

The use of economic evaluations in NHS decision-making: a review and empirical investigation

I Williams, S McIver, D Moore and S Bryan



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The use of economic evaluations in NHS decision-making: a review and empirical investigation

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The research reported in this issue of the journal was commissioned by the National Coordinating Centre for Research Methodology (NCCRM), and was formally transferred to the HTA Programme in April 2007 under the newly established NIHR Methodology Panel. The HTA Programme project number is 06/90/11. The contractual start date was in January 2002. The draft report began editorial review in March 2007 and was accepted for publication in October 2007. The commissioning brief was devised by the NCCRM who specified the research question and study design. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the referees for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

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Abstract

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Objectives: To determine the extent to which health economic information is used in health policy decision-making in the UK, and to consider factors associated with the utilisation of such research findings.

Data sources: Major electronic databases were searched up to 2004.

Review methods: A systematic review of existing reviews on the use of economic evaluations in policy decision-making, of health and non-health literature on the use of economic analyses in policy making and of studies identifying actual or perceived barriers to the use of economic evaluations was undertaken. Five UK case studies of committees from four local and one national organisation [the Technology Appraisal Committee of the National Institute for Health and Clinical Excellence (NICE)] were conducted. Local case studies were augmented by documentary analysis of new technology request forms and by workshop discussions with members of local decision-making committees.

Results: The systematic review demonstrated few previous systematic reviews of evidence in the area. At the local level in the NHS, it was an exception for economic evaluation to inform technology coverage decisions. Local decision-making focused primarily on evidence of clinical benefit and cost implications. And whilst information on implementation was frequently requested, cost-effectiveness information was rarely accessed. A number of features of the decision-making environment appeared to militate against emphasis on cost-effectiveness analysis. Constraints on the capacity to generate, access and interpret information, led to a minor role for cost-effectiveness analysis in the local decision-making process. At the national policy level in the UK, economic analysis was found to be highly integrated into NICE's technology appraisal

programme. Attitudes to economic evaluation varied between committee members with some significant disagreement and extraneous factors diluted the health economics analysis available to the committee. There was strong evidence of an ordinal approach to consideration of clinical effectiveness and cost-effectiveness information. Some interviewees considered the key role of a cost-effectiveness analysis to be the provision of a framework for decision-making. Interviewees indicated that NICE makes use of some form of cost-effectiveness threshold but expressed concern about its basis and its use in decision-making. Frustrations with the appraisal process were expressed in terms of the scope of the policy question being addressed. Committee members raised concerns about lack of understanding of the economic analysis but felt that a single measure of benefit, e.g. the quality-adjusted life-year, was useful in allowing comparison of disparate health interventions and in providing a benchmark for later decisions. The importance of ensuring that committee members understood the limitations of the analysis was highlighted for model-based analyses.

Conclusions: This study suggests that research is needed into structures, processes and mechanisms by which technology coverage decisions can and should be made in healthcare. Further development of 'resource centres' may be useful to provide independent published analyses in order to support local decision-makers. Improved methods of economic analyses and of their presentation, which take account of the concerns of their users, are needed. Finally, the findings point to the need for further assessment of the feasibility and value of a formal process of clarification of the objectives that we seek from investments in healthcare.



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List of abbreviations

ACD	Appraisal Consultation Document	MS	multiple sclerosis
CA	coronary angiography	NICE	National Institute for Health and Clinical Excellence
CASP	Critical Appraisal Skills Programme	NSF	National Service Framework
CEAC	cost-effectiveness acceptability curve	NTRF	new technology request form
CHC	Community Health Council	PACEF	Priorities and Clinical Effectiveness Forum
CHOP	cyclophosphamide, doxorubicin, vincristine and prednisolone	PCT	Primary Care Trust
CMA	cost-minimisation analysis	PEC	Professional Executive Committee
CML	chronic myeloid leukaemia	QALE	quality-adjusted life expectancy
FAD	Final Appraisal Determination	QALY	quality-adjusted life-year
HU	hydroxyurea	SPECT	single photon emission computed tomography
ICER	incremental cost-effectiveness ratio	WHO	World Health Organization
MMC	Medicines Management Committee		

All abbreviations that have been used in this report are listed here unless the abbreviation is well known (e.g. NHS), or it has been used only once, or it is a non-standard abbreviation used only in figures/tables/appendices in which case the abbreviation is defined in the figure legend or at the end of the table.



Executive summary

Objectives

This report is concerned with the use of research evidence relating to economic analyses in healthcare decision-making. The research described in this report addresses two principal questions:

- To what extent, and in what ways, is health economic information used in health policy decision-making in the UK?
- What factors are associated with the utilisation (or non-utilisation) of such research findings?

Methods

Systematic review

Major electronic databases were searched up to 2004 and a systematic review of the literature was undertaken. This considered existing reviews on the use of economic evaluations in policy decision-making, health and non-health literature on the use of economic analyses in policy making and studies that have identified actual or perceived barriers to the use of economic evaluations.

Empirical research methods

The research team adopted a predominantly qualitative approach involving primarily the use of case study methods. This included documentary analysis, meeting observation and semi-structured interviewing. Five case studies were conducted in total, including committees from four local and one national organisation. The national case study was the Technology Appraisal Committee of the National Institute for Health and Clinical Excellence (NICE). Case studies were augmented with a documentary analysis of new technology request forms used by local decision-making committees and workshop discussions with members of local decision-making committees.

Results

Systematic review results

Overall, the systematic review exposed the difficulties of attempting systematically to search for evidence when considering topics such as this. Despite these difficulties, the review established the following:

- There are very few previous systematic reviews of the evidence in this area
- A number of previous studies in healthcare have looked at the use of economic evaluations in decision-making. Although these undoubtedly contribute to our knowledge on this topic, there are some concerns about the methodological approach adopted in these studies.
- There is a continuing need for research that addresses the range of policy decision-making levels and which takes an in-depth, qualitative approach to addressing the research question.

Empirical research results: the local level

There are a range of local formulary decision-making committees in existence. These vary in terms of: the geographical and organisational scope of responsibility; level of resource and capacity available to them; their perceived role and functions; and the types of information they request and use. Our main research finding at the local level in the NHS is that it is an exception for economic evaluation to inform technology coverage decisions.

Our data suggest that local decision-making focuses primarily on evidence of clinical benefit and cost implications. Information on implementation is also frequently requested. Cost-effectiveness information is not routinely requested by the majority of committees and was rarely accessed by the committees included as case studies. Outcomes of deliberation rarely, if ever, included disinvestments in current practices.

Case study committees appeared to operate without any direct control over resource allocation, although some committee members were clearly concerned to control spending. This added to the impression that the principal aim was to manage the introduction of technologies into the health economy (via the formulary) rather than making technology coverage decisions based on principles of efficiency and/or opportunity cost. Committee members acted as advocates of sectional, organisational or departmental interests, and demonstrated a limited capacity to access and interpret economic evaluations.

Attitudes and practices of decision-makers are shaped by the institutional constraints in which they operate. A number of features of the decision-making environment appeared to militate against emphasis on cost-effectiveness analysis. These were:

- a lack of clarity as to the objectives of the committees and their relationship to broader structures and processes
- an explicitly political decision-making process that involved the satisfying of interests
- the absence of a defined budget held and allocated by the committees.

These factors, combined with constraints on the capacity to generate, access and interpret information, led to a minor role for cost-effectiveness analysis in the decision-making process.

Empirical research results: the national case study

At the national policy level, our main research finding is that economic analysis is highly integrated into the decision-making process of NICE's technology appraisal programme. This is evidenced by the remit of NICE (to consider cost-effectiveness), the nature of the assessment reports commissioned specifically for NICE and the committee composition. In addition, data drawn from observation and interviews with Appraisal Committee members added considerable support to this overall impression. Attitudes to economic evaluation were found to vary from one committee member to another, and other factors dilute the influence of the health economics analysis available to the committee. There was strong evidence of an ordinal approach to consideration of clinical effectiveness and cost-effectiveness information. Some interviewees considered the key role of the cost-effectiveness analysis to be provision of a framework for the decision-making process. The NICE committee deliberations that we observed saw significant disagreement among committee members and these mainly revolved around the economic evaluation.

Interviewees indicated that the NICE committee did make use of some form of cost-effectiveness threshold but expressed concerns around both its basis (especially where the threshold in use currently might have come from) and its use in decision-making. Overall, interviewees praised the processes employed by NICE and indicated, in general terms, that the appraisal process worked very well. However, frustrations with the appraisal process were expressed in terms of the scope of

the policy question sometimes being addressed. The suggestion was made that an opportunity to clarify and identify clearly the relevant policy question should be a more formal part of the appraisal process.

Interviewees generally felt that the committee included a sufficient number of professional health economists on each branch. There was less agreement concerning levels of expertise in health economics amongst the broader committee. A number of interviewees indicated that they were concerned not only by their own personal lack of understanding of the economic analyses but also the level of understanding by others on the committee. If the economic analysis is to be used effectively to provide the framework for the discussion, then there is clearly a requirement that a minimum level of understanding of the analyses exists amongst committee members.

A particular issue brought up by many interviewees was the great benefit for a decision-making body such as NICE of a single measure of benefit such as the quality-adjusted life-year, in allowing comparison of very many disparate health interventions and in providing a benchmark for later decisions. Particularly in the context of model-based analyses, the importance of ensuring that committee members understand the limitations of the analysis was highlighted.

Conclusions and recommendations for further research

- Research into healthcare organisational forms that can explore the alternative structures, processes and mechanisms by which technology coverage decisions can and should be made.
- The further development of 'resource centres' that can provide information relating to high-quality independent published analyses and are able to support decision-makers with some local re-analysis and interpretation of findings.
- The development of improved methods of economic analysis that take account of the concerns raised by practitioners and users of such analyses in this research.
- The design of more accessible forms of presentation of economic analyses.
- Further assessment of the feasibility and value to be derived from a formal process of discussion and deliberation concerning the objectives that we seek from investments in healthcare.

Chapter I

Introduction

Background and objectives

This report is concerned with the use (or lack of use) of research evidence relating to economic analyses in healthcare decision-making. The central problem addressed by the discipline of economics is that of resource scarcity, and so the purpose of economic analysis is, in a very broad sense, to help decision-makers when addressing problems arising due to the scarcity issue.

Therefore, such evidence is generated with the direct intention of influencing policy – but is that objective achieved? Over recent years, there have been repeated expressions of concern about the usefulness of health economic analyses, and responses have tended to centre on questions of how research by health economists can be made more useful and accessible to policy makers.¹⁻³

Positive versus normative economics

In considering issues relating to the use and impact of economic analyses, it is helpful to reflect on the division of activity undertaken by economists: ‘normative’ economics and ‘positive’ economics. In the former, value judgements about what in general ought to be done in society are made and inferences are drawn in order that specific courses of action are recommended. In a normative sense, the aim of the economist is to indicate the nature of the resource allocation decision that ought to be followed if certain objectives are to be achieved. In contrast, positive economics is less value laden in the assumptions of the analysis and is intended to be entirely predictive of observable factors. It provides information that can help address resource allocation problems, but does not generate recommendations concerning any particular policy. It can only point out the observable consequences of policy.

These two approaches are not mutually exclusive: the community of health economists is engaged in both positive and normative economics and results of an analysis may be presented in both disaggregated and summary form. However, the desired objective of health economic analyses is

frequently to indicate the nature of the resource allocation decision that ought to be followed. An important prerequisite for such a normative stance is that the analyst has a good understanding of the objective function (i.e. what the health service should be seeking to achieve) and the decision rules to be applied. As Culyer⁴ points out, the process of agreeing objectives is not necessarily straightforward:

“In the real world ... policy makers and most other people who seek economic advice do not have well-articulated ideas of their objectives. One of the first tasks of a cost–benefit analyst, for example, is usually to seek to clarify the objectives – even to suggest some.”

Culyer⁴ (p. 254)

Many health economists in the UK have taken Culyer⁴ at his word. The proposal put forward is that the objective of healthcare services should be to maximise population health benefits.⁵ For many this appears not to be a highly controversial suggestion and, in broad terms, receives support from policy makers and the public more generally.⁶ The difficulties and disputes arise primarily around attempts to measure health. Over the course of the last 20 years or so, the subdiscipline of health economics has had a methodological focus on the measurement and valuation of health. The result is a measure of health that can be operationalised for use in policy making, i.e. the quality-adjusted life-year (QALY) or quality-adjusted life expectancy (QALE). The decision rule, therefore, for normative health economic analyses, is to advocate investment in those technologies that produce the largest QALY gains for a given level of cost. In order to inform such decisions, normative analyses tend to provide results in the form of the incremental cost-effectiveness ratios (ICERs), net-benefit statistics and cost-effectiveness acceptability curves (CEACs):

- The ICER reports the ratio of additional costs to additional health effects associated with a new intervention (e.g. cost per QALY gained).
- The net-benefit statistic expresses the additional health effects in monetary units by using an estimate of the ‘maximum willingness to pay’ per unit of health gain, where available.

- The CEAC plots the probability that the intervention in question is cost-effective against threshold values to define cost-effectiveness.

In contrast, a positive analysis generates information on the likely costs and benefits associated with alternative courses of action. Dowie⁷ describes such research as knowledge generating, as opposed to decision-making technologies. For example, the economic analysis reported by Davenport and colleagues⁸ predicts the magnitude of cost savings and the loss in dental health that might result from a policy of less frequent (i.e. 12-monthly) routine dental checks. A distinguishing feature of such positive analyses is that agreement concerning objectives, between the researcher and decision-maker, is not required. In addition, there is no *a priori* requirement for a single objective to be specified. Positive health economic analyses might involve the use of a profile or cost–consequence approach to reporting results. This is where the predicted impacts of the intervention in question are detailed, possibly in a tabular form, without any attempt to summarise or aggregate across different dimensions.^{9,10} This process could be applied to both resource use/costs items (including specific healthcare service use and costs and productivity losses) and health outcomes (including disease symptoms, life expectancy and quality of life). Kernick¹¹ is a strong advocate of such a positive approach:

“Cost consequence analysis emphasises the importance of presenting data on costs and benefits in disaggregated form, implying a recognition of the value judgement from decision makers and an acceptance that benefits and disadvantages cannot always be condensed into a single output measure.”

Kernick¹¹ (p. 314)

Research utilisation

Having looked at factors underpinning the design of economic evaluations, we now turn to broader debates surrounding the influence of policy-related research in general. Research communities across a range of disciplines have sought both to measure and to increase the impact of their findings on policy and practice. As a result, there has been a sustained focus on the projected ‘gold standard’ of ‘rational’, evidence-based decision-making advocated by research communities and the more incremental and ‘irrational’ reality of policy behaviour.

The origins and history of the term ‘rationality’ are too lengthy to be fully recounted here. The degree to which a decision-making body can be considered rational, however, might be gauged by the extent to which its activities are designed to achieve its expressed aims and goals.¹² The potential influence of research evidence and expert analysis in achieving rationality is a recurring theme in policy literature. Commentators such as Bell¹³ have argued that public policy in contemporary society is increasingly informed by ‘technocratic’ information as the social and political environment becomes ever more complex. He cites the example of the US McNamara administration of the 1960s, which employed economic frameworks, such as cost–benefit analysis, in order to restructure and rationalise the operations of the national department of defence. This was seen by Bell¹³ as a precursor to an increasingly information-based approach to decision-making and a growing reliance on the bearers of such analytic expertise. However, Bell’s predictions¹³ have not been borne out to the expected extent and increasingly commentators have begun to recognise the limited impact of expert, technical advice and information on policy makers.^{14,15}

Simon¹⁶ argued that human decision-making was constrained by a variety of factors which combined to reduce the scope for ‘perfect rationality’ as advocated in classical economic theory. He observed that decision-makers frequently seek **satisfactory**, rather than **optimal**, solutions. Thus, ‘administrative man’, in contrast to ‘economic man’ operates with a simplified reality as he is not able to weigh up the merits of every possible option in each decision scenario. Simon¹⁶ refers to this delimited approach to decision-making as ‘bounded rationality’.

Within the context of the NHS of England and Wales, the normative appeal for research to inform policy and practice has been crystallised in the call for healthcare to be ‘evidence based’.¹⁷ The aspiration towards evidence-based policy decision-making evokes a conception of research utilisation defined by Weiss¹⁸ as the ‘problem-solving model’. In this model, empirical and analytical evidence and conclusions are applied directly to a policy problem and, whether ‘off the shelf’ or specially commissioned, supply the information required to enable the optimal solution to be implemented. For the problem-solving model to apply, the recommendations of a normative economic analysis, for example, would need to be

implemented directly by the relevant policy maker and would be seen as the driving force behind the decision reached. Whether applied prescriptively or descriptively, this model considers the generation of empirically based decision recommendations as the main requirement of effective research utilisation. It is assumed that the decision-makers in question are able and willing to act on research findings. It also assumes that the objectives to be achieved by the decision are shared by all relevant participants in the policy process. Therefore, as Weiss¹⁸ indicates:

“... when this imagery of research utilisation prevails, the usual prescription for improving the use of research is to improve the means of communication to policy makers.”

Weiss¹⁸ (p. 428)

Dowie⁷ sees the issue of communication as arising from the fact that researchers and policy makers (or ‘practitioners’) occupy very different positions on both the ‘cognitive mode’ and ‘task structure’ dimensions:

“... research results are developed in the more highly analytic and well structured modes, whereas action occurs in the distinctively less analytic and ill-structured modes characterised by practice.”

Dowie⁷ (p. 9)

This position is also seen in the work of Drummond and Weatherly,¹⁹ who talk in terms of researchers occupying a ‘scientific paradigm’ and decision-makers a ‘policy paradigm’. Much valuable work has been done on techniques for reducing or bridging the gap between these two communities.^{20,21}

However, there are a number of weaknesses with the problem-solving model. In addition to those identified by Simon,¹⁶ authors such as Etzioni²² point out that organisations – in this case decision-making bodies – are not monolithic. Rather, they comprise a combination of interests and opinion, and as a result are subject to internal disagreement and dissension. The internal political dimension of decision-making bodies can influence policy outcomes, for example through phenomena such as ‘group-think’.²³ Patterns of internal disagreement may reflect the dominant professional and structural interests within healthcare. Thus, for example, the influence of research may be offset by the imperative to protect the interests of senior clinicians and/or managers. It could be argued that the greater the perceived importance of a decision, the greater is the pressure to answer to interest groups – both

internally and externally. In this context, it is difficult for decision-makers to operate with single, explicit objectives when formulating policy. Weiss¹⁸ further calls into question the likelihood of establishing single, agreed objectives in decision scenarios, pointing to a number of interconnecting conditions required for the smooth execution of problem-solving research use. These are:

- a well defined decision situation
- a set of policy actors who have responsibility and jurisdiction for making the decision
- an issue whose resolution depends on information
- identification of the requisite information need
- research that provides information in terms of matching circumstances of choice to be made and
- research findings that are clear-cut, unambiguous, firmly supported, timely, understandable and not counter to strong political interests.”

Weiss¹⁸

Although many economists may adopt a normative view that the problem-solving model has much to recommend it, it has to be recognised that, for these reasons, the real world rarely lives up to that aspiration. For example, in a review of UK studies into factors affecting evidence-based policy-making, Elliott and Popay²⁴ concluded that many policy problems are often intractable or not clearly enough delineated to be tackled directly and comprehensively. They also found that research evidence is frequently unlikely to be sufficiently clear-cut and unambiguous to translate directly into policy. They also called into question the assumption of a straightforward policy process in the problem-solving model and concluded that dissemination of health services research results has been hampered by a preoccupation with the rational, problem-solving model. In these circumstances, Weiss’s¹⁸ ‘interactive’ model of research utilisation, in which policy formulation is understood as a non-linear process involving multiple agents and influences, has far greater descriptive validity.

The distinction between problem-solving and interactive models of research utilisation correlates, to some extent, with the binary of normative and positive approaches to health economic analyses. The requirement for agreement of purpose and objectives between researcher and decision-maker is a defining premise of both normative economic evaluation and rationalist conceptions of policy research utilisation. Positive approaches to evaluation, on the other hand, may be seen as more helpful to decision-makers involved in policy processes that are marked by interaction and competing or

multiple objectives. An understanding by the analyst of the nature of the policy environment into which the analyses are being placed is required. This will allow more informed choice to be made concerning the appropriate approaches to analysis and presentation of results.

Providers and users of economic evaluation information in the UK

In a UK context, the principal providers of economic evaluations include the NHS Health Technology Assessment Programme, the pharmaceutical industry, academic departments with health economics units and consultancy organisations.²⁵ Although a certain level of central direction is given to the NHS through the Department of Health, most decisions about the use of health treatments and technologies have traditionally been taken in a decentralised manner. Given this position, there is a need for the generation and dissemination of information on the effectiveness and cost-effectiveness of healthcare interventions. This is currently being met through a number of initiatives, including the Effective Healthcare Bulletins (reviews of the evidence) and the NHS Economic Evaluation Database, that contain reviews of published studies.

The commissioning brief for this project indicated a focus on ‘policy level’ use of economic analyses, and **not** their use in decisions regarding treatment for an individual patient. The use of evidence in clinical decision-making has been explored elsewhere.^{26,27} At a national level, the establishment of the National Institute for Health and Clinical Excellence (NICE), a body that makes recommendations concerning the use of new and existing technologies throughout the NHS, represents a very significant policy user of economic studies. At a local level, Primary Care Area Prescribing Committees make policy recommendations on the use of health technologies, and at a hospital level, formulary decisions will tend to be made by Drugs and Therapeutic Committees or the closely related Medicines Management Committees. However, this omits Strategic Health Authorities, which retain a ‘strategic role’, and Primary Care Trusts, which, as principal dispensers of healthcare resources, have the final say in resource allocation.

A study by Leach and Leach²⁸ suggests that hospital-based committees are likely to have clinical expertise, GP representation and some

pharmacy support, and many will be linked to a formulary for the trust. They surveyed a sample of committee representatives, asking them to rank four criteria for assessing their effectiveness of their committee. These were:

- compliance with the formulary
- peer persuasion by Drugs and Therapeutic Committee members
- interest shown by prescribers
- compliance with the drug budget.

Of these four, respondents typically attached least importance to ‘compliance with the drug budget’ in assessment of their effectiveness as a committee. This is an important finding, which may have implications for these committees and in particular their willingness to consider economic evaluation when making their decisions.

The problem to be addressed

As a framework for exploring these issues, we have broadly grouped barriers to the use of economic analyses in healthcare decision-making under two headings:

- **accessibility** of the research evidence including issues such as interpretation difficulties, the aggregation of results, difficulties in accessing information, timeliness and shortage of relevant skills
- **acceptability** of the research evidence including a whole range of barriers which prevent or disincentivise the implementation of cost-effectiveness study findings.

The necessary requirements for economic evaluation research evidence to be used in decision-making, under both problem-solving and interactive models of research utilisation, therefore relate both to accessibility and acceptability.

