling is to draw together all relevant evidence and bring this to bear on the decision problem. By its very nature the development of the health economic model requires additional information beyond clinical efficacy as illustrated in Figure 1.



Figure 1. Types of parameter values

Reimbursement decisions are made on the basis of a broader set of issues over and above simply “does it work”. The way in which this is done can have a fundamental impact on the results of the model and ultimately the decision outcome. Whilst clear methods have been developed for reviewing efficacy evidence (1, 2), the same is not true for other types of evidence which are used as sources of evidence to inform model parameters.

A number of issues need to be considered when reviewing evidence to inform the specification and population of cost-effectiveness models. Timelines for HTA may be restrictive so efficient methods are needed. In addition the methods need to be systematic, transparent and reproducible with attempts made to reduce bias in order to produce more reliable results. If model results are to be considered credible, then researchers need to be transparent about how that model came about and why certain inputs should be considered reliable. Sources of evidence may include: randomised controlled trials, observational evidence and other clinical studies, registry databases, elicitation of expert clinical judgement, existing cost-effectiveness models, routine data sources, health valuation studies, grey literature and other sources. Although reviewing processes are often used to identify data for economic models it is less usual for model reports to describe and justify how they have identified and synthesised the evidence beyond the efficacy data or for reports to set out *a priori* criteria against which to assess the quality of the evidence (3). Methodological guidance from the National Institute for Health and Clinical Excellence (NICE) is vague, stating: "For all parameters (including effectiveness, valuation of HRQL and costs) *a systematic consideration of possible data sources* is required" (4). This absence of clarity presents considerable challenges to organisations submitting evidence to NICE as the definition of what is relevant within a model will differ between decision problems.

Information specialists, systematic reviewers and health economic modellers are all involved in producing health technology assessments although the level of involvement for each in identifying evidence to inform models will vary by project and centre. Depending on the timing and size of the requests for additional information there can be considerable difficulties ensuring that the necessary information is reviewed in a timely and systematic fashion. There is tension between available time and resources to develop models and the need to ensure transparency, reproducibility and rigour in the methods used to draw together information to structure and population them. Populating certain elements of a model may require different levels of resource depending on their importance.

Although some of the issues surrounding reviewing evidence for models have been highlighted in detail (5-10) there appears to be very little formal guidance with regard to best practice in this area. Cooper et al (5) state that little is known about current practice regarding evidence identification and selection strategies, except that it is neither uniform nor transparent. Criticisms include inadequate reporting on how evidence was identified, a lack of justification regarding how evidence was selected for use in the model and a lack of quality assessment of the evidence used. Phillips et al (6) suggests that the search process and the methods for ascertaining parameter estimates should be clearly described and that in principle the results should be reproducible by another researcher. A feasibility study on searching for model parameters (11) concluded that determining the most appropriate resources to search was dependent on the model question and that multiple database searching using focused search strategies may prove more effective in finding relevant data than thorough searches of a single database. Searching should be efficient, that is given resource constraints searching should focus on those parameters that are expected to have the largest influence on the results of the model, although whether or not a parameter is important to the model results will be to a large extent dependent on what has been assumed for the other model parameters. Coyle and Lee (7) demonstrated that using different sources of data can have a large impact on the results and highlighted that there is lack of agreement as to what constitutes good evidence for specific data inputs in economic models. Chilcott et al (12) argue that one potential source of errors in health technology assessment models is the separation of the information gathering, reviewing and modelling functions.

Owing to time and resource constraints it may be necessary to use rapid review methods to identify and select evidence to inform certain model parameters. Watt et al (13) raise the point that as with the use of rapid review methods in other areas a key issue is to increase the transparency of the methods used for each review. The basic principles of systematic

reviewing: searching, appraisal, synthesis and analysis (14) may be applicable to the identification of model parameters as a full systematic review may be neither feasible nor necessary. This aim of this paper was to identify relevant key issues associated with reviewing evidence for cost-effectiveness models, particularly with respect to informing estimates for model parameters, to make recommendations for good practice and to identify areas in which further research is required.

Methods

A focus group was held with 17 researchers with extensive experience in health technology assessments including five systematic reviewers, two information specialists and nine health economic modellers in January 2010. The researchers were all from the School of Health and Related Research (ScHARR) at the University of Sheffield. A range of different people with different areas and levels of expertise were purposively invited to attend the focus group in order to reflect the breadth of input into the model development process. Ethics approval was obtained from the University of Sheffield. A topic guide was developed to structure the discussion within the focus group. The topic guide included questions covering current practice, adequate information, the timing at which reviewing activity takes place, ideal practice and areas in which further research is required. The focus group was facilitator led (EK) and was recorded using digital media with the recordings transcribed verbatim. Qualitative framework analysis (15) was used to draw out themes from the transcribed data. The transcripts were coded and a framework approach applied. A subsequent seminar was held in June 2010 and used as a member checking device. All of the 17 researchers were invited to the seminar where further discussions were held on each of the key themes identified in the focus group.