Accessibility

For the information to be accessible, it is required that the results of the economic analyses can readily be understood and interpreted by end-users. This is mainly concerned with issues of the presentation of information. There are two aspects of the results of cost-effectiveness studies where presentational issues are important: (1) base-case result and (2) uncertainty around the base case. As indicated earlier, the spectrum here extends from the profile approach, whereby the disaggregated profile of all costs and consequences are revealed, to the single summary indicator, such as the ICER,

net-benefit statistic or CEACs. Particular difficulties are likely to exist in notions of uncertainty in the results of analyses, primarily because policy makers typically are not trained in research methods and so statistical representations of uncertainty are liable to be misunderstood.

Work in other areas of medical research has shown the sensitivity of decisions to the style of presentation of information. For example, Elting and colleagues²⁹ examined the effect of the method of data display on physician investigators' decisions to stop hypothetical clinical trials. Their findings indicate that more correct interpretations were placed on the data when presented using icon displays.

Acceptability

For the information to be acceptable, it is necessary that economic analyses provide information that is seen by end-users to be relevant (i.e. providing data on parameters that are likely to influence the decision of the policy maker), information that is appropriate to the decisions they face, taking into account relevant contextual factors (e.g. budgetary arrangements commonly seen in the NHS) and that such analyses are seen as providing information in a timely fashion.

In highlighting the failure of health economists to consider issues of the acceptability of the data they generate, Kernick¹¹ argues that:

“The history of any movement determines its structure and the way in which meaning is generated within it. Health economists tend to adopt a straightforward view ... Just as the NHS was configured in part to reflect the needs of doctors and not patients, the development of health economics was set to reflect the requirements of the academic discipline and not the realities of the emerging health care environment.”

Kernick¹¹ (p. 312)

Research questions

The research described in this report is designed to address two principal questions:

- To what extent, and in what ways, is health economic information used in health policy decision-making in the UK?
- What factors are associated with the utilisation (or non-utilisation) of such research findings? (e.g. is the use of such information sensitive to the style of presentation adopted?; to what extent is personal skill base and/or organisational context important?).

The five specific objectives of this research are:

- To identify and review previous theoretical and empirical work concerned with economic evaluation and policy-level decision-making in healthcare and in other sectors (Chapter 3).
- At a local level in the NHS, to explore the use of economic evaluation information in resource allocation decisions concerning adoption of drugs and other therapies (Chapter 4).
- At a national level (using NICE), to explore the use of economic analyses and its influence on its technology appraisal decisions and judgements (Chapter 5).
- To explore with decision-makers how the impact of economic analyses might be increased, particularly in relation to issues of accessibility and acceptability (Chapters 4 and 5).
- To make recommendations for improvements in the use of economic analyses by decision makers in the NHS (Chapters 6 and 7).

Chapter 2

Methods

Defining research terms

Previous research has demonstrated the multi-layered and diffuse nature of healthcare decision-making. In a UK context, Coast³⁰ presents findings of qualitative interviews with professionals from healthcare and related sectors. These indicate that at a meso policy level the process of decision-making can be characterised as “a system of equivocation involving a complex set of interactions in which there are a number of obstacles” (Ref. 30, p. 168). The phrase ‘decision-maker’ is called into question by evidence of practices designed to postpone, defer or ‘pass on’ difficult decisions. These complex structures and practices limit the scope for direct research into decision-making bodies. Our approach concentrated on the introduction of **new technologies** and how decisions in this area were taken. This had the value of reflecting an area of NHS activity for which explicit decision-making bodies are formed – such as NICE and local level Medicines Management Committees. However, this is only one aspect of NHS resource allocation decision-making and there is a need for exploration of the role played by economic analyses in all aspects of healthcare policy.

We decided on this focus for two reasons. The first was an acknowledgement of the project’s time and resource constraints. It was felt that in order to generate findings of sufficient depth and coverage, it would be preferable to select an area of activity with relatively well-defined decision-making processes. Second, we were aware that the provision of economic information on new technologies is a substantial output of the health economics discipline. We therefore concentrated on decisions over which health economics might currently be expected to have some influence.

The focus for the project is on the use of ‘economic evaluation’ or cost-effectiveness information, broadly defined, in decision-making contexts. The working definition employed includes information on the inputs or costs and the outputs or consequences associated with alternative healthcare interventions or procedures. Such a broad definition is important in order to allow

consideration of all forms of economic evaluation and a wide range of styles of presentation, including summary measures and profile approaches. Summary measures of results include:

- the ICER, which is the ratio of additional costs to additional health effects associated with a new intervention (e.g. cost per QALY gained) and
- the net-benefit statistic, which expresses the additional health effects in monetary units by using an estimate of the ‘maximum willingness to pay’ per unit of health gain, where available.

A profile, or cost–consequence, approach to reporting results sets out the impact of the intervention on resource use and costs (including specific healthcare service use and costs, and productivity losses) and health outcomes (including disease symptoms, life expectancy and quality of life) in a tabular form, without any attempt to summarise or aggregate.^{9,10}

Research strategy

The research strategy was designed to explore current processes involved in resource allocation decisions in the NHS and, in particular, the influence of economic evaluation results on those decisions. It was further intended to facilitate the development or refinement of alternative approaches to increasing the accessibility and acceptability of economic evaluations.

The research strategy was selected to develop and improve upon previous research. It was hoped to do this by capitalising on the advantages of a range of methods and the triangulation of these. It was considered important to achieve both breadth and depth in the research in order to maximise its contribution to academic debate in this area and also to the development of strategies to support health economists and professionals involved in healthcare resource allocation decisions.

There were four core elements to the research:

- stage 1: systematic review of previous studies

- stage 2: the collection and analysis of information pro formas used by decision-making committees across primary and secondary care sectors of the NHS
- stage 3: in-depth case studies of a sample of decision-making committees
- stage 4: workshop discussions with decision-makers.

Qualitative case studies of decision-making committees were the primary source of data. The selection of a qualitative case study approach is consistent with our concern to explore **how** and **why** decisions by NHS policy-making bodies are made.

We conducted multiple case studies, drawing on a full range of sources and data collection techniques. We aimed to research the perspectives of participants in the decision-making environment and also the process of decision-making followed. As decision-making bodies and processes do not exist outside of the ‘social actors’ contributing to them, we aimed to explore how collective decision-making is constituted of multiple and sometimes competing views that come together to produce a socially constructed policy process.

We also sought to generate a detailed comparison of the similarities and differences between case study organisations and to identify and describe the contexts and variables that shape the extent to which case study analyses constitute ‘like-with-like’ comparisons. This enables both the researcher and others involved – including the consumer of the research findings – to judge the extent to which research findings are transferable to other bodies and settings. We aimed to identify and explore factors influencing the research outcomes, for example differences relating to the remit, financial responsibilities and composition of the case study committees and also the types of organisations they serve.

Systematic review

This section summarises methods for the systematic review including the search strategies and periods over which databases were searched. Further detail on search strategies is included in Appendix 12.

Review of existing reviews in health-care

Reviews were identified from sources listed in the ARIF Search Protocol for Reviews plus

handsearching of the *Journal of Health Services Research and Policy*, 2000–2. Search strategies for MEDLINE and EMBASE are detailed in Appendix 12. Using text words such as ‘decision-making’ or ‘policy making’ and combined with ‘cost effectiveness’, ‘economic evaluation’, etc., the following sources were also searched in order to inform all four stages of the review:

- Office of Health Economics – Health Economic Evaluations Digest (OHE HEED).
- World Health Organization (WHO) library database.
- The World Bank – the information library was contacted by email.
- Experts in health economics and those on the advisory group for this project within the UK were contacted by email for information on existing publications, and ongoing and unpublished research.
- Additional experts were contacted for information within the Treasury Department of the UK Government.

The titles and abstracts of the results of these searches were also browsed for potentially relevant articles. Hard copies of potentially relevant reports were obtained and where necessary translations were undertaken of part or all of foreign language articles to facilitate the selection process. Reviews to be included in this review were selected based on the criteria below:

1. Study design:
 - (a) any review, particularly those with a systematic approach.
2. Population in included studies in review:
 - (a) healthcare decision and/or policy makers.
3. Focus of studies included in the review:
 - (a) evaluation of effectiveness of initiatives using economic evaluations OR
 - (b) studies attempting to assess the barriers to the use of economic evaluations OR
 - (c) studies attempting to assess how decision-making bodies make their decisions in relation to the use of economic evaluations.

Two reviewers independently applied the inclusion criteria and disagreements were resolved by discussion. A third reviewer was available to provide additional input if necessary. All decisions were recorded. All excluded articles were assessed for relevance to other sections of this review. The quality of included reviews was assessed using a recognised critical appraisal tool [Critical Appraisal Skills Programme (CASP)]. Two

reviewers independently undertook quality assessment and disagreements were resolved by discussion. A third reviewer was available to provide additional input if necessary.

Formal data extraction was not planned for this stage of the review due to the perceived small number of included reviews and the likelihood that the reviews would not be directly comparable. The quality and findings of the included reviews were reported textually, highlighting important strengths and weaknesses of the review and commenting on the external validity with regard to the objectives of this review.

Review of existing reviews in non-healthcare fields

The objective of this stage of the review was a systematic review of existing reviews on the use of economic evaluations in non-healthcare decision/policy making to test whether there was any useful literature outside the health sector. Given the breadth of this task, the review was limited to the following areas: social care, education, transport, environment and criminal justice areas. These were decided *a priori* by the consensus of the project steering group as those areas most likely either to contain reviews on use of economic information in decision/policy making and/or to be most relevant to health care decision/policy making.

One of the difficulties in undertaking the reviews of non-healthcare studies is the relative lack of electronic databases compared with healthcare and the unsophisticated nature of those databases that are available. As such, searching the databases is cruder due to the absence of or limited indexing terms and unsophisticated search engines with which to probe the databases. Hence the identification of relevant articles is less precise with more subjective searching than in healthcare. With regard to this review, in order to overcome the limitation, a pragmatic approach to searching was undertaken. Databases were searched with a trade-off of high sensitivity against poor specificity such that as far as possible any relevant articles were captured but not at the expense of having to sift through unmanageable quantities of search results. Websites were searched where possible using supplied search facilities and using the most appropriate text term(s). Where no search facility was provided on the website or where that provided appeared imprecise, websites were systematically browsed targeting the pages most likely to contain relevant sources of information.

The search strategies for each subject area can be found in Appendix 12.

Search strategies

Full search strategies for all sectors and an indication of the number of hits are recorded in Appendix 12. A record was kept of the search terms used, the date the searches were executed and the quantity of results from each search. Articles identified through websites were browsed online for relevance. Hard copies of potentially relevant articles were obtained for formal application of the inclusion/exclusion criteria. The criteria for each subject area were similar and analogous to those used in healthcare.

Review of empirical studies in healthcare

Searches were undertaken of the following sources.

- Electronic Databases: MEDLINE, EMBASE, EconLit, Social Science Citation Index, the NHS Economic Evaluation Database (NHS EED), the Office for Health Economics Health Economic Evaluation Database (OHE HEED) and the Health Management Information Consortium (HMIC) database.
- Handsearching of key methods journals: *Health Economics*, *Journal of Health Economics*, *Pharmacoeconomics*, *Milbank Quarterly*.
- Bibliographies of all reviews and provisionally included articles retrieved were scrutinised.
- Research Registers.
- The Project Advisory Group was asked if they are aware of any relevant studies.

Searches of electronic databases used free-text terms and keywords (and where appropriate MESH headings) for decision/policy making and economic evaluations. Electronic searches were conducted from inception of the database. No language restrictions were applied. The titles/abstracts were scanned for relevance and duplication of previously identified articles. The search strategies for electronic databases are given in Appendix 12.

Given the difficulty with the way in which the literature in this field is poorly served by keyword indexing and the broad spectrum of possible search terms, once developed the search strategies were piloted to ensure that they were able to identify relevant studies/articles that were already known to the authors. If not, minor modifications were made but care was taken to ensure that sensitivity of the searches was not lost. In addition,

relevant articles were identified from searches undertaken to inform all stages of the review.

Given the large volume of search results, a pragmatic approach was taken to focus on the most relevant studies. The titles of the results were browsed from the database on-screen by one reviewer for potential relevance to the review using criteria for the population and the intervention.

Inclusion criteria

Hard copies of potentially relevant studies were obtained and where necessary translations were undertaken of part or all of foreign language articles to facilitate the selection process. Studies to be included in this review were selected based on the criteria below.

- A. Study design
 1. Does the study adopt a research design (including surveys and case studies) that assesses the use of economic evaluations by healthcare decision- and/or policy makers?
 2. Is it an experimental or quasi-experimental study which utilises a control/comparator group to assess the use of economic evaluations by healthcare decision- and/or policy makers?
- B. Population
Healthcare decision- and/or policy makers.
- C. Intervention
Using economic evaluations.
- D. Outcomes
Any considered.
- E. Exclusion
Any article that is solely a literature review or discussion piece.

If a study met all of the criteria A–D and not E it was included in the review of experimental/quasi-experimental studies (stage 3). If a study met the criteria except A2 and E it was included in the review of non-experimental studies (stage 4). If a study met criteria B–E but not A1 it was marked for assessment for inclusion in the review of reviews in healthcare (stage 1). These criteria were applied by one reviewer and independently checked by a second. Any disagreements were resolved by discussion and involving a third reviewer if required.

Quality of included articles

For experimental and quasi-experimental studies, the methodological quality was to be assessed utilising the framework employed by the Cochrane Library, which aims to assess threats to validity in

the areas of selection, performance, attrition and detection bias. For non-experimental studies, the potential value of quality assessment for this component of the review was less clear. After deliberation and consultation, the research team decided against formal quality assessment of included studies, opting instead to present a detailed account of methods used by studies and to identify potential areas for further improvement in the literature – for example, through the use of different methodological approaches.

Data extraction and reporting

Formal data extraction was only likely to be possible for studies included in the review of experimental and quasi-experimental studies, and a data extraction pro forma was constructed *a priori* for this purpose. All relevant data for studies included in this component of the review were to be recorded and tabulated. For the review of non-experimental studies, only basic key study characteristics were to be tabulated. Analysis for both stages was qualitative, based on patterns of results revealed in the tabulated data. *A priori* we believed that quantitative summary is unlikely to be helpful even in attempting to assess the effectiveness of initiatives to use economic evaluations.

The research team agreed on the basic study characteristics to be tabulated. These were study aims, methods, the study population, the types of economic evaluation included in the study and the study results including reported barriers to use of economic evaluation and strategies for improving its use.

Local decision information pro formas

The research team sought to obtain a measure of the extent to which local level decision-making bodies routinely requested information on the cost-effectiveness of technologies included on their formularies. We devised an approach involving mailing each NHS Trust within England requesting that they return blank copies of any pro formas currently used in gathering information about a proposed addition to their formulary. The aims were:

- to identify local NHS decision-making committees operating in the UK area and the organisations they serve
- to identify what, if any, pro formas are used by these committees

- to ascertain what information, if any, is routinely requested by these committees when making decisions on the inclusion of new technologies
- to gauge the extent to which cost-effectiveness analyses are included within this information
- to make contact with individuals and organisations with a view to further involvement in the research.

The research team was aware at the outset that further in-depth qualitative research methods would need to be employed to supplement this survey. Binley's database of NHS organisations was used to identify primary and secondary care respondent organisations. The letters contained a basic description of the research project and explained in detail the types of 'pro formas' requested. A reply slip was attached which requested that respondents provide their name, designation and willingness to be further involved in the research. Respondents were supplied with an addressed return envelope.

Organisations that had not sent a response within 3 months of the first letter were sent a reminder letter repeating the request for information and again attaching a reply slip and return envelope. Individuals were not sent the reminder if a colleague had responded to the first letter. The letters are shown in Appendix 1.

Organisations that did not respond to either the initial letter or the reminder letter were telephoned by a member of the research team. The objective of these telephone calls was not necessarily to obtain copies of pro formas from the non-responding organisations but to gauge the reasons for non-response and the implications of this for the overall sample. Identified reasons for non-response were recorded and tabulated.

Case studies

Recruitment of case study committees was partly influenced by practical considerations inasmuch as the project required that the studies were

conducted within a pre-identified time-frame. We also employed theoretical sampling to enable the development of comparison and explanation. The main considerations guiding sampling were the need to:

- include both national and local decision-making committees
- achieve some geographical coverage
- include committees operating in or across both primary and secondary healthcare sectors.

A total of six committees were approached, with five consenting to participate as shown in *Table 1*.

Some detail on each committee is provided in Chapters 4 and 5, and Appendix 9. This should allow an assessment of the transferability of results to different settings.

In each case, a member of the research team contacted a key member of the organisation or committee in question and discussed the possibility of conducting the case study. Following this, the research team produced a draft protocol for the proposed case study and attended a committee meeting where both the research and members of the project team were introduced to the committee. Verbal consent was obtained from committee members at this stage. Written consent was then sought from the committee Chair and from individual committee members partaking in interviews.

We used three main research methods in the case studies:

- documentary analysis
- observation of committee meetings
- semi-structured interviews with committee members.

The case study of the NICE Technology Appraisal Committee involved substantially more fieldwork than the others. This reflected the fact that NICE was the sole example of national policy making within the sample.

TABLE 1 *The five completed case studies*

No.	Case study	Location
1	County-wide Priorities Committee	South Central England
2	Hospital Medicines Management Committee	North West England
3	Primary Care Medicines Management Committee	Midlands, England
4	Interface Medicines Management Committee	West of England
5	NICE Technology Appraisal Committee	England and Wales

Documentary analysis

The research team requested that all documentation provided to case study committees pertaining to technologies under consideration be made available for the project. This included meeting agendas, minutes and copies of paperwork attached to applications for the inclusion of a new intervention. Further relevant literature such as committee mission documents and annual reports was accessed where available. These sources informed the data collection process and have been cited throughout the report of research findings.

For each case study, it was felt that attention to documentary analysis would yield useful insight into both the committee's stated terms of reference and procedures and specific informational inputs into its decisions. In addition to providing an 'official' account of structures and processes, committee documentation supplies much of the context to data derived from interview and observation. It does not, therefore, have the epistemological status of primary research but is a useful complement to data generated from interviews and observations.

Observation

Observations of case study committees involved "the systematic, detailed observation of behaviour and talking: watching and recording what people do and say".³¹ A major strength of this approach is that it provides the research team with information on a crucial stage of the decision-making process and allows observation of research subjects in their natural setting. It also can serve to highlight potential discrepancies between data generated from documentary and interview research (what individuals and organisations **say**) and observed behaviour (what people and organisations **do**).

The team adopted an overt approach in which the respondent organisations were aware of both the researchers' presence and the objectives of the observational exercise. However, beyond providing an initial introduction, the research team adopted an unobtrusive approach to observation. It was felt that the committees involved would be used to the presence of observers and would not expect or necessarily welcome active involvement by research team members in their discussions.

Pilot observations were conducted before beginning the research proper. As a result of these pilots, we opted for a free note-taking approach as opposed to using schedules designed to enable

quantitative coding of individual behaviour within group settings.³² The team took general notes on observed discussions and detailed notes on committee references to costs and cost-effectiveness. Although it was not always possible to ensure that more than one note-taker was present at all observations, this was the preferred approach.

Interviews

Unstructured and semi-structured interviews help the researcher to "understand the world from the subject's point of view, to unfold the meaning of experiences, to uncover their lived world".³³ Semi-structured interviews are recommended where there is a balance required between a free-flowing and a directed conversation. We used this format in order to ensure that the research questions were addressed in full while allowing the flexibility to pursue other issues or concerns raised by respondents.

Interviewees were approached after a general introduction of the research team to the committee had taken place. In general, the research team aimed to achieve a representation of the different interest groups represented on the committee. Potential participants were given the choice of face-to-face or telephone interview and all interviews were tape recorded after assurances of confidentiality were provided. Interviews sought to draw on respondent' experiences, opinions, beliefs, feelings, knowledge and perceptions.³⁴

Local decision-making committees

For each local case study, the research team observed a small number of committee meetings. These occasions were used to collect data on parameters such as:

- reference made to economic analyses in the discussions and deliberations
- the role and influence of the economic analyses in the decision taken
- discussion of issues concerning the accessibility and acceptability of health economic analyses, and evidence relating to such factors
- other information drawn on in making decisions.

Interviewees were asked both about their individual experiences of, and approach to, health economics, and their perceptions of the workings of the committee as a whole. We were interested in exploring the weight placed on the economic evaluation information provided, when thinking about whether to recommend a new technology.

Interviewees were asked to explain the considerations that most influenced them, and how much 'importance' they attached to the economic evaluation, in addition to how if at all this differed in their perception from the weight attached to it by other members of the committee. We also asked them whether they felt that they and others on the committee understood the health economics presented and to identify areas where they thought the use of economic evaluation might be improved. The interview schedule used is given in Appendix 2.

National case study

Consent for the research to be undertaken was given by the NICE Executive Board, and all those invited for interview were given an information sheet and consent form. Interviews were only conducted after consent forms had been signed. At the outset of the case study, the research team conducted interviews with the NICE Technology Appraisal Programme Director and the Chair of the Appraisal Committee, and carried out a group discussion with members of its technical support team. The main purpose of these interviews was to achieve a sound and detailed understanding of the technology appraisal process and the specific roles and responsibilities of the parties involved. At this stage, members of the research team also attended a meeting of both branches of the Appraisal Committee, where a brief verbal introduction to the research was provided. These initial observations were used to familiarise ourselves further with the workings of the committee and also to refine data collection instruments. This process also helped inform the selection of the seven prospective technology appraisals to be included within the case study.

Topics were selected in order to:

- cover appraisals carried out by both branches of the committee
- encompass a range of technology 'types' (i.e. not exclusively drugs)
- encompass appraisals involving a varying number of comparators
- include appraisals with varying quantity and complexity of health economic analyses.

All documentation prepared for the committee and pertaining to the seven identified appraisal topics was reviewed by the research team prior to the committee meeting at which the topic was first discussed. This assisted us in establishing the nature of the economic analyses undertaken and how the results were reported. For each appraisal

studied, the following documentation was requested:

- industry submissions
- patient and/or professional submissions
- report of the academic review team.

The team observed committee meetings relating to the selected topics. In observation of these meetings, the research team took notes on the following:

- general content of the discussions
- reference made to economic analyses in the committee discussions and deliberations
- the role and influence of the economic analyses in the decision taken by the committee
- discussion of issues concerning the accessibility and acceptability of health economic analyses and evidence relating to such factors
- other information drawn on in making decisions.

Semi-structured interviews were conducted with committee members involved in each of the technologies appraised. Interviewees were selected to reflect key groups involved, including for example, clinicians, health economists and patient representatives. Between two and four committee members were interviewed for each technology appraised. These interviews were used to explore issues concerning the accessibility and acceptability of health economics (and other) information and to provide a context to observed data deriving from the appraisal process. Interviews were approximately half an hour to an hour in duration and involved tape-recorded telephone discussion in most cases, although a small number of face-to-face interviews were conducted where this was preferred by the interviewee. In addition, a small number of non-technology-specific interviews were conducted with committee members who were willing to be interviewed but had not hitherto been approached. These interviews followed the same interview schedule as before but without questions relating to specific technology appraisals.

In total, 30 interviews were undertaken. Interviewees were asked to reflect both on specific appraisal topics and on the appraisal process in general. The research team deliberately did not specify definitions of terms such as **economic evaluation** or **cost-effectiveness** in order to allow the meaning, either explicitly or implicitly adopted by respondents, to emerge from interview.

As with the local case studies, we were interested in exploring the weight placed on the economic evaluation information provided when thinking about whether to recommend a new technology. Full interview schedules are given in Appendix 3.

Workshop discussions

Case study data were supplemented with two workshop discussions that explicitly used group interaction to generate further research data. They enabled the research team to focus on specific research questions and issues as these emerged from prior fieldwork and provided a separate source of data with which to compare existing research information. Group discussion is an important source of qualitative data, and one which differs from both observation- and interview-based research. The exploration of research topics through group dialogue can generate a greater breadth of information than is typical of face-to-face interviews. It also enables the researcher to hear multiple perspectives in a single research exercise. However, the constraints of an 'audience' can place limits on the depth and level of candour of participants' contributions.

A total of 15 participants took part in the two workshops. Those involved were drawn predominantly from primary and secondary care sectors, with one respondent from a mental health trust.

The specific aims of this further research were to:

- supplement data derived from case studies on the barriers to use of economic evaluation information
- specifically generate further data on strategies for overcoming these barriers.

Each participant had returned new technology request forms and expressed an interest in being further involved in the research and so may have been inclined to see economic evaluation as potentially valuable for their decision-making. The research team felt this bias in the sample was acceptable as long as it was acknowledged. It was further felt that this group would contribute to a discussion that had a particular focus on **overcoming** barriers to the use of economic evaluation.

Participants in these discussions were contacted by telephone and email by a member of the research team. The two discussions took place on

4 and 5 March 2004 with eight and seven participants, respectively. A full programme of the workshops is given in Appendix 4. The feedback components of the workshops were tape recorded by the research team. A senior researcher then used the flip charts and tape recordings to write detailed notes from the workshops. These were analysed for recurring themes under the broad general headings of barriers and ways of overcoming the barriers.

Ethics and confidentiality

Research ethics committee approval of the study was obtained from the West Midlands Multi-Centre Research Ethics Committee.

Local case study organisations have been anonymised in this report. This decision was taken after one case study site requested that their committee not be named. It was agreed that for consistency the other three local case studies would also be reported anonymously. As the sole decision-making body of its kind, it was considered unrealistic to report the case study of the NICE Technology Appraisal Committee anonymously. The committee was named with prior consent from NICE.

Documentary analysis accessed during the fieldwork was treated as confidential. In the case of NICE, the research team did receive some paperwork that was deemed 'commercial-in-confidence'. These documents were included in analysis but treated as confidential. Interviewees were required to provide written consent to involvement in the research in four of the five case studies. Verbal consent was obtained from interviewees from the remaining case study and from participants in the workshop discussions. We adopted the principle of 'informed consent' whereby participants were given a full account – both verbal and written – of research aims and the uses to which data would be put. Interviewees were provided with a basic interview schedule in advance of interview. All interviews were tape recorded with the permission of participants and the resulting recordings and transcripts were stored anonymously. It was decided not to tape record meetings of case study committees. This would have been impractical and potentially intrusive. Where possible, all research data were stored electronically with access restricted to the research team. A full archive of research data is not attached to this report for reasons of maintaining confidentiality.

Data analysis and reporting

The data analysis process employed was chosen to reflect the level of prior understanding of the research topic. Prior conceptual frameworks, in this case based on a reading of existing research literature identified in the systematic review, were influential in the research design and provided some context to data analysis. The approach to data collection also borrowed from grounded theory³⁵ in its adoption of the following features:

1. The attempt to apply a systematic method of content analysis
2. The generation of categories in an ongoing, iterative process of interpretation in which research data are both an outcome and a shaper of fieldwork undertaken.
3. Examining data with a view on as many possible interpretations as could plausibly be advanced.

Each case study involved data collected using different methods, including interviews, observation and documentary analysis, so that triangulation of data could be attempted. Within case studies, findings from different research exercises were analysed and reported in discrete sections and comparisons used to tease out areas of consistency and divergence.³⁶ Analysis of data was performed by a minimum of two researchers operating independently, who then compared their findings and discussed any differences in the themes each had identified. Furthermore, the write-up of each local case study

was sent to lead participants for comments and similarly a draft of Chapter 5 was sent to three senior members of NICE for comments.

The documentary analysis exercise, the local case studies which included data collected through interviews, observation and documents, and the workshop discussions drew data from the same or similar tiers of policy making. Comparison of data derived from these sources enabled the research team potentially to identify limitations in each. For example, case studies of four local decision-making committees suggested that new drug/technology applications did not always come with the full range of information requested on the committee's pro formas. At the same time, the documentary analysis provided the research team with some indication as to how typical the information requirements of the four local case studies sites were.

In both national and local case studies, the research team avoided use of verbatim quotation of committee discussion when writing up findings. Verbatim interview data were used, however, to illustrate themes and findings. Where a point was made by a large percentage of interviewees, this is indicated in the text and supported with a sample of quotations. Where a point was made by a smaller number (or in some cases a single committee member), this is also clearly noted. There is no strict correlation between the number of interviewees expressing an opinion and the number of supporting quotations included.

Chapter 3

Results from the systematic review

Introduction

The review reported in this chapter sought to identify and review previous theoretical and empirical work concerned with economic evaluation and policy level decision-making in healthcare and in other sectors. It was agreed at the outset of the project that, in order to meet this objective, we would need to conduct a systematic review of the literature relating to the use of economic evaluation research in public policy. This would serve to inform and underpin the design of the empirical research conducted by the research team and would also assist in interpretation of findings. The review had four stages:

- Stage 1 – a review of existing reviews.
- Stage 2 – extend stage 1 to databases and sources outside the health sector.
- Stage 3 – to review systematically all existing empirical studies on the use of economic evaluations in decision-making in healthcare.
- Stage 4 – to use existing overviews and a review of surveys and observational research to identify potential barriers to the use of health economic evaluations.

Review of existing reviews (stages 1 and 2)

The searches for reviews in healthcare identified 506 articles (*Figure 1*). On application of the inclusion criteria, only one article met all three criteria.³⁷ This one included review was:

- Spath HM, Allevet B, Carrere MO. Using economic information in the health sector: the choice of which treatments to include in hospital treatment portfolios. *J Econ Méd* 2000;**18**:147–61 (in French).

The best near-miss reviews were:^{38–41}

- Coyle D. *Increasing the Impact of Economic Evaluations on Health-care Decision-making*. Discussion Paper 108. York: Centre for Health Economics, University of York; 1993.
- Drummond M. Evaluation of health technology: economic issues for health policy and policy

issues for economic appraisal. *Soc Sci Med* 1994;**38**:1593–600.

- McDonald R. *Using health economics in health services: rationing rationally?* Buckingham: Open University Press; 2002.
- Prosser LA, Koplan J, Neumann P, Weinstein MC. Barriers to using cost-effectiveness analysis in managed care decision-making. *Am J Managed Care* 2000;**6**:173–9.

A list of excluded studies can be found in Appendix 12. The main reasons for exclusion were lack of adherence to the criteria for population and focus of the review.

Included reviews

The review by Spath and colleagues³⁷ was published in French with the abstract also published in English. In order to assess both the internal and external validity of the review, the remainder of the article was translated into English and the translation of the abstract was checked for accuracy. Critical appraisal of the review using the translation revealed that it contained methodological elements that suggests that, in part, it was undertaken systematically.³⁷ The search strategy is recorded and appears to be comprehensive with regard to the electronic databases searched. It was augmented by handsearching the journal *Pharmoeconomics* and scanning the reference lists of ‘pertinent’ articles. It does not appear that lead authors of included studies or other experts were contacted for additional studies or information.

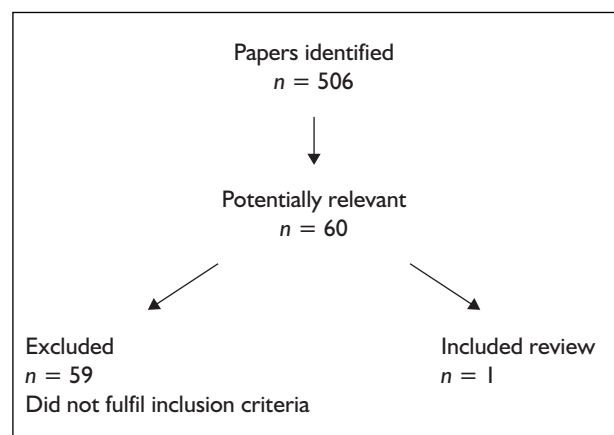


FIGURE 1 Flow chart of selection of reviews in healthcare

With regard to the scope of decision-making, the review only covers decisions about the inclusion of drugs into formularies and not wider policy decisions. The review was not limited to the use of economic evaluations but covered any 'economic information'. As such, studies reporting the use of drugs costs in the formulary inclusion decision process were included. The report of the review appears to use the terms 'economic information' and 'economic evaluation' interchangeably, and therefore it is not clear to which it refers. We have endeavoured to employ the same term as the review when documenting the specific findings.

The review included 34 studies (22 from electronic database searches, eight from handsearching and four from reference lists). The total number of articles identified by the searches is not mentioned. Twenty-seven articles (79%) were descriptions of decisions made using economic information. The nature of the remaining seven articles is not mentioned. Most of the articles ($n = 25$, 73%) originate from the USA, with no more than two articles from any other setting. Only half the articles appear to have been written from the perspective of the decision-maker, with the majority of the rest written from the view of producers of information. The methodological quality of the included studies does not appear to have been formally assessed or described.

The review documented, amongst other outcomes, the frequency of description of specific obstacles to the use of economic information within the included articles. The most commonly reported barriers were:

- The methodology of the economic evaluation (internal validity) was inadequate.
- Transferability of economic information to the context of the decision is limited.
- Decision-makers' knowledge of health economic information is poor.
- Access to and time to interpret economic information are limited.
- Collaboration between economists and decision-makers is inadequate.
- Doctors do not like to be seen to be refusing treatment.
- Wider pressure from outside the pharmacy service to constrain budgets.

The shortcomings of the review and the failure to consider the bias of the included studies need to be taken into account in assessing the strength of these conclusions.

Key excluded reviews

Given that there was only one included review and that this did not fully address the question at hand, we discuss below other reviews that represent the best 'near misses'.³⁸⁻⁴¹

The literature review by McDonald⁴⁰ is part of a wider work on the use of health economics in health services in the context of rationality and models of decision-making. No methodology is given in the review, therefore assessment of robustness of its findings is not possible. The review identifies a number of barriers to the use of health economics in decision-making from existing studies but also tries to place the available literature in the context of decision-making at the health authority level. Information barriers include lack of information, inability to interpret information and the scale of uncertainty around information. Organisational barriers include the ability and willingness to implement findings (i.e. conflicting agendas, inflexible financial regimes, implementation not adequately considered in economic evaluations and authors not understanding the limitations of healthcare decision-making). The limited scope of the context in which economic evaluations are aimed and the limited appreciation of the decision-makers' perspective by authors of economic evaluations have not been fully addressed by those undertaking research into the use of economic evaluations. Thus, McDonald indicates limitations in the research on the use of economic evaluation in decision-making.

The article by Coyle³⁸ is a discussion paper on increasing the impact of economic evaluations on the healthcare decision-making process. It contains three sections on the process by which research information can be utilised in decision-making, a review of previous literature which has addressed the issue of impact made by economic evaluations and consideration of the factors which are believed to influence the level of impact which were raised in the previous sections. It is the literature review that was most relevant to this stage of the review. The article was not formally included in our review as it did not appear to target the use of economic evaluations by decision/policy makers. No methodology is given regarding how the review was conducted. The section that concentrates on the impact of economic evaluations on health care decision-making concludes that:

"Much of the ... literature includes little comment concerning the issues of impact or has been

concerned solely with direct impact. To measure the level of indirect impact made by economic evaluations we would need to know the weight which decision makers give to ... research information The level of indirect impact can only be monitored by studying the actions of decision-makers”

Coyle³⁸ (p. 17)

At the time Coyle undertook this review, it is unclear whether any such research was available. Furthermore, there is the issue that studies addressing the impact of economic evaluations on decision/policy making may not address the subsequent questions regarding reasons for and remedies to any limitation in impact.

A narrative review by Drummond³⁹ considers how economic appraisals could be made more relevant to decision-making so that the results of studies can be more often turned into action. Again, there is no methodological detail provided to outline how the review was undertaken and limited citations are given to support the points made. The review discusses various factors and concludes that methodological standards need to be maintained, economic evidence needs to be produced in a timely manner, relevance to the local situations needs to be increased, dissemination of studies needs to be improved and more note needs to be taken of the available policy instruments. This review highlights areas that require more investigation.

One excluded article aimed to describe and discuss barriers to using cost-effectiveness analysis in decision-making in managed care organisations.⁴¹ Although managed care organisations are more prevalent in the USA, similar organisations have appeared in other countries. As with the reports above, no detail is supplied regarding the methodology of how the information in the article was compiled. The article is probably best described as a discussion piece, although it does serve to outline the barriers to the uses of cost-effectiveness analysis. Using existing discussions and surveys, it tries to highlight these barriers. However, it is not immediately apparent which barriers are supported by research data and which are judgements by the author. The barriers indicated are outlined below:

- Whether decision-makers are equipped to evaluate cost-effectiveness information or understand its value.
- Little internal incentive to utilise cost-effectiveness evaluations in the face of conventional strategies to achieve cost control.

- Public perception of organisations being obsessed with cost – revealing that economics and costs are taken into consideration in decision-making is seen as a public relations mistake.
- Untimely nature of economic evaluations, with the technology already established before the evaluations are available.
- The perspective of the economic analysis is not from the viewpoint of the care organisations.
- End-points, such as QALYs, are not seen as appropriate from the organisation’s perspective.

The findings of this review of reviews are that the identified reviews:

- Do not give much information on interventions to improve the use of economic evaluations in healthcare decision-making.
- Contain little on what might be used to assess whether new measures to increase use of economic evaluation are successful.
- Contain considerable commonality about general barriers to use.

Non-healthcare reviews

Given the absence of systematic reviews on the use of economic evaluations in healthcare decision- and policy making, the review was expanded, as planned, to identify similar reviews in non-healthcare fields (namely social care, education, transport and the environment). The yield of articles from the searches varied depending on the database/website and the non-healthcare area searched. The greatest number of search results came from the social care area, primarily because of the more extensive coverage of the topic by available databases and more sophisticated search engines associated with these databases. Furthermore, social care feels as if it has a more active research profile than some of the other non-healthcare areas.

Scanning the search results revealed very few articles of sufficient relevance to be applied to the formal inclusion/exclusion process. Most of these articles came from the social care field and do not necessarily note more relevant research being undertaken in this field but might be the result of a greater number of search hits from a relatively more comprehensive collation of research in the databases searched. Furthermore, many of the articles for which hard copies were obtained and thus to which the inclusion/exclusion criteria were applied were only obtained due to lack of information with which to exclude them from the title/abstract alone.

Further information regarding the databases/websites searched, the quantity of search results and the number of relevant articles from each search is contained in Appendix 12. On application of the inclusion/exclusion criteria, no articles were subsequently included in the review. A list of studies identified and excluded is available on request from the authors of this report as space does not permit them to be printed here. The primary reasons for exclusion were that articles did not address the use of economics in the context of the decision-making process.

Overall, this review identified no reviews on the use of economic evaluations in the non-healthcare fields assessed. This suggests that no such reviews have been undertaken in this area, or that reviews have been undertaken but the available bibliographic databases that were searched are not extensive/comprehensive enough to catalogue them. It is interesting to speculate why there appears to be no such literature. A further option is that reviews have been undertaken but that the findings are nested within larger reports and thus not easily identified. However, it is our feeling that reviews on the use of economic evaluations in decision-making in these areas are unlikely to have been undertaken. Therefore, as with the healthcare area, there appears to have been no robust evaluation and summary of the research on the use of economic evaluations in decision-making. On this basis, we decided that it would not be efficient to extend the searches for primary literature on stages 3 and 4 outside healthcare databases.

Review of empirical studies in healthcare (stage 3)

The definition of an empirical study was one which includes studies using a control or comparator group in addition to those with no comparator group, for example case studies and surveys. Over 29,000 articles were identified through the original searches (*Figure 2*). After scanning the titles, 114 articles were considered potentially relevant. Hard copies of these reports were formally subjected to assessment against the inclusion criteria, resulting in no studies being included in the review of (quasi-) experimental studies and 27 in the review of non-experimental studies. The primary reasons for exclusion were: the document not reporting empirical research, the population group of the studies not being policy makers, the study not specifically measuring the use of economic evaluation and the

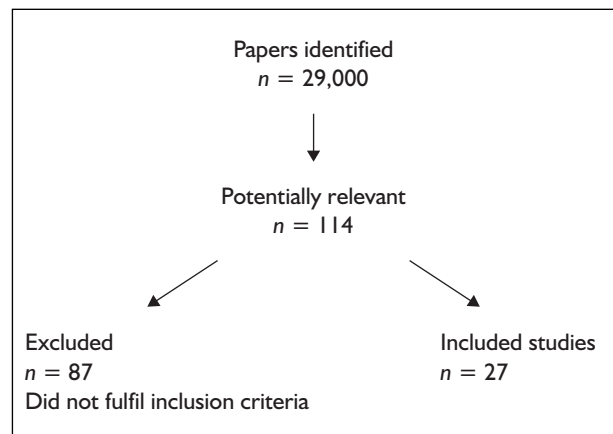


FIGURE 2 Flow chart of selection of empirical studies in healthcare

document reporting research findings already reported in another included document. A list of excluded studies can be found in Appendix 12.

The details of the 27 studies that met the inclusion criteria are given in Appendix 12. Several of the studies were conducted in 2000 as part of the Euromet survey.⁴² One study was reported in 1984 and the rest date from 1995 onwards. More than half of the studies were conducted with decision-makers in either the UK or the US health systems.

Each study had aims relating to the measurement or explanation of the impact of economic evaluations on healthcare decision-making. The majority of studies reported modest or low use of economic evaluation among decision-makers at all levels of healthcare policy. A number of studies suggested barriers to the use of economic evaluation and a smaller number suggested strategies for improvement.

Many studies did not define what they meant by 'economic information' or 'cost-effectiveness' in the report of research. Of those that did, each of the Euromet studies specifically asked respondents about cost-effectiveness, cost-utility and cost-benefit analysis,⁴³ as did Odedina and colleagues.⁴⁴ In interviews with decision-makers, Duthie and colleagues³ reported using stimulus material that had a 'cost-benefit component'. Two studies provided respondents with abstracts from published economic evaluations as part of the research process.^{43,45} Two further studies asked respondents for their own definitions of economic information or cost-effectiveness.^{1,37} Finally, one study, by Walley and colleagues,⁴⁶ provided its own broad definition.

Policy makers researched had a variety of backgrounds and frequently included Hospital Pharmacy Directors and Health Authority/Board representatives. Local decision-makers were more frequently researched than national policy makers, although the latter were included in a small number of study populations. Methodological approaches varied to some extent but surveys were the most common data collection technique.

The Euromet study collected survey data from decision-makers drawn from local decision-making levels (and in some cases national decision-making) in a range of European countries. This involved the use of a standard questionnaire (albeit adapted in some instances), which covered the following core questions:

- To what extent are the methods of economic evaluation known among the healthcare decision-makers?
- To what extent are results of economic evaluation being used in healthcare decision-making?
- What are regarded as the main barriers in the use of economic evaluation in decision-making?
- What factors might encourage the use of economic evaluations?

In some instances, the survey was augmented with data generated using other research techniques. In a summary of findings of the Euromet Project, it is concluded that:⁴³

- Knowledge of the methods of economic evaluation, overall, was poor.
- Actual use of economic evaluation in decision processes was low, although most respondents believed that it should be an influencing factor.
- The five most important obstacles to use of economic evaluation are: difficulty in transferring funds, concerns about bias in industry analyses, other budget constraints, study savings are anticipated and not real, and concerns about the assumptions made in economic studies.
- The five most important incentives for improving use are: more practical explanation of study relevance, training in health economics, more comparability of studies, more flexible healthcare budgets and easier access to studies.

Five surveys of US decision-makers and their use of pharmacoeconomics were also included in the review. These adopted either postal or telephone surveys and – like the Euromet Project – reported a widespread willingness to use economic information. However, this finding was again tempered by less evidence of actual use.^{44,47–51}

However, these studies indicated a higher level of usage of economic evaluation than the Euromet survey – especially in managed care organisations. In one case in particular, no barriers to the use of economic evaluation were reported.⁴⁴ By contrast, however, Sloan and colleagues⁵² reported limited use of economic information among US hospital decision-makers.

Two surveys conducted at different times in a UK context produced less equivocal findings.^{53,54} Both found that at local levels of decision-making, economic information had a limited impact. These findings were echoed in a study of senior provincial government bureaucrats in Canada.⁵⁵ Where they existed, barriers were reported in each of the surveys referred to. In all cases, these barriers were selected by respondents from a list pre-set by the authors. This raises questions about their validity. There are also concerns about sample size and representativeness. Walley and colleagues⁴⁶ supplemented a survey of primary care prescribers in the UK with focus group discussions. This study suggested that clinical data were seen as more important in informing decisions than cost-effectiveness information and suggested that usage of the latter was rare. The main barriers reported were inflexibility in health service structures and a perception of a lack of credibility in economic evaluations.

Apart from those arms of the Euromet Project that used interviewing, there were four more studies which made use of this technique. Duthie and colleagues³ conducted interviews using stimulus material with pairs of representatives from primary and secondary care in the UK. Their study confirmed a high level of stated interest from respondents but concluded that “current methods of economic evaluation and the communication of the results do not assist pragmatic decision-making”. The main barriers reported here derived from the difficulties presented by short-term contracting cycles and inflexible budgets. Decision-makers’ concerns about using a utilitarian approach presented a further barrier. Ross¹ used structured interviews to identify how economic evaluation was being used by decision-makers at state and national levels in Australia and found that use was limited. This was again seen as a result of economic evaluations either not being, or not being seen to be, relevant to the circumstances of policy decision-making. Spath and colleagues³⁷ interviewed pharmacists from public and private hospitals and clinics in France and concluded that “economic data appeared to be a minor decision-making factor”.

Reported barriers varied from budget inflexibility to difficulties in accessing studies and concerns about study bias. Drummond and Weatherly¹⁹ used secondary sources, a postal questionnaire and semi-structured interviews to research the use of economic information by health authorities in the UK. Again, this study found that these forms of information were considered “highly relevant” and yet were not regularly used. The main reported barriers were that policy makers found studies hard to access within the decision-making time-frame and found results of studies difficult to transfer to their own circumstances and, therefore, difficult to implement. Political factors were also seen as a competing influence on decisions. In this study, a number of recommendations were put forward. These included using economic evaluation to formulate national guidelines as local decision-makers are more able to adhere to these. The authors also advocate further training in health economics.