Results

Framework analysis, using the topic guide questions as an initial framework was used to draw out the focus group themes. Six main themes were identified from the focus group: [1] problem structuring, [2] current practice in model parameter reviewing, [3] determining when there is adequate information, [4] appropriate timing for the specification of parameters, [5] ideal practice for identifying evidence for model parameters and [6] areas identified for future research. These themes were further separated into subthemes.

Problem structuring

Structuring the decision problem and specifying which parameters are relevant in representing the decision problem are important parts of the process according to the focus group participants. Respondents stated that some of the important parameters could be anticipated from the outset and that problem structuring should begin early enough to facilitate shared planning and understanding within the project team. A key issue for problem structuring was defining what constitutes a relevant parameter and what process was required to uncover that relevance. It was suggested that the model structure and definition of model parameters needs to take place before systematic attempts are made to identify values for the parameters. One respondent suggested that the main objective of problem structuring activity is to develop a model that is generalizable to real world practice; this was deemed to be a task for the whole research team rather than the solely the modeller or economist. Respondents felt that an evidence-based conceptual model should be explicitly developed and that searching and reviewing is required to inform this development.

Current practice

Respondents reported that at the beginning of the modelling process the team may start off with background reading and clinical input to determine the disease natural history and develop a general understanding of the area and then think about which evidence sources should be consulted to inform model parameters. One modeller felt that the whole process

of populating relevant parameters can be quite subjective so it is important that there is transparent and adequate reporting of the decision process for selecting parameter values. Not only is it important to report how the searching was done and the search results but there needs to be a clear reporting of the systematic process used to select the parameters values that are used. This should include quality assessment. Respondents raised concerns about the quality of rapid searching done by individuals who have not been formally trained as information specialists.

The choice of clinical experts was felt to be important for identifying information to inform model parameters as this will have an impact on the appropriate specification and population of model parameters. Clinicians were thought to vary considerably with respect to their level of expertise in interpreting evidence and their opinions concerning the use of specific technologies. Sometimes two or three clinicians acted as project advisors and attended project meetings to allow the opportunity for extensive discussion aimed at reaching a consensus of opinion. Whilst it was acknowledged that the choice and use of expert opinion required caution, expert clinical advice was considered to be an essential and ongoing part of the model development process although participants did not mention asking clinical experts to review identified model parameters.

The dynamics of the research team were considered important and this was felt to vary across individual projects and across different research centres. Some roles may be shared among the team. The background and level of expertise of the reviewer was considered to have a relevant impact on how the model is developed. There was reported variation in the degree of separation between the tasks of reviewing and the broader process of model development and in the extent to which these processes were integrated. Although it was mentioned that systematic reviewers have considerable experience in reviewing large amounts of material, some modellers mentioned that they felt that sometimes they had to find all parameter values themselves. In contrast, for the sake of efficiency, one modeller felt

that it may be more appropriate for the modeller to identify and appraise evidence for model parameters.

Some respondents stated that they develop a list of tasks for the research team at the beginning of a project and divide the tasks between the reviewer and the modeller depending on expertise and available time. It was felt that for some parameters the modeller was better placed to find appropriate values whilst for others this activity would be more appropriately undertaken by the reviewer. The respondents' experiences with respect to this division of tasks seemed to vary between projects. The process was described as "iterative" as more information may be needed later as the model is developed. Respondents stated that the team becomes more focussed on the parameters that are shown to be sensitive and new issues are identified throughout the model development process as attempts are made to reflect parameter uncertainty. However an issue was also raised that the sensitivity of one parameter will to some extent be dependent on the values of the other parameters. Therefore caution should be advised in using this approach to focus reviewing efforts. A common view amongst the focus group respondents was that the reliance on simple sensitivity analysis (e.g. one-way or restricted multi-way analysis) represents an insufficient basis for assessing parameter importance and may indeed produce misleading findings depending on the extent to which other model parameters have been systematically identified, selected and used within the model. All respondents agreed that it was inappropriate for the systematic review to be undertaken in complete isolation and then handed over to the modeller with no communication between the two; instead it was agreed that this needs to be an integrated process.