Two further studies of UK health authority decision-makers took a slightly different approach. Hoffmann and colleagues⁴³ used focus group discussions in an attempt to establish a “best case scenario” in which respondents would be able to envisage effectively using economic evaluations. This study again found that despite the feeling that these were useful in principle, “in practice their usefulness may be limited”. This was found to be a result of the lack of generalisability of studies and of the complexity of decision-making situations.

In a series of case studies of health authority organisations, Nixon and colleagues⁴⁵ sought to improve access to economic evaluations by making the latter available to decision-makers. In a positive finding, they reported that having access to cost-effectiveness information did assist local-level decision-makers in their work.

Finally, McDonald’s study⁴⁰ involved in-depth and long-term participant observation of the decision-making process within a single UK health economy. McDonald concluded that health economics and the NHS are fundamentally incompatible and cast doubt on the value of persisting to seek to inform decision-making with the use of economic evaluation.

Discussion

Review of reviews

An important issue for the existing reviews is just how rigorous the evidence is concerning the

barriers. Also, this review of reviews raises the issue of just how helpful have been the reviews on this topic that do not possess a clear statement of method. One suspects that many reviews have been more systematic in approach than their reporting suggests. However, while acknowledging this, in the absence of clear statements about what types of literature have been sought and included, there is uncertainty about whether the ‘review’ is truly an attempt to summarise existing research or merely a vehicle for expressing or developing ideas. It could be suggested that this does not matter. However, in this topic where the volume of primary research is so small, the importance of explicitly linking views expressed by influential researchers to an evidence base is vital.

Review of empirical studies

The review identified a small number of studies in a variety of settings. Levels of usage of economic evaluation by decision-makers were found to be low in the majority of studies.

The most commonly used research approach was the postal or telephone questionnaire. This has the advantage of breadth but yields little by way of interpretative material to contextualise and explain research findings. This means that apparently contradictory findings are left unexplained. For example, the Euromet Project asked respondents to rank in order of importance a list of barriers to the use of economic evaluation, and then to repeat the exercise with a list of incentives for increasing its use. The results of these exercises did not appear to match inasmuch as the most highly ranked improvements did not address the most frequently cited barriers. Avoidance or exploration of these apparent discrepancies would require a more in-depth approach. Similarly, the consistent finding that decision-makers **value** but do not actually **use** economic evaluation is not fully explored or accounted for in quantitative research exercises.

Those studies that employed more in-depth methodologies^{19,40} consistently reported a low impact of economic evaluation on decision-making. For differing reasons, neither of these studies produced concrete recommendations for the improvement of this situation. This is therefore an area that requires further work.

Overall, despite concerns about the research methods employed, the body of work identified reveals that a number of barriers appear consistently to impede the use of economic evaluation. Studies consistently find that inflexible

and/or limited budgets prevent the implementation of study findings. Concerns about bias, assumptions and relevance of studies are also consistently cited as barriers in the literature. Finally, difficulties in accessing and interpreting economic studies present a barrier for decision-makers.

These findings are again qualified by concerns about the methodology for identifying what the barriers to using economic evaluation might be. The provision of a pre-set list of potential barriers enables responses to be quantified but also circumscribes the range of possible responses. Failure to include real-time observation of decision-makers leads researchers to rely solely on data generated by interview or questionnaire.

Conclusions

Overall, the review exposed the difficulties of attempting systematically to search for evidence

when considering topics such as this. Despite these difficulties, the review established the following:

- There are very few previous systematic reviews of the evidence in this area. We were able to identify only one. Most reviews have been conducted in a non-systematic manner or are more accurately described as opinion pieces.
- A number of previous studies in healthcare have looked at the use of economic evaluations in decision-making. Although these undoubtedly contribute to our knowledge on this topic, there are some concerns about the methodological approach adopted in these studies. Studies using surveys, in particular, frequently raise more questions than they answer.
- There is a continuing need for research that addresses the range of policy decision-making levels and which takes an in-depth, qualitative approach to addressing the research question.

Chapter 4

Results from local research

Introduction

This chapter reports findings regarding the use of economic information by local decision-makers. It includes a review of new technology request forms used by primary and secondary care providers when considering policy decisions about the use of new drugs. In addition, the chapter has a write-up of the case studies of local decision-making committees which examined a number of factors, including the importance attached to economic evaluation and the way in which it is used by the committees. The chapter also describes the workshops held to discuss the barriers to use of economic analysis and ways of overcoming them.

Review of new technology request forms used by local decision-making bodies

This section is concerned with the information routinely requested by local decision-making bodies when considering policy decisions relating to the use of new drugs. The objective was to obtain information from all secondary care providers (including hospital trusts, community health trusts and healthcare trusts) and primary care trusts (PCTs) in England. Partnership trusts were excluded from the sample. We requested a copy of the form used locally when a new drug was considered by a drugs and therapeutics committee, medicines management committee or other similar decision-making body.

The coverage and response is described followed by a description of the types of committees covered and the extent of use of formal pro formas by committees. For those that do use a form, we detail what general types of information tend to be requested and what proportion formally request cost-effectiveness/economic evaluation information. For those that routinely request cost-effectiveness information, we have analysed the wording of the questions in order to assess the types of information that tend to be requested. These findings are reported separately for secondary and primary care settings.

Response and coverage

Figures 3 and 4 indicate for secondary care and primary care organisations, respectively, the number of requests for information made and the response and coverage of organisations achieved.

For secondary care (*Figure 3*), we approached 188 secondary care providers, of which 116 responded; 12 indicated that their organisation's committee did not make use of such a pro forma, 101 provided the relevant pro forma and three responses gave information that was not relevant or helpful. However, from the responses, it became clear that we additionally had information that related to five of the non-responding organisations because there was a shared committee with one of the responding organisations. This means that in total we have relevant information (including the statement that no such form is in use) for 118 secondary care organisations, giving us a coverage rate of 63%. Reasons for non-response were ascertained from approximately 50% of non-responders. The most commonly cited reasons were that the individual mailed no longer worked there, that they were too busy to respond, that they had no recollection of receiving the letters and that no Chief Pharmacist was employed by the trust.

For primary care (*Figure 4*), we approached 308 primary care organisations, of which 165 responded; 114 indicated that their organisation did not make use of such a pro forma, 40 provided the relevant pro forma and 11 responses gave information that was not relevant or helpful. In line with the secondary care data, we again had information that related to non-responding organisations because of the existence of committees shared with responding organisations – there were 30 non-responding organisations accounted for in this way. This means that in total we have relevant information for 184 primary care organisations, giving us a coverage rate of 60%. Reasons for non-response were ascertained from over half of non-responders. The most commonly cited reason was that the individual mailed no longer worked there.

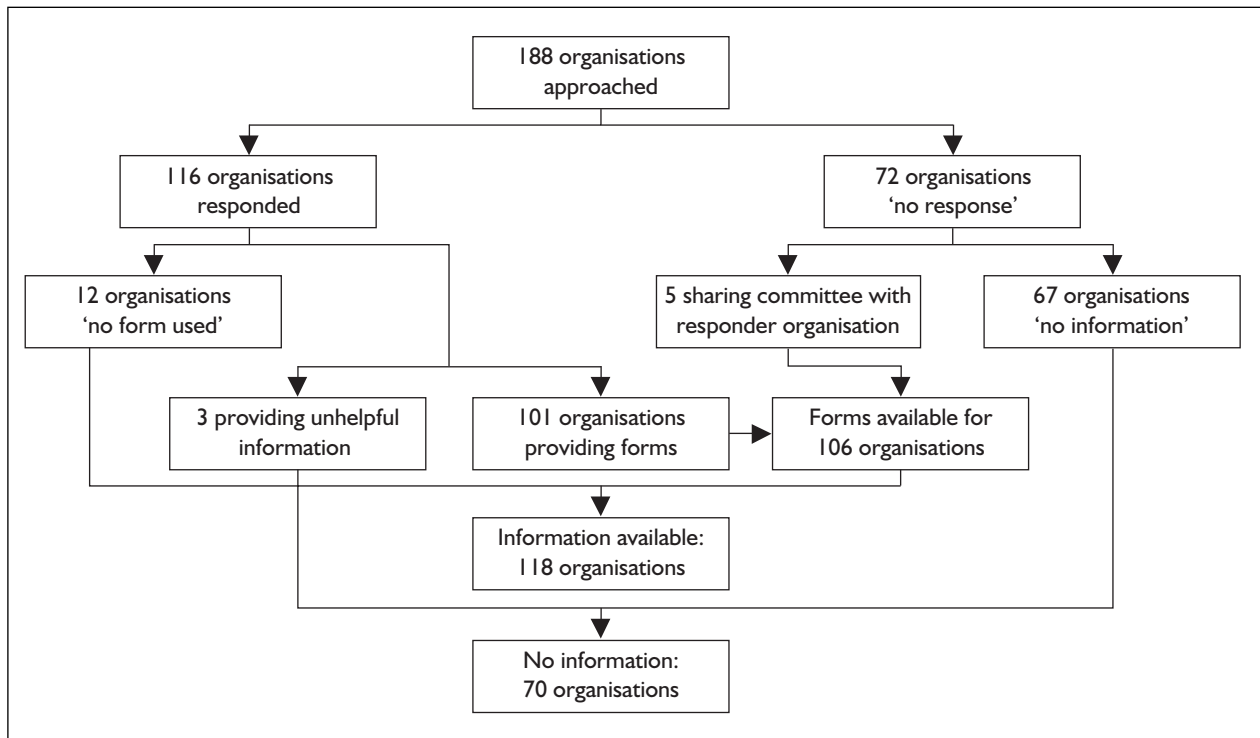


FIGURE 3 Coverage and response – secondary care

Where respondents replied to a letter addressed to an organisation in a different sector, for example, a response on behalf of a PCT from the secondary care arm of the survey, the information has been categorised in its appropriate sector. This

happened in only a handful of cases. There are instances where respondents were asked to provide a form for an organisation in one sector but have attached the form relating to a different healthcare sector. For example, PCT prescribing

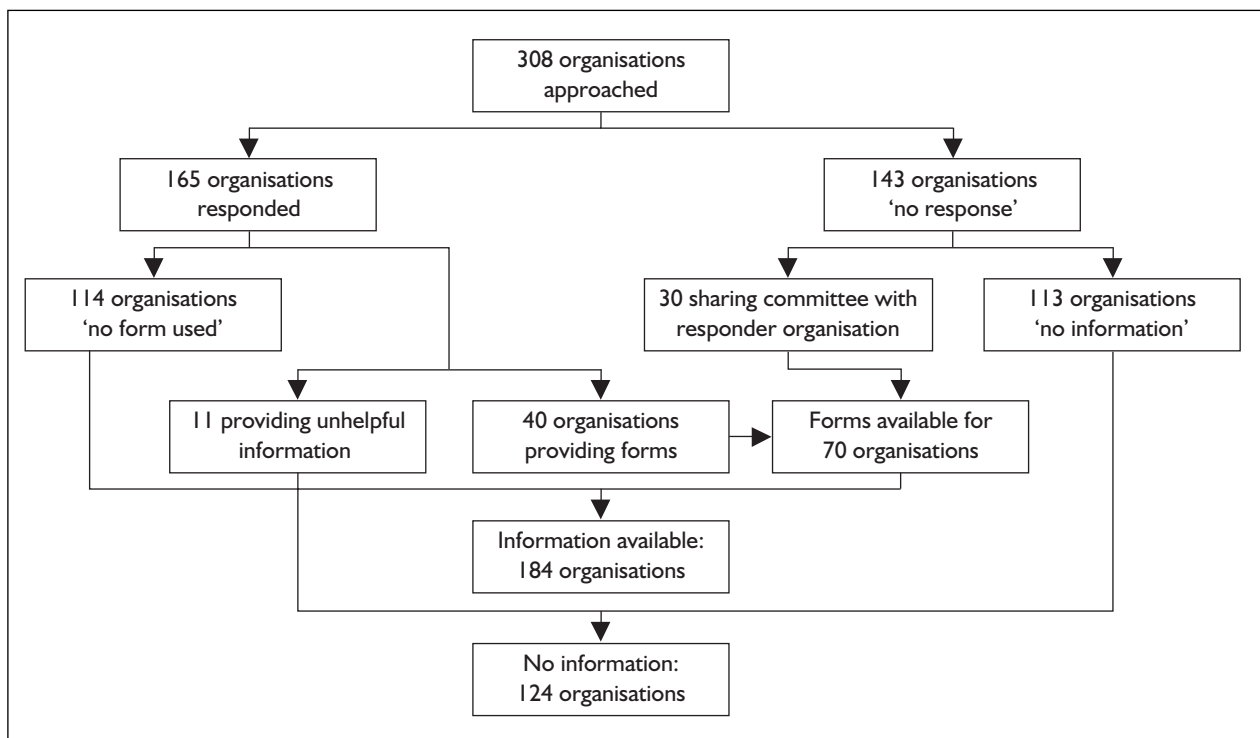


FIGURE 4 Coverage and response – primary care

advisors who sit on committees in secondary care organisations have in some instances attached a hospital-based information pro forma. The research team have attempted to establish the healthcare sector(s) covered by the committees and the pro formas. The different remits of the committees include secondary care, primary care and cross-sector. Where the specific remit of the committee reported was not clear, it is assumed that it primarily covers the sector in which the respondent is based.

Types of committees covered

Table 2 shows the more common committee names identified in the survey of secondary care organisations. The majority use a traditional name of 'Drugs and Therapeutics Committee' or something very similar. Although many committees were concerned solely with a single secondary care provider, it is clear from some of the committee names that single committees are being established either to work across a number of hospitals or to work jointly across primary and secondary care (e.g. 'Area Prescribing Committee', 'Locality Prescribing Committee').

Table 3 shows examples of the titles of pro formas commonly used across the secondary care committees. For ease of presentation, the names have been grouped under broader headings when the variation is not important.

In the primary care setting, in comparison with secondary care, the names used by prescribing committees are rather different, with much more variation indicating both that such committees are less well established and that they perform more varied roles (Table 4). Where committees are referred to as prescribing committees prefaced by the name of the area covered, these have been categorised as 'area prescribing committees'. Where

TABLE 2 Names of secondary care committees

Name	No. of committees
'Drugs and Therapeutics Committee' (or something similar, such as 'Drugs, Therapeutics and Clinical Technology Committee')	56
'Prescribing Committee' or 'Formulary Committee' (or something similar, such as 'Pharmaceutical Advisory Committee')	15
'Medicines Management Committee' (or something similar, such as 'Area Medicines Management Committee')	12

TABLE 3 Names of secondary care pro formas

Name	No. of pro formas
New product/drug/medicine/indication request form	35
Formulary addition form	29
New product/drug/medicine/indication application	11
New drug product/drug/medicine/indication evaluation	4
Submission to Drugs and Therapeutic Committee/other committee for a new drug	3
Business case for new drugs/medicines	2

it is evident that a committee has been referred to in more than one pro forma, they are counted only once.

The terms 'area', 'interface' and 'joint' are commonly seen in the committee names, supporting the view that joint working across primary and secondary care is increasing.

The titles of pro formas used in primary care tend to be similar to those used in secondary care,

TABLE 4 Names of primary care committees

Name	No. of committees
Area Prescribing Committee/Forum	6
PCT/Primary Care Prescribing Group/Forum	6
Health Economy/Area Medicines Management Committee/Board	6
Drug/Medicine/Prescribing Interface Committee	4
Drugs and Therapeutics Committee	3
Priorities Subcommittee	2
Joint Prescribing Committee	2
Area/District Drugs and Therapeutics Committee	2
Area Joint Formulary Group	2
Area Priorities and Clinical Effectiveness Forum (PACEF)	1
Area Prescribing and New Technologies Strategy Group	1
New drug panel	1
NICE implementation and new technologies group	1
Submission for drug evaluation prior to prescribing	1

with terms 'request', 'application', 'assessment', 'introduction' and 'addition' being used frequently.

Use of forms and information requested

All forms asked for some details of the product/therapy in question and indications for use. Further information categories and the frequency with which forms requested this information are given in *Table 5* and included in full in Appendix 6. As we are interested in information being used in the health sector organisations, the organisation is our denominator and so we have counted more than once cases where the same form is known to be used by a number of organisations/committees. Thus, we have included organisations that did not respond themselves but where responses from other organisations provided information on the particular form used.

Table 5 reports, in broad terms, the nature of the questions included on the information pro formas. The items in *Table 5* are ordered in terms of how frequently the questions are asked (in the secondary care setting). The pattern of questions appears to be similar in both secondary and

primary care settings. A focus on evidence of benefit comes through clearly, with most organisations requiring evidence in order to consider a new technology. Other issues frequently considered are the size of the clinical problem and the scale of the potential investment, highlighted by the question concerning the expected number of potential patients. Implementation considerations also play an important role in many committees, with the concern to limit access by restricting who can use or prescribe commonly asked. Again on the implementation topic, the signature of the budget holder is required on many forms, indicating that the support of senior colleagues is crucial in bringing about successful adoption. There is potential for conflicts of interest in these settings with many new drugs and/or devices proposed by clinicians who may have received incentives from manufacturers to promote the product. It seems that many committees recognise this potential problem and uncover it through such conflicts being stated in writing.

It is also clear that most committees on which we have data raise cost issues. The main focus appears to be on the cost to be covered

TABLE 5 Analysis of 'information pro formas'

Question on pro forma	Number (%) of organisations where the question is used	
	Secondary	Primary
General questions:		
What is the evidence of clinical benefit?	84 (79)	41 (59)
Expected number of patients to receive treatment	82 (76)	20 (29)
Is the technology an add-on or replacement?	79 (74)	22 (31)
Implications for other sectors (e.g. primary care)	64 (60)	32 (46)
Conflicts of interest	59 (56)	14 (20)
What are the 'advantages' of the new technology?	52 (49)	23 (33)
Signature of budget holder required	51 (48)	12 (17)
Should there be restrictions on who should prescribe?	49 (46)	24 (34)
Request for licence information	44 (41)	23 (33)
Length of treatment course	34 (32)	7 (10)
Place in therapy	23 (22)	19 (27)
Prior identification of funding if technology supported	16 (15)	6 (8)
Does it represent a 'therapeutic advance'?	12 (11)	2 (3)
Clinical experience of the technology locally	11 (10)	3 (4)
Discussion with/support of colleagues	11 (10)	5 (7)
Previous appraisal by NICE/national guidance	7 (7)	8 (11)
Numbers-needed-to-treat	2 (2)	1 (1)
Questions specifically concerning cost information:		
Some requirement for cost information	91 (86)	39 (56)
Cost impact of technology	62 (58)	33 (47)
Costs when compared with alternatives/current treatment	44 (41)	18 (26)
Price of technology	33 (31)	11 (16)
Potential savings from using technology	22 (21)	8 (11)
Total	106	70

immediately rather than the longer term savings that might be generated.

Cost-effectiveness information requested

A relatively small number of committees using a form on which information is available [$n = 19$ for secondary care (19%); $n = 16$ for primary care (23%)] routinely ask for evidence on cost-effectiveness information. For those that do, the actual wording of the questions asked is presented in Appendices 7 and 8. Some of the questions concerning cost-effectiveness are very vague (e.g. "Does this drug provide good value for money?") and it is unclear what information would be given in response to the questions and how such information might sensibly be used by the committee in reaching its judgement. However, many of the questions are more focused and request evidence of cost-effectiveness in the form of published papers and other supporting materials. For example:

"Is there evidence that this proposed new treatment is more cost-effective than standard treatment already in use? Yes ... No ...

If yes, please provide supporting references."

In some cases, it is not evidence on cost-effectiveness that is requested but a judgement call on 'value for money' by the clinician putting forward the case. The assumption would appear to be that if evidence on cost-effectiveness is available it would have been read and digested by the proposer who is then asked to respond to a question as follows:

"What will be the cost benefit (£ spent vs £ saved), cost-effectiveness (£ per unit of health outcome), cost utility (£ per QALY), and opportunity cost of using this drug (what could have been done instead?)."

The broad pattern of not routinely requesting formal information on cost-effectiveness and only in a small number of cases asking for evidence from economic analyses is a pattern that seems to be common to both the secondary and primary care settings.

Findings from case studies

This section presents summary findings from the four local case studies specified in *Box 1*. A detailed report of each case study is given in Appendix 9.

BOX 1 Case study committees

Case study A: County-wide Priorities Committee

- Established in July 1999.
- Met monthly.
- Members included senior representatives of each NHS trust and PCT in the area, in addition to other stakeholder organisations.
- The committee reported directly to each member trust and PCT, which then decided whether or not to implement its recommendations.

Case study B: Hospital Medicines Management Committee

- Developed from a long-standing NHS Teaching Trust Drugs and Therapeutics Committee.
- Met monthly.
- Committee membership consisted of hospital pharmacists, a small medicines management team and a representative of each clinical directorate. Membership from outside of the trust included university and primary care representatives.
- The committee decided what technologies were introduced on to the trust formularies but did not control the budget for new technologies – this authority resided with individual directorates.

Case study C: Primary Care Area Medicines Management Committee

- Established in 2002.
- Met bimonthly.
- Members included pharmacists, PCT prescribing leads, secondary care consultants and specialists in pharmaceutical public health.
- The committee reported to the PCT Professional Executive Committees (PECs) and the hospital Clinical Governance Committee on a quarterly basis. The committee's role was advisory.

Case study D: Interface Medicines Management Committee

- Established in 2002.
- Met bimonthly.
- Membership included PCT prescribing advisors and clinicians, hospital medical directors, local Medical Committee and local Pharmaceutical Committee representatives and finance representatives.
- The committee reported to the boards of the trusts in the area through their representatives on the committee regarding medicines' management issues, particularly those affecting the interface between primary and secondary care.

Decision-making

Researchers attended a minimum of two meetings for each case study site. In total 11 meetings were observed and 31 people from across the four committees were interviewed. Each of the committees had some responsibility for deciding on new technologies and each was responsible for the management of a formulary. The relationship to funding streams of member organisations for the three committees was through their respective representatives (see *Box 1*). The Acute Trust Medicines Management Committee requested that applicants seek authority for the funding of the new technology within the trust as part of the application.

A similar process was followed by each of the case study committees. Papers relating to proposed formulary additions were distributed and a presentation was made to the committee by the applicant. Questions and discussion ensued before a decision was reached in closed session. Each committee had some process for reviewing decisions. There was, however, significant variation in the depth of information submitted, with one committee receiving a one-page application supported by a short supplement from the trust information manager and, at the other extreme, the Priorities Network receiving considerable detail in both the application itself and the supporting information. All four committees had some in-house data-generating capacity but levels of this capacity varied.

Observation and documentary analysis confirmed that committees were concerned with both the implementation and the evaluation of technologies. Information and discussion explicitly focused on patient numbers and budgetary implications and also differences between geographical locations within the health economy. Again there was variation, with the Priorities Network apparently making more use of health technology assessment and other research evidence. Other committees focused less on published evidence and more on practical implementation issues of whether and how to restrict usage and control prescribing. The extent of variation in levels of scrutiny applied to each application was reflected in the number of decisions taken: whereas the Priorities Network averaged two decisions per meeting (with some decisions postponed over several meetings due to lack of evidence), another committee made decisions on 12 applications in the course of the two meetings observed.

Many committee members saw their role as being to represent their particular organisation and/or healthcare sector, in addition to considering the objective merits of an application.

“My job is to put on the agenda things which are of interest to (name of PCT), review the background papers, or take my share in producing the background papers and essentially contributing to the debate on behalf of (name of PCT) and arguing for that point of view when it comes to the committee making a recommendation.”

(CA 9)

“I take things pertinent to nurse prescribing because I’m the nurse prescribing lead for (name of area). So if we have issues, you know, around formularies, new products, then I’d see it as my role to take the issues there on behalf of all the nurses.”

(CC 2)

“I’ve got two roles, really. One is to come at it as a GP, what I would consider to be appropriate and reasonable for me to prescribe and what would be in the normal competencies of a GP to be able to do, and to advise the committee from that point of view. I also come at it from the PCT point of view: perhaps our financial or clinical governance aspects.”

(CD 1)

“I drive the primary care agenda and make the secondary care physicians aware that the repercussions of the drugs they are recommending and how they prescribe them do quite often fall on to the heads of general practitioners and primary care trusts.”

(CB 5)

This partiality was reflected in the discussion which frequently involved achieving consensus and satisfying the specific concerns of stakeholders. There were a number of possible outcomes of committee deliberation. These included:

- agreement to add the technology to the formulary
- a decision not to provide coverage – usually on the grounds of lack of evidence of effectiveness
- a decision to postpone a determination until more evidence became available
- agreement to cover a technology subject to development of a treatment algorithm for prescribers
- agreement to cover a technology subject to prescribing restrictions (for example confining use to a clinical speciality within a trust).

There were no instances where it was agreed to disinvest in a technology or remove any intervention from the formulary.

Committees were unanimous in citing evidence of a technology's clinical benefit to patients as the primary factor influencing the decisions. With some variation in emphasis, cost implications of introduction were identified by interviewees as being the next most sought after information – although no technologies were refused on these grounds during the case studies.

“For me it's about the clinical benefits of a drug: are they really demonstrated as being much better than what we've got already? What is the quality of the evidence?”

(CB 4)

“Well basically the quality of the published evidence. The published trials: the number of patients involved, the number of centres involved, preferably fewer rather than greater, whether the trial was sponsored by the manufacturer of the drug. Cost is obviously something that needs to be considered these days.”

(CB 2)

“A summary of the product characteristics is a useful starting point. You need to know something about obviously the cost of the product, it's safety and efficacy profile, the latest evidence about it, projected costs if they are available, what the impact is going to be on our local economy, those sorts of things.”

(CC 3)

“I would consider that the safety and the therapeutic indication, and the benefit of it, that those would be the critical issues. The cost is of secondary importance, but is there. The critical issues are who is it going to help, by how much, and what are the risks in doing it?”

(CD 1)

As indicated in previous studies, other factors did seem to influence the committees, such as the perspectives of committee members, especially clinicians. Interview responses seemed to suggest that the approach to decision-making adopted by the committee did not permit the development of precedent or case law to inform prospective recommendations. Therefore, each application was considered on its merits, effectively from a 'blank slate' position. In this context, it was felt by some respondents that the committees were susceptible to powerful personalities on, or attending, the committee.

Levels of understanding of health economics

Responses to the question, “do you feel you understand the economic evaluation presented to the committee?” indicate significant variation in committee members' familiarity with economic evaluation, with many reporting a lack of expertise

in this area. Although a small number of interviewees expressed concern at their subsequent difficulty in critiquing economic evaluations, the majority felt their work was relatively unhindered by this constraint.

“Could I sit and describe to you precisely what modelling went into a QALY? No I couldn't. Could I sit and say that I have an appreciation of what a QALY means? Yes I could. It's a bit like yes, I can tell the time, but I've no interest in knowing how a watch works.”

(CA 5)

“There's a lot of jargon in health economics. If you said at the committee 'the health economics was done by a Markov model', people wouldn't know whether that was good or bad. And if you started talking about a Monte Carlo analysis or bootstrapping or anything like that, people would say, 'I don't know what the bloody hell that means'. But if you said, 'it's a randomised, double-blind cross-over trial', then most people would have a good understanding of that.”

(CC 4)

“I understand QALYs enough to know that they are a measure of the cost-effectiveness and affordability rate of a particular product. I don't know enough about the influencing factors within the model to be able to make a reasoned approach to it.”

(CD 5)

At the time of research, the committees had few or no specific health economics experts in attendance. Observations of meetings seemed to suggest that this presented the committee with difficulties when processing economic evaluation information in the small number of instances where this was forthcoming.

Use of economic evaluation

Individual members of two of the four committees had some health economics expertise. For a third committee, a member with health economics expertise had recently left. However, although the specific co-opting of health economics expertise seemed to be viewed as beneficial, it was not considered essential by the interviewees. Two of the four (the Priorities Network and the primary care based committee) included a request for health economics information as part of its new technology request form (NTRF). However, the main sources of economic evaluation in all four cases were NICE guidance and company-sponsored evaluations, with interviewees indicating only limited access to other sources. Reference to published cost-effectiveness analyses was rare in committee discussion, and the actual accessing of these forms of analysis did not occur

in the course of the case studies. The Priorities Network was the only body which reported previously having commissioned a review incorporating cost-effectiveness analyses.

Our data reveal some confusion among committee members over the terms ‘economic evaluation’ and ‘cost-effectiveness’. Despite this, it appeared that economic evaluation was attributed more importance in interviews with Priorities Network members than the other bodies. In all four cases cost impact – the implications for allocation of resources locally – seemed to be of greater concern. Formal cost-effectiveness analysis appeared to be less frequently accessed and less highly valued than other forms of cost information.

“We very rarely look at cost-utility calculations, mostly because they’re not available, and they’re quite often very difficult to do. Occasionally we may get QALY-type stuff, but it’s usually straight numbers of lives saved per pounds spent, or numbers of admissions avoided per pound spent.”

(CA 9)

“The big problem is that most of the applications we get for drugs are at the time they are first launched and such data really doesn’t exist at that point other than guesstimates from the drug companies.”

(CB 2)

“I don’t think we actually need raw analysis for every application, because that’s not necessary and it’s just extra work for the applicant and for ourselves, when the decision could actually be quite easily made around other measures for that product.”

(CC 3)

“A lot of NICE guidance has an element of health economic data but I think many commissioning managers look at the additional financial cost implications of NICE guidance rather than the health economics data. So even when it is available in that local commissioning kind of environment it probably isn’t used as much as it should be.”

(CD 2)

Using an open-ended question, interviewees were asked to identify the barriers to use of economic evaluation. The most commonly cited barriers related to the accessibility of analyses: cost-effectiveness analyses were rarely available, especially within the strict time-frames in place. The next most commonly cited barrier concerned the potential for biased analyses. This reflected the view that available evaluations had most often been conducted by manufacturers of the technology under consideration. Those respondents who had been able to access independent studies reported problems relating to

the inability to realise, in practice, savings identified in analyses in addition to difficulties interpreting the cost-effectiveness analyses. Other less frequently cited barriers identified included excessive variation in health economics methodologies, concerns about the robustness of analyses and ethical objections to the perceived underlying values of health economics.

“I think that what would be critical is having the information available. What we don’t have as a committee is the resources to be able to go and find the information and put it together, assess it to make sure that it’s robust and then deliver it to the committee. We don’t have the team to be able to do that sort of work.”

(CD 1)

“A lot of the models that I’ve seen come out with a bottom line cost which is difficult to extract in cash terms. Saving beds is not, at this moment in time with the pressures on the NHS, going to realise any savings at all, because that bed will be used for the next pressure that’s coming in.”

(CD 5)

“Quite often this sort of information is available from the actual drug companies themselves, isn’t it? I see that as a weakness with it. Because if a drug company is driving a product there may be the risk of bias.”

(CC 1)

“To be realistic I almost think the term needs to be changed ... A lot of clinicians think that pharmacy’s all about money, that’s really all we’re concerned about, and if you say ‘economics’ well that’s money really. So it’s difficult to actually try and get away from looking at benefits to the patient without tying those to a financial element.”

(CB 4)

Respondents did talk about ways of overcoming these barriers. The need for a clear, standardised and generally accepted format for the presentation of economic analysis, including greater clarification about the assumptions that go into models, was emphasised. A national resource centre and archive of health economics tools and models that could be used was proposed, together with information about the benefits of using these tools. Training for committee members, and the co-opting on to the committee of health economics expertise in cases where this was required, were also suggested.

However, these prescriptions – which echo those reported in previous studies – do not address all of the stated or revealed reasons for the lack of use of economic evaluation. For example, in each case study example there was an absence of

consideration of the opportunity cost of decisions taken. Committees rarely conducted formal comparison of new technologies with current practice and were rarely if ever in a position to recommend disinvestment in existing technologies. A small number of interviewees – particularly those involved in the Priorities Network – expressed concern at this.

“If you’re making an investment in something that doesn’t come ring-fenced with money it inevitably, in a fixed budget, means a *de facto* disinvestment in something else. We’re less clear about, as I see it, what we’re disinvesting in.”

(CA 5)

“No-one has yet found a way of taking money out of anything. The whole time I’ve been working I’ve never ever found a situation where we’re able to say ‘we no longer need to do that.’”

(CA 6)

“We’re just adding to the formulary. That’s the problem with formularies: people will just carry on adding things and adding things until it ceases to be a formulary and ends up just being a directory of all the drugs known to man. Waste of time.”

(CC 7)

This avoidance of the ‘hard choices’ that cost-effectiveness analysis is geared towards informing was perhaps a further disincentive to its use. Similarly, although the case study sites routinely requested information on costs associated with new technologies, it is not clear how this was intended to be used given that – with the partial exception of the Priorities Network who held a ‘NICE implementation budget’ – they did not directly allocate resources and merely advised those charged with financial decision-making. Despite all having remits that to some extent included the power to recommend exclusion of, or disinvestment in, technologies, in practice the committees were more likely to focus on **how**, as opposed to **whether**, new treatments should be introduced. Decisions frequently took the form of prescriptions for the development of guidelines, protocols and/or shared care policies across primary and secondary care. In this context, it is difficult to assess and prescribe the value of decision-making frameworks such as those generated by economic evaluations.

Workshop discussions

The research team facilitated two workshop discussions with the aim of providing additional

data on the barriers to the use of economic information in decision-making and identifying strategies to overcome these barriers. Participants were recruited by writing to pharmacists who had responded to the NTRF exercise and expressed an interest in being further involved in the research. A total of 15 participants took part in the two workshops. Those involved were drawn from both primary and secondary care sectors and one participant was from a mental health trust (see Chapter 2 for further information on sampling and other methods used in this part of the research).

Barriers to the use of economic analysis and ways of overcoming them

Is health economic evaluation necessary?

Participants considered that the government does not acknowledge that rationing and prioritisation have to take place and so there is little understanding in society that this type of analysis is necessary. If rationing is not explicit then health economics information is not important.

“We are not allowed to make these decisions (about rationing treatments) because they can be over-ruled at will ... You have to take into account the response of the press.”

“It’s something that hasn’t got off the ground. I’ve been doing this for 10 years and only now am I getting someone to help me. It hasn’t been seen as a priority.”

“You go to a lot of trouble to produce guidelines (e.g. the NICE decision about beta interferon) and then patient pressure overturns it, and the politicians stand behind the patients.”

It was very important to participants that this barrier was overcome by a more explicit approach to rationing from the Department of Health and NICE.

“Can we have right at the top of the list that we need an admission that we need it? Prioritisation has to occur in the NHS so there is a need for health economic information. Can the DH please admit this up front and help us with our jobs?”

“There are currently contradictory messages from the government. On the one hand the customer has choice and on the other, the budget must be met.”

Levels of understanding

A second point was that because this type of information was not given a high profile, no-one understood what health economics analysis was about. It was not part of professional education and training.

“Although health economics information has been around for two decades or longer, I don’t think it is included in any of the healthcare training. So nobody embraces it. No one understands it.”

Several suggestions were made about how this problem could be overcome:

- Short, easily assimilated courses constructed in consultation with practitioners to make sure they were practical, understandable and relevant.
- Including health economics in undergraduate training for health professionals.
- Training on decision-making with health economics as one of the tools, for prescribing committees and other similar committees using the same model as training for Local Research Ethics Committees (LRECs), where all members were expected to have a basic knowledge of research ethics.
- Promotion of health economics by professional bodies such as pharmaceutical societies.
- Funding for this training will need to be ring-fenced as trusts will not prioritise it – LRECs usually have the funding, not the trusts.
- Joint training (across a health economy) is important so prescribing committees are a good idea as representatives of different organisations will be members.
- Mentorship by academics for those who wanted to go further into the subject, for example pharmaceutical advisers of drugs and therapeutics committees. This would help both academics and practitioners.

There is no incentive to use it

There is often no incentive to use health economics information and analysis. A number of reasons for this were given. First, clinicians tend to only consider effectiveness for individual patients:

“One thing it is very difficult to get across to them is that a new drug that is better than an old drug can still not be cost-effective. Sometimes the less effective drug because it is a lot cheaper means that you treat more patients and so have better outcomes for a larger number of patients. They think that can’t be right. Clinicians are not on board to the value that the NHS is about the greatest good for the greatest number of people.”

Linked to this is the fact that most clinicians have a ‘**silo mentality**’ and do not see the whole picture. They are only concerned with their own particular speciality and not with the way in which the budget is divided between different areas. The organisation of the NHS can add to this tendency

to compartmentalise because there is competition between trusts for resources. The benefits of a particular course of action that is cost-effective may not accrue to the healthcare providers who made the decisions. The lack of a unified budget meant that benefits could be in social care. In fact it may not be possible to see the benefits at all because:

“... a bed day saved in the NHS is just a bed given to somebody else.”

The cost of carrying out health economic analysis was also mentioned, plus the fact that the organisation may not be able to afford the drug so it was sometimes better not to examine existing practice:

“It is best not to have it clarified as immediate budget constraints will probably prevent implementation.”

This was considered to be a difficult barrier to overcome, but training and education were thought to be important in addition to the government giving the subject a higher profile; also perhaps if there was national guidance about how to approach economic data. A national depository of health economics tools and models that could be used was suggested. Benefits of using these tools needed to be made clearer. Two factors were identified that might help and these were: if health economics information was more easily available and if it were more relevant.

It is not available

Participants thought that much health economics information was difficult to get hold of when it was needed. Also, finding information that could be relied on because it was from an independent source was hard as much health economics information was produced by the pharmaceutical industry.

“Sorting out which data is good quality and keeping up to date is difficult ... it takes time and we are very busy.”

“Information is not available when you need it.”

“We don’t have the time or resources to make use of this information. It’s never a formulaic decision. It’s always value based at the end of the day.”

It was difficult to review decisions when new information became available because there were always new drugs to review and no time to go back and assess whether previous decisions were still the best ones.

An information centre was suggested, but there was disagreement about where this should be located. A national independent drug information centre with a website and message board was preferred by many of the participants who wanted up-to-date, easily accessible information about specific drugs from a credible source. Others wanted a regionally based resource that could disseminate national information to the local level and which would be available to answer questions. The ARIF and Bandolier examples were given, where it was possible to ring up someone with research expertise and ask whether, for example, a particular paper was important or credible.

The exchange of local information between committees was also discussed, but although this was seen as desirable, it was also perceived to be difficult and time consuming. Harmonisation of decisions across organisations in the same health economy was considered a goal to be aimed at but not practical unless formally facilitated.

What is available is not appropriate or relevant

The type of information available in health economic analysis was considered to be not always relevant for various reasons:

- They do not take account of the extra costs of adverse drug reactions.
- Models are not transparent about what is included.
- One way of presenting is QALYS and another is cost per event prevented – there are other and more useful ways of presenting cost-effectiveness information.
- Budget impact is also important in addition to cost per QALY.
- The level of risk also comes into the equation.
- No one completes the loop and carries out longer term follow-up to find out if the analysis turned out to be correct.
- A clearer breakdown is needed in health economic analysis about which budget will be experiencing the savings and which not.
- They should be closer to the real world – for example, taking into account implementation problems such as the implications of spending and the increase in demand when technologies are approved.

It was suggested that health economics analysis could be improved by making it more sensitive to the questions that health providers needed answers to and by making clearer the assumptions that went into models.

NICE is too distant from NHS providers

Participants thought that NICE was not making decisions about interventions that were of most importance to healthcare providers. The decisions they faced were to do with mental health, coronary heart disease and sexual health, yet NICE mainly tackled cancer treatments and other expensive drugs. In this respect, NICE was compared unfavourably with the Scottish Intercollegiate Guidelines Network (SIGN), which dealt with everyday ordinary interventions.

The setting up of intermediary organisations between NICE and local healthcare providers was suggested as a way of overcoming some of the problems caused by this distance.

Summary

The review of pro formas used by local decision-making bodies, the case studies of local decision-making committees and the workshops with local decision-makers show that local decision-making focuses primarily on evidence of clinical benefit and the cost implications of introduction. Issues frequently considered were the size of the clinical problem and the scale of the potential investment. A relatively small number of committees routinely ask for evidence about cost-effectiveness, and case study research suggests that even those requesting this information are not necessarily receiving it with any regularity. Main sources of written health economic information are the manufacturers of technologies under consideration, and guidance produced by NICE, with only limited access to other sources of economic evaluation. Data from the case studies support the idea that these local committees are not duplicating the decisions taken at a national level by NICE but rather are concerned with those technologies not covered by NICE determinations, and with issues of implementation arising from NICE guidance and guidelines.

Barriers to better use of health economics include limited resources and capacity to generate or locate evaluations in time to inform decisions, problems relating to the inability to realise savings identified in analyses, concerns about biases due to the source of the analysis, the robustness of analyses or appropriateness of the comparators used. These problems arose within a general context of a lack of incentives to use economic analysis and a lack of skills and understanding.

Ways of overcoming the barriers suggested were the need for a clear, standardised and generally accepted format for the presentation of economic analysis, including greater clarification about the assumptions that went into models. In addition, health economics analysis could be improved by making it more sensitive to the questions for which health providers need answers. A national resource centre and archive of health economics tools and models that could be used was proposed together with information about the benefits of

using these tools. Training for committee members and the co-opting on to the committee of health economics expertise in cases where this was required were also suggested. The lack of incentives for use of economic evaluation is partly an issue of the **remit** of committees. Without some clarity and standardisation as to specific functions – especially in relation to finance and budgets – of decision-making committees, it is difficult to prescribe a strategy for optimal usage of economic evaluation.

Chapter 5

Results from the NICE case study

Introduction

One of NICE's core functions is to appraise new and existing health technologies and to produce guidance on new and established medicines and treatments. This is performed via the Institute's appraisal process. The key decision-making element of this process is carried out by the Appraisal Committee, which consists of experts appointed by NICE. For each technology appraised, NICE receives an independent assessment of evidence, which includes an economic evaluation. The committee also takes submissions from interested parties ranging from the sponsor of the technology to patient representative and expert bodies (www.nice.org.uk).

The Appraisal Committee meets to discuss the evidence and listen to further testimony from clinical and patient representatives before producing a provisional determination [the Appraisal Consultation Document (ACD)] as to the technology's clinical and cost-effectiveness. This is made publicly available for consultation and typically forms the basis of the committee's Final Appraisal Determination (FAD). At its most definitive, this guidance will either recommend the routine use of the technology in all appropriate clinical situations, or recommend the NHS not adopt the technology. Alternatively, guidance will recommend restricted use, for example, in certain patient categories only or as part of ongoing research.

Interviews with the Appraisal Programme Director (PD) at NICE and other members of the appraisal team were used to obtain information on the process.

On the issue of selection of people to serve as members of the Appraisal Committee:

"The selection of the members initially was determined by discussion between us at NICE about the kinds of background for individuals we would want ... as well as taking advice from professional societies, the colleges and so on. We came up with a list of individual names, and selected them from that list as opposed to the present process which of course requires advertisement and CVs and so on."

(Chair)

On the selection of topics that are considered by NICE:

"That is done via the Department of Health. They essentially send us what we term the 'remit' for the appraisals ... so NICE doesn't actually select the technologies themselves, that's outside of our remit."

(NICE PD)

Once topics have been selected, two members of the Committee are appointed as the 'lead team' and have responsibility for verbally presenting the evidence and analyses from the appraisal reports to the rest of the committee.

"... we have one member of the lead team who concentrates on the economic issues and another one who concentrates on either the clinical or the clinical effectiveness issues and then both of them concentrate on those other issues that impinge on both the information and the decision that needs to be made ... The lead team will receive absolutely everything The rest of the committee will receive the assessment report, the summaries of manufacturers' submissions and the professional and patient submissions. They don't automatically receive the full copy of the manufacturers' submissions but these are available on request."

(NICE PD)

Another committee member described the process of preparing the ACD and FAD as follows:

"The ACD is part drafted before the meeting. It's a twenty-page document that's derived from the factual material. The thing that has to be added is the final decision. Then immediately after the committee meeting there is a period of two or three days when the ACD is re-written, by the chairman and by the technical leads (i.e. the secretariat). Much more happens because the decision is not as it were written off until after (a) the ACD, (b) the email discussion on the draft ACD, (c) the submissions of all the complainants about what the ACD said, (d) the FAD meeting and (e) the discussion by email around the FAD meeting. The FAD meeting itself is a complex procedure which could have another iteration with TAR [Technology Assessment Review] teams and further calculations being made and then finally of course the appeal."

(NICE 1)

The seven technology appraisal topics

The seven technologies selected for consideration are listed in *Table 6*, along with the dates of the first and second Appraisal Committee meetings. Appendix 5 provides a summary of economic analyses for each of the NICE appraisal topics studied.

Capecitabine and tegafur with uracil for colorectal cancer

NICE guidance stated that “Oral therapy with either capecitabine or tegafur with uracil (in combination with folinic acid) is recommended as an option for the first-line treatment of metastatic colorectal cancer”. Overall, it seems that the guidance reflected a number of factors which emerged in both the observations and interviews with the committee. These included the weakness in clinical and quality of life data and, therefore, the difficulty in separating the treatment alternatives on cost-effectiveness grounds. The economic analysis performed was generally understood and accepted as valid by the committee and as such this appraisal was seen as unusually straightforward. Although interviewees emphasised the importance of establishing the cost-effectiveness of any recommended technology, it was felt that in this case the economic analysis generated few areas of particular concern or debate and, therefore, committee discussion focused, to a greater extent than is usual, on issues of patient preference and choice.

Capecitabine for breast cancer

Following the second appraisal meeting, NICE issued its FAD, which contained the following guidance:

“In the treatment of locally advanced or metastatic breast cancer, capecitabine in combination with docetaxel is recommended in preference to single-agent docetaxel in people for whom anthracycline-containing regimens are unsuitable or have failed.”