Frequent project team meetings were suggested as an opportunity for discussion and for making decisions concerning the need for more information. For example, after identifying parameters that have an impact on the model results, discussions about a more systematic reviewing approach for that parameter may be needed. Some reviewers said that they

flagged up information that they thought would be important for the model but were not clear as to how or if this information was used by the modeller.

Adequate information

A specific focus of the discussion within the focus group concerned what constitutes “adequate” information. One issue concerned the danger of relying on only one clinical advisor. Although clinical advisors were seen as an important source of information and potentially more appropriate than the use of routine data sources or the literature for some but not all parameters, more than one expert was needed and there had to be a level of understanding of the condition on the part of the team to ensure that the most appropriate decisions were made regarding model parameters. This was also felt to some extent to be dependent on geographical variation and local enthusiasms for particular technologies. The use of an expert panel was suggested as a possible means for avoiding this potential source of bias. Also mentioned was the need to ensure that all levels of health care delivery were represented, for example hospital specialists as well as GPs as opinions on treatments and approaches can be quite different across different settings. Respondents also raised concerns regarding determining the level of variation in the pathway of care and the extent to which the model should reflect this. A related issue raised by the respondents concerned tensions between internal and external validity in models, with particular reference to the potential gap between costs and outcomes of treatments sourced from clinical trial data and actual clinical practice. The respondents suggested that attempts need to be made to ensure that the uncertainty around each of the parameter estimates is characterised appropriately.

A major concern raised by the respondents was that a team could potentially make an assumption that they had identified all relevant information for a model parameter when in fact they may have missed important evidence. Conversely it was agreed that comprehensiveness was not the goal as it was not necessarily important to find all sources

of information nor would there be time due to the constraints of most projects. Finding the best source of evidence was an issue felt to be sometimes down to serendipity and sometimes down to taking the time to determine what was the most reliable or realistic source of information. Respondents felt that there was a difference between transparency and credibility in that the wrong model might be developed and yet be clearly reported. As well as identifying the most suitable sources of information it was considered also important to report the thought processes involved in the development of the model and why specific choices had been made. Quality assessment of evidence was mentioned as being important.

Timing of reviewing activity

The respondents noted that judgements regarding the importance of specific parameters are sometimes made quite late in the development of a model and respondents suggested that it can be very difficult to plan for this in advance. When one parameter is changed another parameter can suddenly become more important to the results. Some can be identified early on by putting estimates into the model but this approach needs to be treated with caution. Judgements need to be made regarding the efficient use of time and resources in such cases. There is a danger that parameter values may be identified in a less than systematic way due to these constraints. One recommendation was that it is important to plan and give the team an idea early on as to what additional parameters values to be looking for. The development of a conceptual model at the start of the project was considered very useful for this reason and it was felt to be important to incorporate some contingency time for unexpected parameter values.

Ideal practice

Several points were identified regarding ideal practice. First, problem structuring methods should be considered in order to identify what is relevant early on in the modelling process. Communication was felt to be very important and everyone in the team should be involved in

the development of the model structure from the beginning and work closely together. This was considered to be an iterative process though the level of iteration differs between projects and teams. It was felt that iterative team working helped to ensure that the most relevant parameter values were identified. The reviewers are also aware of the requirements of the model during data extraction for the clinical efficacy review; this was seen as a benefit of structuring the process in this way. It was considered particularly useful if at least some members of the team have expertise in the disease area. Reporting of the process of reviewing for model parameters was thought to be essential in demonstrating that it had been done in a systematic and reproducible fashion.

Some modellers stated that they would like to be more involved in the searches that informed the model. For some projects there may be a need for focussed searches. Although not every piece of evidence for every model parameter will be identified, decisions need to be made as to the type of searching and sifting that the time constraints of the project allow.

Also mentioned was the possibility of “tagging” potentially relevant sources during the sifting of references. At the start of a project when reviewers are sifting references for the clinical efficacy review they can also look for other relevant references which may be used for populating model parameters. If there was a list of parameters, keywords could be used to aid the rapid identification of relevant studies for specific parameters. One potential problem with tagging was the possibility of the reviewer missing potentially appropriate information sources and the modeller assuming that there was no relevant information in the database of references because it had not been identified by the reviewer.

Respondents felt that forward planning was important where possible. Although requests for more information may come late on in the project, some of these needs can be anticipated. One final suggestion was for a repository for key parameter values.