As with the prior appraisal of treatments for colorectal cancer, this appraisal guidance relies heavily on patients and clinicians to exercise choice as to the appropriate treatment – albeit within constraints. Key issues arising from this appraisal appeared to echo the previous appraisal: limits to the clinical evidence base, a non-controversial cost-effectiveness profile for the new technologies, and a recourse to patient preference in the absence of evidence of superiority between the new technologies.

Olanzapine and valproate semisodium for the manic phase of bipolar I disorder

NICE’s final guidance stated that:

“Olanzapine and valproate semisodium, within their licensed indications, are recommended as options for control of the acute symptoms associated with the manic phase of bipolar I disorder.”

This appraisal had a number of features that echoed the previously observed decisions – limited data leading to an inconclusive cost-effectiveness

TABLE 6 The seven selected technology appraisals

Technology	Date of first Appraisal Committee meeting	Date of second Appraisal Committee meeting
Capecitabine and tegafur with uracil for colorectal cancer	13.11.02	11.02.03
Capecitabine for breast cancer	13.11.02	11.02.03
Olanzapine and valproate semisodium for the manic phase of bipolar I disorder	25.02.03	29.05.03
Fluid-filled thermal balloon and microwave endometrial ablation techniques for heavy menstrual bleeding	12.03.03	15.05.03
Rituximab in the treatment of aggressive non-Hodgkinson’s lymphoma	24.04.03	01.07.03
Imatinib for chromosome-positive chronic myeloid leukaemia (CML)	15.05.03	10.07.03
Myocardial perfusion scintigraphy for the diagnosis and management of angina and myocardial infarction	01.07.03	27.08.03

analysis and ultimately to an inability to make differential recommendations for the alternative new drugs under review. The scope of the appraisal was felt, in retrospect, to be too narrow in terms of time-frame considered.

Fluid-filled thermal balloon and microwave endometrial ablation techniques for heavy menstrual bleeding

NICE guidance stated that:

“Fluid-filled thermal balloon endometrial ablation and microwave endometrial ablation are recommended as treatment options for women with heavy menstrual bleeding in cases where it has been decided (by the woman and the clinician responsible for her treatment) that surgical intervention is the appropriate next step in management of the condition.”

This appraisal raised similar issues to those that preceded it. First, it involved some discussion as to whether the appraisal scope had included all of the potentially relevant comparator technologies. Second, the cost-effectiveness analysis again did not permit a ranking of the new technologies, leading the committee to promote the importance of patient choice, and dialogue between patient and clinician in the selection of appropriate treatment options. This was the first appraisal that saw significant disagreement between those who felt the committee should take more account of the results of the cost-effectiveness analysis, which in this case indicated the dominance of hysterectomy over other treatment options, and those on the committee who felt other factors were more important.

Rituximab in the treatment of aggressive non-Hodgkin's lymphoma

The guidance document produced by NICE following the committee's deliberations concluded:

“Rituximab is recommended for use in combination with a regimen of cyclophosphamide, doxorubicin, vincristine and prednisolone (CHOP) for the first-line treatment of people with CD20-positive diffuse large-B-cell lymphoma at clinical stage II, III or IV (see section 2.3). Rituximab is not recommended for use when CHOP is contraindicated.”

Despite some concerns over data shortages, there was widespread agreement within the committee that the technology was both clinically effective and cost-effective in first-line treatment. The level of accord between the economic analyses of the manufacturers and the academic review team was seen as an unusual feature of the appraisal.

The issue of precedent arose with the committee made explicitly aware of the constraints of previous decisions taken in relation to this technology.

Imatinib for chromosome-positive chronic myeloid leukaemia (CML)

Following the second appraisal meeting, NICE issued the following guidance:

“Imatinib is recommended as first-line treatment for people with Philadelphia-chromosome-positive chronic myeloid leukaemia (CML) in the chronic phase.”

This appraisal raised a number of interesting issues. First, it highlighted differences within the committee in attitudes towards the economic evaluations they receive. Despite the importance of the cost-effectiveness information, there were clearly a range of other factors that predisposed sections of the committee to a positive recommendation of this drug. These included:

- the views of the clinical community in defining ‘appropriate’ current clinical practice
- the nature and perceived severity of the condition
- innovation and the orphan status of the technology
- the committee's prior familiarity with Imatinib and its benefits through other appraisals of this drug.

Myocardial perfusion scintigraphy for the diagnosis and management of angina and myocardial infarction

The guidance document published by NICE for this technology was drafted as follows:

“MPS using SPECT is recommended for the diagnosis of suspected coronary artery disease (CAD) in the following circumstances.

- As the initial diagnostic tool for people with suspected CAD for whom stress electrocardiography poses particular problems of poor sensitivity or difficulties in interpretation, including women, patients with cardiac conduction defects (for example, left bundle branch block), and people with diabetes, and for people for whom treadmill exercise is difficult or impossible.
- As part of an investigational strategy for the diagnosis of suspected CAD in people with lower likelihood of CAD and of future cardiac events. The likelihood of CAD will be based on the assessment of a number of risk factors including age, gender, ethnic group, family history, associated comorbidities, clinical presentation, physical examination, and results from other investigations

(for example, blood cholesterol levels or resting electrocardiogram).”

Overall, this was the third of the seven appraisals where there was significant disagreement between committee members regarding the implications of the economic information made available to them. As with the previous appraisal, the dispute appeared to derive from the extent to which other factors could be seen as legitimate modifiers of a strict or ‘purist’ health economics approach. In this case, these other factors appeared to be:

- current clinical practice and the need for guidance not to go directly counter to this
- capacity issues and the implementation of guidance.

Summary across the seven technologies

The case study involved a sample of seven technology appraisals. There are a number of recurring themes that can be highlighted.

Several appraisals considered a number of new technologies that often had results (from the economic analyses) that were broadly similar. Clearly, this posed difficulties for the committee in seeking to recommend one new technology over another on cost-effectiveness grounds. In addition, frustration was repeatedly expressed by committee members at not being able to prioritise between new technologies due to data shortages, particularly in the areas of clinical and quality of life data. However, four of the seven technology appraisals studied appeared to have a broadly non-controversial economic analysis, and as a result the details of the cost-effectiveness analyses were not discussed extensively. When both sponsor and independent economic assessments found similar results, the decision was considered to be considerably easier and more straightforward.

A number of the appraisals were hampered by concerns regarding the scope of the decision. In some cases, the view was expressed that a highly appropriate comparator had been excluded from consideration. In another case, it was felt that the analyses received had adopted too short a time-frame in which to measure the full benefits of treatment options.

Three appraisals saw significant disagreement among committee members. In each case this revolved around the economic evaluation. Each

time this involved the cost-effectiveness analysis favouring the use of a treatment option that was seen as undesirable by some committee members. Subsequent disputes focused on the issue of how to reconcile the ‘economic paradigm’ advocated by NICE and the desire of those on the committee to reject as unhelpful the implications of the commissioned economic evaluation. One resolution to these disagreements was for guidance not to be explicitly supported with reference to cost-effectiveness analysis. This occurred predominantly when the results of the economic evaluation challenged current clinical practice. Other factors that appeared to influence the committee – although not to the same extent – ranged from the severity of the disease, the importance of promoting innovation, patient preferences and implementation issues. The net effect of these other factors tended to be to incline the committee towards a positive recommendation.

A number of other interesting themes recurred throughout the case study. For instance, it appeared that the committee were to some extent bound by decisions taken in previous appraisals and also practices considered legitimate in other appraisals such as the use of indirect comparisons. Also, final published guidance regularly recommended funding of the technology but restricted access to certain patient subgroups.

Data from NICE interviews

The following sections present results from interviews with the committee. The focus is on general themes, in contrast to the topic-specific issues presented hitherto. Interviewee responses are compared with data drawn from observation of committee meetings where relevant.

Cost-effectiveness analysis as a key driver

The research confirms that economic analysis is highly integrated into NICE’s technology appraisal process. This is indicated by the stated remit of NICE to consider cost-effectiveness, the nature of the assessment reports commissioned specifically for NICE and the composition of the Appraisal Committee. The committee is in the highly unusual situation of having, for every technology they consider, an independent economic analysis undertaken specifically for their purposes, in addition to having senior and experienced health economists as permanent committee members. This helps to address

potential difficulties relating to access to appropriate and relevant cost-effectiveness studies, and to interpretation of complex analyses. Obtaining a study within the required time-frame, for example, presents less of a challenge to NICE than is the case for most, more local, decision-making bodies in the NHS.

These resources enable NICE to access and process studies to a perhaps unprecedented extent. The committee is not required to consider in detail implementation issues relating to their decisions, enabling them to concentrate on the results of the review and economic evaluation. This tightly defined remit also distinguishes NICE from other bodies making technology coverage decisions.

Some interviewees suggested that although it was the case that the decisions were highly influenced by the cost-effectiveness analysis, this had evolved over the lifetime of the committee. For example:

“People have come to accept that the economic evaluation is more crucial than they thought. I think a lot of them came along with the idea that ... you had to listen to the economist say something ... they’ve moved to saying ‘God this is all complicated, just tell us what the ICER is!’ because they’ve actually realised that it is a crucial issue.”

(NICE 26)

Our data, drawn from both the observation and the interviews with committee members, add considerable support to the overall impression of economic evaluation being central to the final determinations reached.

“I’m conscious that what NICE is concerned about is cost-effectiveness because it is about deciding whether or not medication should be reimbursed, or universally available on the NHS.”

(NICE 19)

“I think economic evaluation was regarded as being important from day one.”

(NICE 21)

“It [the economic evaluation] seems to me to be the clincher really. If it’s too high then it’s not going to get funded.”

(NICE 30)

One of the main positives indicated by many respondents in relation to the cost-effectiveness analysis was that it helped the committee members to manage the complexity in the decision problem. Thus, the economics facilitated the process of moving from receipt and consideration

of the broad range of evidence on the technology in question to arriving at a decision on coverage. This is not to say that the committee members were only interested in the ICER and did not want to consider the underlying model and assumptions. In fact, our observations demonstrate that in some instances the economic analysis and modelling work were used as a means of structuring the discussion – this was particularly the case for the myocardial perfusion scintigraphy topic – and in others, much of the debate centred on issues relating to, or highlighted by, consideration of the economic analysis and/or its implications – examples of this include the endometrial ablation techniques topic and the manic phase of bipolar I disorder topic.

Understanding of cost-effectiveness analyses and roles of the committee members

Concerns were expressed relating to the complexity of the economic analysis presented and many interviewees indicated that they spent considerable amounts of time seeking to digest the analysis and its results. The view was also put forward that virtually all committee members do consider and take account of the economic analysis, although not everyone will focus primarily on that aspect of the assessment report. A number of interviewees indicated that they were concerned both by their own personal lack of understanding of the economic analyses and the level of understanding by others on the committee. In some instances this was expressed in stark terms and implied that some parts of the assessment report were not read by some committee members. Asked to reflect on both their own and others’ level of understanding of the analyses they receive, interviewee responses ranged from those who considered the committee to be sufficiently and impressively conversant, to those who expressed concern at what they considered low levels of appreciation amongst some on the committee. Health economists were amongst both groups.

“The rest of the committee members who haven’t had formal training in economics, because its such an important part of the discussion, have now, to my view, got a very, very good feel and understanding for what’s important in an economic evaluation.”

(NICE PD)

“I think there’s an incredibly high level of understanding of health economics. Of any group of non-economists that I’ve ever sat with, that’s the highest level.”

(NICE 20)

“I think it’s fair to claim that everyone on the committee has a basic understanding of QALYs, costs per QALYs, thresholds if you like and the cost-effectiveness acceptability curve and the ICER and so on.”

(NICE 25)

“Some of the people round the table I would think ... are probably not all that clear as to how it is done ... and some people do keep very quiet when the health economics is being talked about and that’s very noticeable.”

(NICE 17)

“I think my knowledge is poor and I know quite a number of other people on the committee feel theirs is poor as well, so I think the people representing nursing, general practice and even quite a number of the medics would feel their understanding is poor.”

(NICE 2)

This range of opinion was expressed despite a broad consensus that the non-economist committee members had increased in their understanding during the committee’s lifetime. The observation of the committee meetings reinforced the general impression of limited understanding of the economic analysis for some members of the committee. For example, the meeting to consider olanzapine and valproate semisodium for the manic phase of bipolar I disorder was presented with analysis results in the form of a CEAC. There was very little discussion of this aspect of the report and what discussion there was centred on seeking clarification on how to interpret it rather than making use of it to guide the decision.

The extent to which variability of understanding of cost-effectiveness analysis is a serious barrier depends on the role that committee members are expected to play and the overall approach to decision-making being adopted. Therefore, the issue of members’ roles was explored. All interviewees indicated that the committee members were selected as bearers of particular expertise and/or experience deemed relevant to the decision-making process. Within this there appear to be two identifiable roles which inform the selection of the committee members: the ‘technical expert’ and the ‘advocate’ or ‘representative’. Experts were seen as applying their particular skills and knowledge, for example, in clinical medicine, statistics and nursing. Representatives, in a less clearly defined role, were expected to consider the implications for particular constituencies (most obviously, patients).

The breadth of experience and skills was seen by some interviewees as a strength of the committee

as it enabled a range of perspectives to be brought to bear on appraisals and for different aspects of a decision scenario to be considered fully. Within this conception, aspects of the decision process and/or the evidence base informing it are discrete and correspond to specific individual areas of expertise.

“The health economists ... are more keen on that side of the information than perhaps other committee members ... We have people who are more concerned with the financial impact, there will be clinicians who will be wrapped up in the evidence itself, GPs wrapped up in the practicalities of implementation and follow-up. So there’s actually a very good mix around the table.”

(NICE 3)

“I always focus on the clinical effectiveness side of it first because that is more my area of expertise. I believe that’s why I’m on the committee – to represent patients and healthcare in that capacity.”

(NICE 13)

“I’m a pharmacist and so I guess I’m there to pick up details around medicines administration and I also work in both secondary and primary care so I tend to pick up issues about prescribing across the interface.”

(NICE 3)

This model for processing information allows for health economists to be responsible for the critical interpretation of the health economics and the other Committee members to defer to them in this area.

“I don’t think it would be possible to bring the health economic evidence into that decision-making if you didn’t have health economists there to interpret it and they have played an incredibly important part in helping the rest of the committee to deal with it in layman’s terms ... Eventually, the argument is dominated by those people who obviously have a very high knowledge of the health economics.”

(NICE 10)

This approach to processing the cost-effectiveness analysis was challenged by a minority of interviewees. The first objection derived from the assumed obligation of a policy-making committee to act in full knowledge of the evidence. One committee member suggested that all members require an understanding of the decision model if they are adequately to carry out their role.

“I do think this is not the way a public decision body should operate in the sense that you have people proudly almost saying ‘Oh well I’m not a health economist’. It seems to me that if you’re in this

position you jolly well ought to be pretty competent in these things that we're talking about."

(NICE 26)

There is some support for this stance to be drawn from NICE's stated approach to reaching a determination which involves reaching a consensus within the committee and taking a vote where a consensus is not achieved. The implication is that, in theory, all members of the committee have an equal say in determining the outcome of the appraisal process – that is, they are acting not just as expert advisors or advocates but as decision-makers who are entrusted to make national policy for the NHS. Hence, in order to fulfil this decision-maker role, all committee members are required to understand in full the nature of the decision problem, the results of the alternative analyses and the key evidence that is driving the results; in short, they are obliged to understand the economic analysis.

A commonly expressed concern relating to poor levels of understanding of the cost-effectiveness analysis was that too much faith might be placed in it. This reflected a weakness, mentioned by many of the interviewees, of poor-quality data commonly being available for the economic analysis. There was a frequently expressed view that economic analyses tended not to reflect fully the uncertainties inherent, given the poor-quality data being used in the analysis. Particularly in the context of model-based analyses, the importance of ensuring that the committee members understand the limitations of the analysis was highlighted. The suggestion is that the results of model-based analyses are not interpreted with due caution. The potential for misleading results when inappropriate structural assumptions are made in modelling exercises was also indicated as a serious problem.

"What worries me most about the whole process is all the assumptions that get built into the economic model. I think there's a real danger that the economic analysis gets taken as fact, and it is not fact. There are so many assumptions and judgements made that I think that makes it very difficult."

(NICE 2)

"The structural issues I think are more devastating because if the structure is wrong then it doesn't matter what you put in, it's going to be nonsense."

(NICE 12)

"Sometimes the quality of the data isn't all that it should be. But that's just a consequence of the fact that sometimes the sort of trials that needed to be done have not been done so there are gaping holes

and things that are incomplete. And that therefore requires the statisticians and the health economists to model things and having to make quite a few assumptions."

(NICE 29)

The call from committee members was for those conducting clinical trials to be more aware of, and concerned with, the needs of those conducting economic analyses in order to avoid, where possible, the need for model-based analyses to rely on too many assumptions and/or poor-quality data. Interpretation of the economic analyses was thought by a small number of interviewees to be further hindered by the general lack of consistency in the methods employed by different assessment teams. One interviewee highlighted the need for greater consistency, and called for the NICE Appraisal Committee to spend some of its time discussing, and coming to agreement on, principles concerning the methodology to be used.

"Every time we get the assessment, at the end we could look at some sort of sensitivity and major determinants and the variation around the cost per QALY, in exactly the same format every time, because we'd learn to use it better."

(NICE 23)

"There should be a very standard way of doing something so that it will be feasible and justifiable to expect every member of the committee to understand what's happening in the presentation. At the moment it varies from case to case: what we get, how it's presented, etc."

(NICE 26)

These difficulties were reflected in a series of interviewee suggestions for improvement, including greater levels of training for new and existing committee members. There was also a call for presentational improvements. The sensitivity analysis was highlighted in particular as a very useful aspect of the analysis but which needs to be made more accessible. The use of summaries was promoted but the call more generally was for overviews that do more than simply repeat what is in the report but are designed to be user-friendly and address the specific questions that committee members are likely to have. Graphical representations of the model were thought to be particularly helpful, where possible.

Ordinal approaches to the consideration of evidence

The precise nature and extent of the committee's adoption of a strict health economics approach is an area that requires further consideration. Within the range of interview responses, there were two

rather different but recurring conceptions of how the economic analysis was used as part of the decision-making process; each is now discussed in turn.

Many of the interviewees espoused the view that there was a strong ordinal approach to the way the evidence and analyses were considered: first, the clinical evidence and then the economic analysis. Data drawn from observation of committee deliberations supported this view, with the clinical 'hurdle' relating to both expert opinion and evidence. That is, the first hurdle for the technology in question was that of clinical value and effectiveness – does it fit sensibly into clinical practice and deliver improvements in health (or some other measure of clinical effect)? Thus, a concern with cost-effectiveness was considered not to be appropriate unless the issues of clinical value and effectiveness had been demonstrated. This was most common among committee members with a clinical background.

“My first consideration when I look at this is ‘does this treatment actually work?’ Obviously it has to appear to be clinically effective and to be shown to be clinically effective. Once you’ve decided that something is effective or it isn’t effective, the decision on whether to recommend is an economic one.”

(NICE 10)

“If it doesn’t get through the clinical effectiveness hurdle then I’m not that interested in the economics.”

(NICE 22)

For some interviewees, this ordinal approach reflected their own weighting of the relative importance of the clinical factors and the technology’s effectiveness over the cost-effectiveness evidence, with the latter seen as important but a secondary consideration. This was seen in observation of three of the seven technology appraisals where there were challenges to the cost-effectiveness analyses because of the perceived clinical sense of the implied recommendation. An example of this is the appraisal of imatinib for chromosome-positive CML. In this case, the economic analysis suggested favourable results for a treatment option that was seen as clinically less desirable by some Committee members and/or expert clinical advisors.²⁴ Although imatinib was shown to be cost-effective when compared with interferon- α , it was markedly less so when compared with hydroxyurea (HU). This led some committee members to question the grounds for an appraisal determination recommending routine use of

imatinib. Responses from those in favour of recommending imatinib fell into two broad camps: (1) those arguing that interferon- α is superior to HU on the basis that it is currently the preferred option of clinicians working in this area; and (2) those who suggested that HU is not an appropriate comparator in this appraisal because, unlike both imatinib and interferon- α , it does not act on the progression of the disease and, therefore, does not extend life. For such appraisal topics that we observed, subsequent committee discussion tended then to focus on how to reconcile the ‘value for money’ remit of NICE with the desire of some of those on the committee to reject as unhelpful the findings of the commissioned economic evaluation. One solution to this problem was for the guidance documents (i.e. the ACD and the FAD) not to base their conclusions explicitly on the cost-effectiveness analysis. For example, in the appraisal of endometrial ablation techniques for heavy menstrual bleeding, despite cost-effectiveness analyses suggesting hysterectomy as the most cost-effective option, the guidance did not recommend this treatment option. In effect, the understanding and perception of the technology’s clinical value by committee members over-rode the results and conclusions from the cost-effectiveness analysis.

For some interviewees, the conflict was less apparent and they tended to emphasise the inter-relatedness of the two ‘hurdles’, acknowledging that clinically effective technologies often tended also to be cost-effective and so the use of two separate hurdles was sometimes of little consequence. One of the health economist interviewees agreed that this ordinal approach to decision-making was commonly the approach adopted by the committee, but argued that this was potentially problematic in that the ordinal approach prevents a technology being deemed ‘cost-effective’ unless there is evidence of an improvement in clinical effectiveness. Therefore, for example, a new drug that brings about large cost savings (e.g. through avoiding repeated hospital admissions for many patients), but is thought to be associated with a very small reduction in effectiveness will not be supported even though it is likely to have an ICER well below the relevant threshold.

“I don’t believe effectiveness should be a criterion for NICE decisions. Now that’s a fundamental conceptual problem with NICE that they require clinical effectiveness before we go on to examine cost-effectiveness.”

(NICE 26)

Economics as the framework for decision-making

The second conception relating to the use of economic analysis by the committee, repeated by a number of respondents, was that it provided the analytical framework within which the key appraisal issues were considered and discussed. That is, the value of the economic evaluation was not limited solely to the fact that it provided an overall result (e.g. in terms of ICERs or CEACs), but that it allowed the discussion to be structured and focused towards the most important aspects of the evidence, be they epidemiological, clinical or cost-related. This perspective on the role and use of economic analysis tended to be expressed by non-clinical committee members, especially those with a background, or some training, in health economics.

“I go straight to that [the economic analysis]. In fact when I read the report I go to the ICER in the summary first and then read backwards and forwards until I get to see how it was derived.”

(NICE 1)

“[The economic analysis] is, if you like, the starting point, the bottom line from which you then say ‘Yeah so that’s it but what else do we need to think of?’ The sensitivity analysis, the patient preference and those other issues.”

(NICE 25)

“The reason why it [*the economic evaluation*] is important is not simply because all we talk about is cost per QALY or the only thing we look at is the economic model. It’s the fact that it provides us with a framework to identify what we should be concerned about and where we should be pushing the argument in terms of, for example, interpretation of the clinical evidence it focuses the discussion on what actually matters: ‘what is it that can actually switch a decision on this?’”