Areas in which further research is required

Several recommendations for further research were identified by respondents. There was considerable support for the need for training for rapid searching methods. Although ideally searches would be undertaken by information specialists this was not always feasible and other members of the team felt that training in this area would be helpful. It was also suggested that it would be useful to have some guidelines concerning where to find information such as a list of websites and a hierarchy of information sources. Training was also needed for scoping searches and focussed searches.

More research was considered necessary regarding methods for problem structuring and ways this process could be communicated. Also mentioned were research into methods for decision making processes around the selecting and reviewing of evidence for model parameter values. Another research area mentioned concerned methods for establishing the standard care pathway or a representative selection of care pathways. Quality assessment methods for different study types, particularly rapid quality assessment tools were also suggested as were methods for validating model parameter estimates. Finally, research into how the use of clinical expert opinion should be managed and incorporated into the model development process was suggested.

Discussion

Summary of main issues identified

The purpose of this paper was to identify prevalent issues and constraints surrounding the systematic consideration of evidence sources used to inform health economic models. Inevitably, comprehensive, systematic reviewing of the evidence for all model parameters is not possible due to time and resource constraints. However the well established components of systematic reviewing searching, appraisal, synthesis and analysis can be utilised to maximise transparency in the choice of parameter values as far as is possible.

The focus group highlighted that activities surrounding reviewing for model parameters represent a central element of model development. Reliance on simple sensitivity analysis was felt to be an insufficient basis for assessing parameter importance and may result in the production of misleading findings depending on the extent to which other model parameters have been systematically identified, selected and used within the model. Further, the extent of a given parameter's importance upon the model results may change as the other elements of the model are further developed and refined. Claxton (16) argues that adoption decisions should be made on the basis of mean costs and health outcomes; in principle a single model parameter which is not subjected to formal searching, synthesis and analysis could produce misleading estimates of costs and outcomes and potentially result in inappropriate policy decisions. The best measure of the credibility of a model's parameters is the legitimacy of the process through which the evidence has been identified, selected and implemented rather than whether it matters to the results at some point in time during model development. This view was directly reflected in the focus group responses.

The International Society for Pharmacoeconomics and Outcomes Research (ISPOR) has produced good practice in modelling guidance (17, 18) which covers some of the issues

outlined in this research. However, little guidance is given where a full systematic review for model parameters is not possible due to time or resource constraints.

A further finding arising from the discussions concerned the nature of the model development process. It became clear from the respondents that the definition of best practice for reviewing evidence to inform model parameters cannot be entirely detached from problem structuring activities to determine which parameters are relevant to the particular decision problem. Given this interrelationship, the focus group respondents suggested that parameter reviewing activity should not lie solely with the reviewer, nor solely with the modeller; instead the respondents suggested that this should be considered as a joint process and that the organisational infrastructure should reflect the need for joint working in this area.

Implications for practice

The methodological and practical issues from the focus group give rise to a number of implications for the practice of health economic model development.

Recognition of the joint relationship between model development and reviewing activity:

Model specification and model parameterisation are intertwined and should not be treated as separate processes; they are both directly concerned with ensuring the credibility of results drawn from the model. Model development should be considered as a broader process than simply model implementation and programming, instead including all aspects of evidence identification, selection and use in addressing the decision problem.

Improved communication and training: There is a need for reviewers and information specialists to understand the principles of health economic modelling as well as a need for modellers to understand the principles of searching and systematic reviewing. This may have training implications for modellers, information specialists and reviewers.

Transparency and consistency: There is considerable variation in the way that models are developed and in how reviewing for model parameters is undertaken. However, greater

degrees of consistency and transparency are desirable in ensuring model credibility. The identification, selection and use of particular evidence sources to inform model parameters should be explicitly justified. It is reasonable to further argue that decisions concerning the model specification, that is the definition of which parameters are relevant within the model, should also be explicitly described in the form of one or more conceptual models.

Areas for future research

It is important to recognise that this research is based on one focus group in one research centre, and as such, the findings of this study should be considered exploratory in nature. Current practice in reviewing model parameters, and indeed the broader process of model development may vary between academic centres and other health outcomes and consultancy groups. It is essential to explore these issues in more depth with other centres who may have different approaches to the modelling process. Nevertheless several areas where more research is needed were identified. The first involves the use of problem structuring methods for the identification, specification and prioritisation of relevant parameters. Another area of research identified is the systematic identification of evidence to inform model parameter estimates. This includes guidance on appropriate searching methods. Research into methods for reviewing model parameter data in a systematic fashion are also needed and include critical appraisal and rapid review methods. Finally, guidance in the appropriate reporting of review methods and decisions and judgements made for the identification and selection of evidence are needed.

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