(NICE 12)

A related issue raised by several interviewees was a concern with the uncertainties inherent in the economic analysis – what level of confidence could or should the committee place in the economic analysis results? In the context of discussing this issue, many interviewees highlighted the value they attached to extensive sensitivity analyses being included as part of the economic analysis.

Some of those interviewees who saw the cost-effectiveness analysis as providing a framework for considering the evidence also indicated that in theory the analysis might be developed iteratively to help clarify the decision problem at hand. Frustrations with the appraisal process were

expressed in terms of the scope of the policy question sometimes being addressed. There was a repeated concern that the definition of the policy question, and the development of the appraisal scope, were not given sufficient time or resource and often led to problems in the committee meetings themselves. For example, in the appraisal of olanzapine and valproate semisodium for the manic phase of bipolar I disorder, some members of the committee felt that hospitalisation rates should be a key driver of the cost-effectiveness analysis, but this was not allowed for in the analysis since, as a consequence of the relatively short 3-week time horizon, hospitalisation was assumed to be the same for all drugs being compared. The suggestion was made that an opportunity to clarify and identify clearly the relevant policy question should more formally be part of the appraisal process. Building on this suggestion, some interviewees proposed a ‘two-stage’ process that could address difficulties in identifying appropriate appraisal questions:

“For a long time I’ve been arguing for a two-stage process where you actually do some work which is targeted primarily at framing the right question then you do the rest of the work. It’s almost like we’ve got to have a mini-appraisal half-way through to tease these things [*the relevant policy question*] out and then go back into the modelling. Ideally they would devote a lot more resources to the assessment. That would actually build in some sort of modelling and then a period of reflection and then further modelling.”

(NICE 21)

This conception of the place of cost-effectiveness analysis differs markedly from the ordinal approach. It assumes that the principal role for cost-effectiveness analysis in technology coverage decision-making is to provide a framework by which the committee discussions and deliberations are structured. This was recognised with concern by some committee members who felt that discussions were often framed and dominated by those with a strong background in, and understanding of, economics.

“It can feel sometimes like the cost-effectiveness does tend to dominate – maybe because I haven’t been able to voice my concerns within that arena. The whole tenor of the reviews and the lead presenters’ reports and everything is about the economics, so you don’t have much scope to dissent in that sense.”

(NICE 14)

“The risk is that we are at the mercy of what is said by people in an expert position in the room.”

(NICE 8)

Cost-effectiveness analysis concepts

The acceptability of cost-effectiveness analysis concepts was also explored through observation and interviews. The two principal factors that were observed or discussed directly by the committee were the QALY and equity. Each of these is discussed below.

QALYs

A particular issue brought up by many interviewees was the great benefit for a decision-making body such as NICE of a single measure of benefit such as the QALY, in allowing comparison of very many disparate health interventions and in providing a benchmark for later decisions. It was also felt that the concept was broadly familiar to those in the NHS and in other stakeholder organisations. However, the value of QALYs was tempered by concerns.

“The use of QALYs does seem to mean that at least there’s a currency that people are familiar with, generally. The key stakeholders, whether they be clinicians, economists, drug companies or manufacturers, all seem to have a certain familiarity and ability to understand and work with QALYs.”
(Health Service Manager – HM15)
(NICE 15)

“This is where I think the qualms about QALYs come in and the incommensurability of alleviating different kinds of woe. You’re comparing hip replacements with postponement of death and cancer and so on, which you can’t of course.”
(NICE 19)

“I think they’re grossly flawed in hundreds of different ways but they’re the best we’ve got and what they allow us to do is to make a comparison.”
(NICE 9)

A theme relating to the limitations of QALYs, identified by several interviewees, was the concern that they fail to capture some important aspects of benefit. Using the example of patients with motor neurone disease, one committee member explored the weaknesses of QALYs in terms of their failure to incorporate issues of disease irreversibility.

“When it comes to something like motor neurone disease our measures of health outcome don’t capture everything of concern to us. For example, with motor neurone disease there is an issue of irreversibility, and if we could incorporate the value of the option of keeping somebody in a better state for a little bit longer with this disease then we’d be attaching greater weight to their health outcome without citing equity concerns.”
(NICE 12)

Using the same clinical example, the same interviewee moved on to consider the limitations of QALYs in assessing benefits in the situation of very severe conditions.

“The additivity assumption underlying QALYs may be really important when people are looking forward over that really quite dire prospect of health outcome that having a few weeks or a few months of better quality of life during that period might be valued much more highly than just assigning a QALY weight in the same way as you would do in any other profile.”
(NICE 12)

Similarly, another interviewee used the example of multiple sclerosis (MS) to consider the adequacy of the QALY measure.

“MS is a very good example ... the drug was supposed to limit the rate of relapse. And what patients would tell you is, ‘it’s not the fact that I only had one relapse in the last two years, it’s the fact that I came to believe it and I had the confidence to go out and go on holiday for a week because I wasn’t scared of relapsing’. You try building that into a QALY!”
(NICE 23)

Our observation of the endometrial ablation topic meetings also highlighted this point. The issue of the comprehensiveness of the assessment of benefits, measured using QALYs, was raised in discussion. It was suggested that there are some aspects of benefit for the second-generation ablation technologies that were not fully captured in the economic analysis. The particular issue highlighted was the convenience aspect associated with their delivery in outpatient settings.

A general theme of interviewee comments appears to be that the patient experience is not captured fully or adequately in the QALY measure.

“The huge gaps are in the utility measurements – they [*data on patient experience*] are just never there. And the measurements that are being used for utility historically, and so far without exception, have nothing to do with patient experience.”
(NICE 8)

“It’s very easy for a group of people to sit around and assess life states and what they’re worth when they’re theoretical and they’re not the people who are ill.”
(NICE 23)

Once again, the observation data support this finding. The observation of discussions on the analysis undertaken for the manic phase of bipolar I disorder topic revealed that QALYs would be inadequate as a measure in this condition. Thus,

the committee were supportive of the decision by the analysts not to attempt to estimate QALYs.

Further on a negative note, the highly aggregated approach of the QALY was not the preference of some committee members. The presentation of information and/or results of analyses in a disaggregated manner, using something akin to a cost–consequence format, was seen as appropriate. However, this was seen as an addition rather than as an alternative to a cost per QALY analysis.

“I think sometimes it doesn’t need to be simplified down to the QALYs. I think if you gave people a sort of list and said ... ‘this drug will cause you to have so much diarrhoea and vomiting for so long’ and just give a list of the good and the bad points of the drug and then the cost, ‘are you willing to take this on?’ I think the committee themselves too could perhaps look at it in that way ... I mean the cost per QALY is a tremendous simplification of human life really – turning it all into one number at the end of the day is sometimes too simplistic, it seems to me.”

(NICE 17)

Equity concerns

On the issue of incorporating equity concerns in cost-effectiveness analyses, most of the interviewees who discussed this topic indicated that equity tends not to be formally considered by the committee for a variety of reasons. For example, one committee member indicated that he did not have a clear view on what the appropriate equity arguments are and, even if there was greater clarity on the nature of the arguments, there exists no agreement on how they might be included in the economic analysis. The observation data supported this general finding.

“I’m not convinced of what the legitimate equity issues are. So what it is that needs to be highlighted in the report in terms of equity I don’t exactly know. Even if we did know what it was it’s definitely not clear how those could be incorporated formally into the analysis.”

(NICE 12)

Support was given by another interviewee for the concern that robust methods for equity weighting are currently not available.

“I think there’s a sort of recognition at the moment, that we have no basis for doing the weighting.”

(NICE 28)

Inconsistency in the application of equity issues and variation in the circumstances in which equity arguments are evoked were concerns that were

also raised. One interviewee commented on this in the context of endometrial ablation for menorrhagia.

“People didn’t say ‘these are women who have a hard time, we should be giving them more’. Whereas when we’ve looked at particularly life-enhancing interventions, say in cancer treatment where people have a very low life expectancy, quite a few people around the panel say ‘well we should be giving these people more weight – they only have six months to live so an extra month or two is going to be more important to them’.”

(NICE 28)

On a similar note concerning inconsistency in the application of equity principles, the issue of interventions targeted at children being given favourable consideration was also mentioned by the same respondent.

“At the end of each of these discussions people say, ‘well we have no basis for doing this so let’s just treat a QALY as a QALY regardless’. But where that isn’t true I think is in relation to children. In relation to children, I think, although people don’t necessarily explicitly state it, I think everybody tends to give it more weight.”

(NICE 28)

Interviewees also made the point that the type of decision being made could influence the process. For example, if it was a life-threatening condition, then ethical considerations such as the ‘rule of rescue’ would come into the discussion:

“The fact that it is an important disease that causes death focuses the mind a little more than perhaps some other technologies we’ve looked at where there may be good randomised clinical trials but sometimes it’s difficult to judge the relative merits of the technology.”

(NICE 27)

The observation data relating to the topic rituximab in the treatment of aggressive non-Hodgkinson’s lymphoma provide some support for this in that the discussion highlighted the severity of the medical condition. One of the committee members again indicated that because this was potentially a very severe condition this helped to ‘focus the mind’.

Cost-effectiveness threshold

On the issue of the cost-effectiveness threshold, virtually all interviewees who spoke about this indicated that the committee did make use of some form of threshold, and also expressed some concerns around both its basis (especially where

the threshold in current use came from) and its use as a basis for decision-making. The line put forward by many interviewees on the threshold subject was that there was not a precise value to the threshold but that when the ICER exceeded £30,000 per QALY this began to signal that the technology was unlikely to be cost-effective.

“There is a feeling when we get beyond £30,000 per QALY we’re running into trouble.”
(NICE 19)

“Any threshold that has been derived is purely, if you like, case law rather than statute. The cost per QALY *per se* does not determine whether or not there is a ‘yes’ or ‘no’ guidance ... and so I think, therefore, clinical need, patient preference, the input from the professionals, do hold sway.”
(NICE 6)

“I do sometimes have reservations about the figure of £30,000 per QALY. Where does the figure come from? Who determines where the cut-off point should be? ... This magic figure of £30,000 keeps popping up but I lack the underlying knowledge to be able to challenge a figure like that.”
(NICE 13)

“If you get below that level [£30,000 per QALY], then usually we have a certain level of comfort.”
(NICE 27)

“Why do people think so bloody categorically as though a threshold was a yes/no thing? Very few thresholds are yes/no things. They are things which go from zero to one and along that line somewhere there are lots of other influences coming in to affect you.”
(NICE 18)

There was a suggestion that where the initial cost-effectiveness estimates are close to the threshold there tends to be further investigation of the data and the assumptions upon which the analysis is based.

“If it is closer to some unmentionable threshold then we might delve more into patient preference and so on.”
(NICE 25)

One of the interviewees made a strong call for the threshold to be more transparent.

“I find the £30,000 per QALY actually very frustrating simply because it’s what everybody uses as a benchmark. I think it is a key driver. Many people on the committee, certainly the people who’ve been there a long time and the more influential people on the committee, I think that’s what drives them, yet it’s not

supposed to exist and I just think it ought to be transparent.”
(NICE 2)

An important consequence of applying the threshold range around £30,000 per QALY was thought, by several interviewees, to be that further pressure was being placed on the NHS at a local level to remain within budget. This was thought to be accentuated by the policy change to make the implementation of NICE guidance mandatory; and so there were real opportunity costs being incurred, and also to be compounded by the fact that, by definition, the main impact of the judgement is experienced at the local level, and so is not seen clearly or fully by those making the decisions at NICE.

“My biggest criticism of the approach used at NICE, in the technology appraisals, is basically we are funding things at a level that actually the NHS cannot afford – that the [cost per] QALY figure is far too high, it should be much lower.”
(NICE 7)

“I think NICE is a worthwhile enterprise, in principle, but the thing that worries me most about it is the fact that advice is, well it’s not advice any more, it’s compulsory ... and it worries me because the opportunity cost notion that’s supposed to underlie economics doesn’t really bite at the NICE level.”
(NICE 4)

Summary of interview data

Data drawn from interviews, in combination with observed committee behaviour, suggest that cost-effectiveness analysis was at the heart of committee deliberations and a key driver of determinations reached. Many interviewees indicated that they found the economic evaluation to be a useful aid to decision-making. This usage of cost-effectiveness analysis was made possible by NICE’s capacity to commission its own economic evaluations and the level of health economics expertise within the committee itself.

The data also suggest that committee members were processing clinical and cost-effectiveness data in different ways and that perceived roles and levels of expertise in health economics varied significantly. A number of committee members criticised some of the techniques, concepts and presentation of economic evaluation. In particular, concerns were expressed about QALYs and the cost-effectiveness threshold. Alongside the clinical effectiveness and cost-effectiveness evidence, a number of other considerations influenced the committee.

Chapter 6

Discussion

Introduction

This research has looked at the way in which health economics information is used in decision-making in the NHS. It has described a number of examples at the local and national levels of the way policy decisions are made concerning the use of drugs and other medical technologies. In this chapter, we summarise the main findings of our research, discuss the barriers to the use of economic evaluation in health policy decision-making and consider how these barriers might be addressed. The strengths and weaknesses of our work are also considered.

Systematic review

The systematic review undertaken as part of our project indicates that the use of formal economic evaluations in health policy decisions concerning the coverage of medical technologies is an under-researched topic. The research data that exist reveal limited usage of economic evaluations in the UK and elsewhere. In terms of methods that might be used to research this issue, exploration using qualitative methods has been used very rarely.

Local-level decision-makers

Levels of use of economic analyses

Our main research finding at the local level in the NHS in England is that it is an exception for cost-effectiveness analysis to inform technology coverage decisions. Such information was being used in the Priorities Network, but even here a number of significant barriers existed. It seems that for cost-effectiveness analysis to become an important consideration in technology coverage at local levels a range of factors – some specific to health economics and others pertaining more generally to bodies making such decisions – need to be addressed. Clearly, there is substantial variation in practice at local levels. However, the review of NTRFs used by local decision-making bodies and the case studies of local decision-making committees show that local decision-making focuses primarily on evidence of clinical

benefit and the budgetary implications of introduction.

We have discussed elsewhere the importance of cost-effectiveness analysis being both accessible and acceptable to decision-makers if its use is to be increased.⁵⁶ Our data suggest that limited use of economic analyses can be traced back, amongst other things, to lack of capacity in three respects: generating cost-effectiveness analyses, accessing and reviewing cost-effectiveness analyses, and interpretation of such analyses. These issues of ‘accessibility’ consistently prevented the majority of local decision-making bodies researched from making full use of health economics information. With the partial exception of the Priorities Network, there was very little capacity to generate and/or access studies, and little formal expertise within the committees to make sense of those that were obtained. The main sources of information on cost-effectiveness were found to be the manufacturers of the product and NICE guidance as there are limited resources available at the local level to commission new locality-specific analyses. Although, in general, respondents from local decision-making environments were receptive to the notion of making greater use of health economics information, levels of understanding and expertise in the subject remained low.

In these respects, our findings are consistent with previous studies examining this issue. For example Walley and colleagues⁴⁶ found that clinical data were more important than cost-effectiveness information in informing decisions in primary care and the Euromet Project,⁴² which found that knowledge of methods of economic evaluation was poor. Previous studies have pointed to an apparent contradiction between the observation that health economic information is rated as being very important but is not used in practice. Drummond and Weatherly,¹⁹ for example, found that these forms of information were considered ‘highly relevant’ yet were not regularly used, and the Euromet Project⁴² and Duthie and colleagues³ found high levels of interest in principle but lack of use in practice. Our findings suggest that there are a number of reasons for this apparent contradiction. These include misunderstanding about what is meant by health economics analysis,

lack of knowledge of how to use the analysis, organisational constraints on use and mistrust of the sources of such analysis.

Issues of accessibility of economic analyses

There were two most commonly cited strategies for overcoming the accessibility barriers. The first of these was to develop a standardised analytical approach which is consistently applied to economic evaluations. This would also involve the use of a routine format for the presentation of results and recommendations. This was seen as potentially enhancing decision-makers' ability to understand and apply study findings. The second strategy cited by interviewees from each of the local case studies was for those involved in policy making to receive fuller and more formal training in health economics. For example, it was suggested in workshop discussions that health economics training should be a compulsory component in the standard medical curriculum. In addition, the case was made for short courses – designed in consultation with practitioners – to be available to current health professionals and managers. It was suggested that this could form part of a broader focus on decision-making techniques and could be provided jointly to the various agencies within a health economy. Mentorship by academic health economists could be provided for those wishing to go further in the subject. Supplementary national initiatives proposed included development of both an archive of health economics tools and models, and a national independent health technology information centre providing credible information on new interventions.

This problem for those working locally was seen to be caused partly by a paucity of high-quality cost-effectiveness studies and by a lack of resources locally that makes it not possible to commission cost-effectiveness studies to inform local decision-making. The database of economic evaluations (NHS Economic Evaluation Database), managed by the University of York Centre for Reviews and Dissemination, was not a resource that decision-makers locally made reference to – value might be derived from further publicising this resource.

Health system and organisational issues

Other aspects of cost-effectiveness analyses that were thought to be poor or missing related to implementation considerations and budget impact assessments. On the latter, the comment was made that cost-effectiveness studies are rarely linked to

budget impact analyses and where they are undertaken such assessments tend to be poor. It is clear from our work that, although there are important issues to be addressed in terms of improving both the accessibility and acceptability of cost-effectiveness studies for health decision-makers, the most fundamental challenges relate to the overall design of the health system and the structure of healthcare organisations – it is not just about tinkering at the margins to make cost-effectiveness studies easier to get hold of and easier to understand.

In terms of health system-level issues, the workshop discussions uncovered some frustration at the local level with perceived failures on the part of the Department of Health centrally to acknowledge the need for rationing in the NHS. A consequence is that the need to make use of cost-effectiveness studies, and the benefits that might be derived from using such analyses, are not well recognised by those working at a local level in healthcare organisations. In addition, even where there might be recognition of the value in using formal cost-effectiveness analyses, there tend to be considerable structural and organisational barriers, the most commonly cited being the inflexible and short-term nature of NHS financial accounting systems – the 'silo mentality' of the NHS was referred to. Hence there is little incentive to make use of cost-effectiveness information as the system modelled in the analysis does not have the constraints and limitations of the system facing the decision-maker in reality. It was felt that for the use of economic evaluation to improve there was a requirement on national government to promote and profile the importance of cost-effectiveness analyses as a means of challenging existing practice.

A further factor which impinges on the use of economic analysis is the committee's overall approach to decision-making and whether or not this follows an agreed and formal process. This is related, in part, to considerations of the **objectives** of the decision-making process.

In the majority of cases we researched, there appeared to be some variation and a lack of consensus over process and roles in the decision-making bodies and committees. There was also little sense that the committees developed precedent in their decision-making. Despite the progress made by NICE on these issues, there remains room for further development of clear and rational decision-making approaches in localities in the NHS.

Returning to the objectives of the decision-making body, Simon¹⁶ characterised decision-making as ‘problem solving’ and pointed out that it is generally carried out more effectively when the ‘problem’ is well structured. Local committees typically operated in a less defined decision situation than NICE. A range of broader considerations – such as the likely impact of decisions on the local health economy – were brought to bear on their deliberations. These committees also had fewer resources to put into the scoping of each decision so that decision options tended to be less well defined.

An important and related issue concerns the remit of the decision-making committees and the extent to which this takes in consideration of budgets and financial flows. It is important here to ask:

- Does the decision-making body (and the relevant committee) have responsibility for a specific budget?
- Do parties or individuals making applications to the committee have to identify a source of funding for the proposed new technology in advance?
- Does the committee have clear links to the financial processes of the organisations represented on it?

Clearly, the answer to these questions will shed some light on the extent to which it makes sense for committees to use cost-effectiveness information routinely in their deliberations. Our research suggests that many of the local committees in the NHS that are making recommendations on the ‘coverage’ of drugs and other technologies (e.g. Drugs and Therapeutics Committees, which make decisions whether or not to list a new drug on a hospital formulary) operate without any requirement formally to consider the financial implications of their decisions – such committees almost never have a direct link to a budget that will be drawn on to fund their decision. This, combined with the information deficits, appeared to result in committees making little attempt to disinvest in or ‘de-prioritise’ existing technologies. Consideration of cost issues was most often confined to a concern amongst committee members that their department or organisation did not bear an excessive financial burden resulting from introduction of a new treatment.

Overall, the current picture, therefore, appears to be one in which information deficits of technology coverage committees, combined with their specific

location within broader structures and processes, render them unreceptive to cost-effectiveness information. This should not be interpreted as a denunciation of such bodies. The use of cost-effectiveness analysis only makes sense if it accords with the objectives and constraints extant at local level. Shifting this broader context to one which incentivises pursuit of economic objectives is not within the power of decision-making bodies themselves.

NICE

Levels of use of economic analyses

At the national policy level, our main research finding is that economic analysis is highly integrated into the decision-making process of NICE’s technology appraisal programme. This is evidenced by the remit of NICE (to consider cost-effectiveness), the nature of the assessment reports commissioned specifically for NICE and the committee composition. In addition, our data drawn from observation and interviews with Appraisal Committee members added considerable support to this overall impression. However, the precise nature and extent of the committee’s adoption of a health economics paradigm is an area that deserves further consideration. Attitudes to economic evaluation were found to vary from one committee member to another, and other factors dilute the influence of the health economics analysis available to the committee. There was strong evidence of an ordinal approach to consideration of clinical effectiveness and cost-effectiveness information. However, many interviewees pointed out that the economic and clinical evidence were inextricably linked. Some interviewees considered the key role of the cost-effectiveness analysis to be in providing a framework for the decision-making process. The NICE committee deliberations that we observed saw significant disagreement among committee members and these mainly revolved around the economic evaluation.

Issues of accessibility of economic analyses

Although issues of accessibility, broadly, were far less acute at the national level, organisations such as NICE still have some important issues to address in this area. In terms of the challenge of interpreting cost-effectiveness analyses, a frequently cited issue was the poor levels of understanding of cost-effectiveness information. The extent to which this is a serious barrier depends, to some extent, on the role that

committee members are expected to play and the overall approach to decision-making being adopted. This suggests the need for engagement with broader debates around the role of evidence in policy decision-making.^{57,58} If the mechanism of arriving at a decision is expected to be through a consensus process, then all committee members are required to understand in full the nature of the decision problem, the results of the alternative analyses and the key evidence that is driving the results; in short, they are obliged to understand the economic analyses.

Members of the NICE Appraisal Committee also expressed views on strategies for improving the committee's use of economic evaluation. It was generally felt that NICE devoted sufficient resources to the commissioning of economic evaluations and that the Appraisal Committee had sufficient numbers of health economists as members. Although some committee members felt formal health economics training would not be welcome or necessary for them personally, a large proportion of interviewees felt this would be beneficial to many on the committee. This was despite greater levels of overall expertise than was true for local decision-making bodies. In line with local decision-makers, NICE committee members expressed support for a greater standardisation of analytical approach from academic and industry health economists. It was felt by some that the economic evaluations they received could be better presented in order to make them more readily understandable – for example, through the use of a standard summary document.

A failing on the part of analysts that was revealed from the research concerned the presentational style of cost-effectiveness studies. It was felt by many, both nationally and locally, that the highly technical nature of the cost-effectiveness studies and the presentation of the results in a less than clear way made them very difficult for the non-economist to understand. The need for improvements in the presentation of cost-effectiveness studies was a view held by many of the research participants. Others cited aspects of cost-effectiveness analyses that make interpretation challenging include the variability in approaches and methods used by different analysts and the highly aggregated nature of the presentation of results. On the latter, some respondents argued for the use of a cost-consequences approach to reporting results whereby results of analyses are presented on different dimensions separately rather than combining everything together in the QALY.

Ordinal and 'framework' approaches to processing cost-effectiveness analysis

Returning to our research, the results confirm that, on the whole, Appraisal Committee members see cost-effectiveness analysis as an integral element of the required evidence base.

Approaches to the processing of this information, however, reflect a dichotomy between those adopting an ordinal method and those who see the cost-effectiveness model as the committee's primary analytical framework. The research has, therefore, highlighted a tension among committee members in terms of the process by which the coverage decision should be arrived at. Dowie⁵⁹ has argued against the use of an ordinal approach, suggesting that it represents reluctance by decision-makers to consider technologies that move into the southwest quadrant of the cost-effectiveness plane. That is, any technology that is both less effective and less costly, regardless of how large the financial savings might be, should not be considered for adoption. He argues that if one accepts the logic of using cost-effectiveness analysis in the case where technologies are more expensive and more effective (i.e. in the northeast quadrant), then there is no reason to accept the same logic in the southwest quadrant. Thus, Dowie argues against the ordinal approach as inconsistent and argues in favour of using cost-effectiveness analysis as a framework for processing information to arrive at a coverage decision. The tension between ordinal and framework approaches has implications for committee deliberations.

Our research observations suggest that clinical opinion (or a 'clinical hurdle') was, in some situations, the most influential factor in discussions such that the perception of a technology's clinical value and benefit could override the results and conclusions based on the reported evidence. In other discussions, economic analysts were more dominant – apparently as a result of their technical expertise in interpreting the cost-effectiveness analysis. Although it is debatable whether these scenarios amount to the exercising of disproportionate influence, it remains important to guard against any one grouping on such committees being granted a dominant position. For example, the adoption of cost-effectiveness analysis as the single 'lens' through which decisions are viewed may result in a reliance on methods incommensurate with societal values, as Coast has argued.⁶⁰

Failure to resolve these tensions with regard to committee processes fuels uncertainty for

members in terms of the role that they are being asked to fulfil. An ordinal approach requires those involved applying themselves to aspects of a decision with which they are most familiar – clinicians focusing on the clinical hurdle alone and economists on the cost-effectiveness hurdle alone, for example. This is asking those involved to act as specialist ‘experts’. The alternative approach, discussed in this study, is to operate with an agreed framework and model within which the decision problem is considered. This approach is more consistent with the notion of seeking consensus, but requires all committee members to have a full understanding of the detail of the decision problem at hand and of the model being used to give structure to the problem. This approach would almost certainly necessitate a greater level of individual expertise in the interpretation of the analyses presented than many interviewees felt they possessed. This then has important implications for the training of those who take on responsibility for technology coverage decisions.

Acceptability of cost-effectiveness studies

A second tier of barriers to the use of economic studies relate to its acceptability to decision-makers. The term ‘acceptability’ as employed here refers to the extent to which decision-makers were inclined to adopt the recommendations of studies that they had accessed and interpreted. Our research has found that economic evaluations were often perceived as ‘unacceptable’ for the following reasons:

- The broad approaches and assumptions underlying much health economic analysis are problematic.
- The commonly applied methods and tools of cost-effectiveness analysis are seen as having important weaknesses and lacking robustness.
- The quality of cost-effectiveness studies is often perceived as being poor.
- The source of the economic evaluation is often considered to be neither independent nor credible.

Comments from those with some knowledge of health economics suggested a belief that underlying all cost-effectiveness analyses was a strong utilitarian principle, and for some this led to a rejection of the whole health economics approach. Some respondents indicated that they had ethical objections to the values implicit in cost-effectiveness studies and espoused the ‘rule of rescue’ as an alternative. More at the national

level, a common concern with the cost-effectiveness analyses presented was that they failed explicitly to consider the opportunity costs of the decisions being considered. The cost-effectiveness analysis presented the problem in terms of a one-off decision concerning the coverage of a given health technology (commonly a new drug) with no explicit consideration given to the sacrifice that would be required in order for the additional resources to be made available (assuming that the incremental cost is positive). There is an attempt to negate this problem by using a cost-effectiveness threshold and defining technologies that have ICERs that fall below the threshold as cost-effective uses of NHS resources (regardless of the true opportunity cost). This issue has been highlighted by several commentators.⁶¹ However, although the necessity of using a cost-effectiveness threshold is acknowledged by most of the NICE committee members, it is viewed as problematic – the basis for the threshold value or range is very unclear and the level chosen is widely viewed by members as being arbitrary.⁶²

Some of the commonly applied methods and tools of health economics have been questioned by our research participants. These issues were mainly highlighted in the national case study. The concerns with QALYs tended to focus on their failure to capture all of the important aspects of benefit from healthcare interventions. An interesting example of this cited by one respondent was, in the context of a chronic disease, the loss of hope associated with disease irreversibility which the QALY is unable to take account of. The predominant focus on efficiency issues in cost-effectiveness studies, and the perceived failure of health economics to develop methods that would allow formal consideration of equity issues, were highlighted as an area of concern. The exclusive focus on efficiency issues in cost-effectiveness studies was seen as particularly problematic as this would tend to disadvantage certain patient groups. One participant raised a concern that treatments for people with very rare diseases will almost always look very unattractive from a purely cost-effectiveness point of view, using currently applied methods.

A number of issues have been raised at both the local and national levels concerning the perceived quality of cost-effectiveness studies. Concerns were expressed about the robustness of methodological approaches (e.g. the use of inappropriate comparators). Although there was general acceptance of the necessity for economic analyses

being based, to some extent, on a number of assumptions (where good data might be lacking), the validity of such assumptions was repeatedly questioned. Hence, there is some concern that the long-term predictions from cost-effectiveness models may be very wrong. This was linked in some people's minds to the issue of transparency of the analyses – a common view was that a lack of transparency of cost-effectiveness studies engenders caution on the part of decision-makers to use them. A related issue that was again raised repeatedly at both local and national levels was the view that cost-effectiveness studies that are undertaken or sponsored by the technology manufacturer are likely to be biased. The difficulty faced by those working locally is that they often have no other access to such analyses.

In our research, a necessary requirement for the 'use' of a cost-effectiveness analysis was widely stated to be that it addressed the policy question facing the decision-maker. At both national and local levels, frustration was expressed at the failure of cost-effectiveness studies (even those specifically commissioned for NICE) to address the correct policy question. The criticism was principally directed at the cost-effectiveness analyst. Examples of issues raised include: cost-effectiveness analysts rarely have a good understanding of the decision-making process in the NHS, the very broad perspective adopted in the cost-effectiveness study often does not match that required for the decision-maker, and the financial 'savings' predicted in cost-effectiveness analyses are often not seen in reality.

Reflections on research methodology

Case studies

It was felt that a predominantly qualitative approach was best suited to addressing the primary research questions. This was supported by an application of Marshall and Rossman's criteria⁶³ for the adoption of a qualitative research design, which they recommend if one or more of the following conditions apply:

- It is important for the researchers to understand the in-depth processes that operate within the body researched.
- The research issues involve poorly understood organisational phenomena.
- The researchers are interested in the differences between stated (**decision-making processes**) and their actual implementation.
- The study seeks to explore variables that do not lend themselves to experiments for practical and ethical reasons.

- One aim of the study is to discover new or hitherto unspecified variables.

Qualitative case studies of decision-making committees were the primary source of data.^{64–66} The selection of a qualitative case study approach is consistent with our concern to explore **how** and **why** decisions are made by NHS policy-making bodies. The approach adopted was intended to yield both exploratory and explanatory data. In other words, the hope was that it would enable the researchers to address directly the research questions but would also be responsive to new and unforeseen issues and areas of interest. Case studies typically entail 'close-range' qualitative research techniques such as observation, participant observation and intensive interview. The case study method in social research is suited to in-depth, microscopic exploration and unsuited to macroscopic investigation. This focus was designed to complement and build upon the more quantitative approach of many previous studies. There is also scope for our findings to inform the design of future studies – be they quantitative or qualitative in approach.

Observation

Observations of case study committees involved "the systematic, detailed observation of behaviour and talking: watching and recording what people do and say".³¹ A major strength of this approach is that it provides the researcher with information on a crucial stage of the decision-making process and allows observation of research subjects in their natural setting. It also can serve to highlight potential discrepancies between data generated from documentary and interview research (what individuals and organisations **say**) and observed behaviour (what people or organisations **do**). A potential limitation of observation as a research method is the likelihood that the presence of a researcher will have some effect on the behaviour of the observed. A further limitation of this approach is that the observer acts as the research instrument and therefore selects and **re-presents** data for collection and analysis. Triangulation of observation data can help to compensate for the intrinsically subjective process of note-taking, and also for the potentially transforming effects of researcher on researched.

The research team were aware of limits to data generated in this way, for example:

- The meetings attended and observed may not be typical of committee activity.

- There may be other, unobserved elements of decision-making processes – for example, less ‘formal’ meetings or communication.

We have attempted to account for the potential gaps in data brought about by these limitations especially where these were highlighted by interviewees.

Interviews

Unstructured and semi-structured interviews help the researcher to “understand the world from the subject’s point of view, to unfold the meaning of experiences, to uncover their lived world”.³³

Semi-structured interviews are recommended where there is a balance required between a free-flowing and a directed conversation. We used this format in order to ensure that the research questions were addressed in full while allowing the flexibility to pursue other issues or concerns raised by respondents. This approach allows the research respondent to present an account of the decision-making environment in their own words and in an environment conducive to production of in-depth knowledge on a range of parameters and topics.

Interviews are a common feature of qualitative research as they can help to highlight new areas of interest for the generation of conceptual frameworks. Semi-structured interviewing is particularly useful when interviewing ‘elites’: in this case policy-making communities. Researchers have reported difficulties in keeping a focus on the research questions when interviewing policy makers, many of whom are articulate and used to verbalising their thoughts.⁶⁷ The use of a semi-structured approach can help to ‘tip the balance of power’ in the direction of the researcher.⁶⁸ We took the further step of supplying a basic interview schedule to respondents in advance of interview. Although this provided the interviewee with the option of ‘pre-preparing’ their responses, the interview schedule was not adhered to rigidly and enabled a re-focusing when the interview moved too far from the primary research questions. The issue of how directive interviewers should be in the interests of retaining control is addressed by Patton,³⁴ who suggests three appropriate strategies:

- knowing what it is you want to find out
- asking the right questions to get the information you need
- giving appropriate verbal and non-verbal feedback.

As with qualitative research in general, semi-structured interviewing does not lend itself to the generation of statistical data. It is important to recognise that the semi-structured interview is a human exchange in which knowledge is generated through dialogue.⁶⁹ Therefore, the researcher should at all times be aware of and account for the role they play in shaping responses. Although it is neither desirable nor possible in this context for the researcher to adopt a position of scientific detachment, it is important to have an awareness of how the interviewer’s behaviour might influence responses and attempts should be made to avoid leading questions. Interviewers attempted to minimise their influence on the interviewees by using a semi-structured interview schedule and attempting to be non-directional in verbal and non-verbal language. However, in a small number of cases, interviewees wrongly assumed that the researcher was a health economist and so in favour of the increased use of economic analysis. Where this occurred, this was explored and any vested interests of the researcher were discussed.

Research sample and design

A number of changes have occurred in healthcare in the period since the study was carried out that have had a significant impact on the topic of technology coverage at local levels. Recent reorganisations and policy guidance have focused on strengthening the commissioning function and this has had most far-reaching implications for PCTs who bear primary responsibility for bringing about the new ‘NHS Local’. Given recent high-profile controversy surrounding technology coverage decisions that have seen PCTs portrayed as unreasonable rationers, there is an increasingly urgent need for local payers to find mechanisms for increasing the legitimacy of the technology coverage decisions they make.

In retrospect, the study would have benefited from a more systematic exploration of the relationship between the local technology coverage committees and the main commissioning bodies in their areas. A study of, for example, PCT Professional Executive Committee decision-making (and also practice-based commissioning) would provide a useful complement to the findings reported here. Similarly, empirical exploration of the relationship between national bodies such as NICE and local decision-makers would help to address gaps in the study design.

Chapter 7

Conclusions

The driving force behind the push to make more use of economic analyses in healthcare resource allocation decisions is the desire to make decision processes, and the decisions themselves, more rational. In turn, greater rationality in the system contributes to openness and transparency, and so better fulfils accountability requirements.⁷⁰ Our suggestions relating to decision-making committees and bodies in the NHS are that they should have clear and agreed objectives, closer links with finance functions in their organisations, systematic processes by which decisions on technology coverage are made, clearer roles for committee members, an ability to recall precedents that have been established and consideration of the full impact of their decisions. The adoption of these suggestions would mean that the decisions taken are likely to be 'better' decisions but also that the decisions can more easily be communicated to stakeholders, including the general public – public bodies have a duty to be accountable for their decisions.

There is a further challenge that stems from the increasing expectation for lay and patient representation on decision-making committees in the NHS. This is seen very clearly in the composition of the NICE Appraisal Committee, which has, for example, members who are described as 'patient advocates'. This development necessitates that the information upon which decisions are based is accessible to a wide audience – the more accessible the information used in decision-making, the easier it is to be inclusive in the decision-making process and the more transparent is the basis upon which the decision is made. This accessibility concern represents one of the challenges to the health economics community but also highlights the training agenda – the case for stronger and more widespread training in health economics for both clinical and managerial professionals in the health sector is compelling. Additional areas of focus for health economists include the need to overcome perceived weaknesses in the methods of their analyses (e.g. are QALYs the best that can be achieved as a measure of outcome?), and the need to work with those in healthcare to ensure alignment between the objectives assumed in economic analyses and the objectives facing decision-makers in reality.

That is not to suggest that the decision-maker always 'knows best', but analyses based on false assumptions regarding objectives clearly serve no purpose. One way for NICE to address this would be to facilitate, at a preliminary stage of the appraisal process, a consensus regarding the design of the cost-effectiveness model in order to prevent the subsequent disagreements (for example on comparators) which arose during the case study. Overall, there is a powerful argument for more emphasis being placed on the work they commissioned so that downstream difficulties relating to analyses can be pre-empted. In the case of early appraisals (for example, of recent technologies), the research supports calibration of decisions to include 'provisional' approvals and ongoing technology monitoring.

Our research supports the view that in order to be useful, analysts need to take greater account of the specific circumstances of local decision-making. A number of features of the decision-making environment appear to militate against emphasis on cost-effectiveness principles. These include separation of appraisal and resource allocation functions and confusion over the relationship between the two. They also include the extent to which decision-making is structured to encourage bargaining between sectional interest groups – for example, over the financial burden of implementation. The study has implications for healthcare systems where similar conditions apply. It further problematises narrow prescriptions for improving decision-making such as increasing either the volume of economic evaluations or providing more health economics training to decision-makers. It highlights instead the need to address the relationship between the attitudes and practices of decision-makers and the institutional constraints in which they operate. There is a corresponding requirement for greater clarity in both the objectives of technology coverage committees and their responsibilities within a broader political and financial context. This would help to establish the terms on which the routine use of cost-effectiveness analysis might become a possibility.

The NICE 'experiment' has seen cost-effectiveness analysis move to the centre ground of national

policy deliberations regarding technology coverage in the NHS in England and Wales. However, our case study implies that there is room for further progress, or at least greater clarity, in the way in which such analyses are integrated into the decision-making process. The current situation whereby two broad but fundamentally inconsistent approaches to the use of cost-effectiveness analysis operate simultaneously within the NICE Appraisal Committee needs to be addressed. This key observation has relevance to other similar technology coverage decision-making bodies in the UK and internationally that are seeking to make more formal use of research evidence as part of the decision-making process.

Recommendations for further research include:

- Research into healthcare organisational forms that can explore the alternative structures,

processes and mechanisms by which technology coverage decisions can and should be made.

- The further development of ‘resource centres’ that can provide information relating to high-quality independent published analyses and are able to support decision-makers with some local re-analysis and interpretation of findings.
- The development of improved methods of economic analysis that take account of the concerns raised by practitioners and users of such analyses in this research.
- The design of more accessible forms of presentation of economic analyses.
- Further assessment of the feasibility and value to be derived from a formal process of discussion and deliberation concerning the objectives that we seek from investments in healthcare.



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Contribution of authors

Iestyn Williams (Lecturer) contributed to the conception and design of the project. He led on data collection and analysis and drafted much of the report.

Stirling Bryan (Professor of Health Economics) was the principal investigator overseeing the conception, design and overall running of the project. He also contributed to data collection and analysis and drafted elements of the report. He acted as guarantor of the final report.

Shirley McIver (Senior Fellow) contributed to data collection and analysis and drafted elements of the report.

David Moore (Senior Systematic Reviewer) was involved in designing and conducting the literature review component of the project.

Paper published in another peer-reviewed journal relating to this research project

Williams I, Bryan S. Understanding the limited impact of economic evaluation in healthcare resource allocation: a conceptual framework. *Health Policy* 2007;**80**:135–43.



References

1. Ross J. The use of economic evaluation in health care: Australian decision makers' perceptions. *Health Policy* 1995;**31**:103–10.
2. Bryan S, Brown J. Extrapolation of cost-effectiveness information to local settings. *J Health Serv Res Policy* 1998;**3**:108–12.
3. Duthie T, Trueman P, Chancellor J, Diez L. Research into the use of health economics in decision-making in the United Kingdom – Phase II. Is health economics 'for good or evil'? *Health Policy* 1999;**46**:143–57.
4. Culyer AJ. *The economics of social policy*. London: Martin Robertson; 1973.
5. Williams A. Intergenerational equity: an exploration of the fair innings argument. *Health Econ* 1997;**6**:117–32.
6. Bryan S, Roberts T, Heginbotham C, McCallum A. QALY-maximisation and public preferences: results from a general population survey. *Health Econ* 2002;**11**:679–93.
7. Dowie J. The research-practice gap and the role of decision analysis in closing it. *Health Care Anal* 1996;**4**:5–18.
8. Davenport C, Elley K, Taylor K, Salas C, Bryan S, Fry-Smith A, et al. The clinical effectiveness and cost-effectiveness of routine dental checks. *Health Technol Assess* 2003;**7**(7).
9. Mauskopf JA, Paul JE, Grant DM, Stergachis A. The role of cost-consequence analysis in health care decision-making. *Pharmacoeconomics* 1998;**13**: 277–88.
10. Freemantle N, Mason J. Not playing with a full DEC: why development and evaluation committee methods for appraising new drugs may be inadequate. *BMJ* 1999;**318**:1480–2.
11. Kernick DP. The impact of health economics on health care delivery. *Pharmacoeconomics* 2000;**18**: 311–15.
12. Parsons W. *Public policy: an introduction to the theory and practice of policy analysis*. 3rd ed. Cheltenham: Edward Elgar; 1999.
13. Bell D. *The coming of post-industrial society: a venture into social forecasting*. Harmondsworth: Penguin Books; 1976.
14. Singer O. Knowledge and politics in economic policy making: official economic advisors in the USA, Great Britain and Germany. In Peters BG, Barker A, editors. *Advising West European governments: enquiries, expertise and public policy*. Edinburgh: Edinburgh University Press; 1993.
15. Henderson D. *Innocence and design: the influence of economic ideas on policy*. Oxford: Blackwell; 1986.
16. Simon HA. *Models of man: social and rational*. New York: Wiley; 1957.
17. Black N. Evidence based policy: proceed with care. *BMJ* 2001;**323**:275–9.
18. Weiss CH. The many meanings of research utilization. *Public Admin Rev* 1979;**42**:6–31.
19. Drummond M, Weatherly H. Implementing the findings of health technology assessments. If the cat got out of the bag, can the tail wag the dog? *Int J Technol Assess Health Care* 2000;**16**:1–12.
20. Lomas J, Sisk JE, Stocking B. From evidence to practice in the United States, the United Kingdom and Canada. *Milbank Q* 1993;**71**:405.
21. Lavis JN, Robertson D, Woodside JM, McLeod B, Abelson J. How can research organizations more effectively transfer research knowledge to decision makers? *Milbank Q* 2003;**81**:221–48.
22. Etzioni A. *The active society: a theory of societal and political processes*. New York: Free Press; 1968.
23. Janis IL. *Groupthink: psychological studies of policy decisions and fiascos*. Boston, MA: Mifflin; 1972.
24. Elliott H, Popay J. How are policy makers using evidence? Models of research utilisation and local NHS policy making. *J Epidemiol Commun Health* 2000;**54**:461–8.
25. Stevens A, Milnes R. A knowledge-based health service: how do the new initiatives work? *J R Soc Med* 1998;**91**:26–31.
26. Bero LA, Grilli R, Grimshaw JM, Harvey E, Oxman AD, Thomson MA. Closing the gap between research and practice: an overview of systematic reviews of interventions to promote the implementation of research findings. *BMJ* 1998;**317**:465–8.
27. Kitson A, Harvey G, McCormack B. Enabling the implementation of evidence based practice: a conceptual framework. *Qual Health Care* 1998;**7**: 149–58.
28. Leach RH, Leach SJ. Drug and therapeutics committees in the United Kingdom in 1992. *Pharm J* 1994;**253**:61–3.

29. Elting LS, Martin CG, Canton SB, Rubenstein EB. Influence of data display formats on physician investigators' decisions to stop clinical trials: prospective trial with repeated measures. *BMJ* 1999;**318**:1527–31.
30. Coast J. Citizens, their agents and health care rationing: an exploratory study using qualitative methods. *Health Econ* 2001;**10**:159–74.
31. Mays N, Pope C. Qualitative research: observational methods in health care settings. *BMJ* 1995;**311**:182–4.
32. Bales R. *Interaction process analysis*. Chicago, IL: University of Chicago Press; 1950.
33. Kvale S. *Interviews: introduction to qualitative research interviewing*. Thousand Oaks, CA: Sage; 1996.
34. Patton M. *How to use qualitative methods in evaluation*. London: Sage; 1987.
35. Glazer BG, Strauss AL. *The discovery of grounded theory: strategies for qualitative research*. New York: Aldine; 1967.
36. Barbour RS. Checklist for improving rigour in qualitative research: a case of the tail wagging the dog? *BMJ* 2001;**322**:115–17.
37. Spath HM, Allenet B, Carrere MO. Using economic information in the health sector: the choice of which treatments to include in hospital treatment portfolios. *J Econ Méd* 2000;**18**:147–61 (in French).
38. Coyle D. *Increasing the impact of economic evaluations on health-care decision-making*. Discussion Paper 108. York: Centre for Health Economics, University of York; 1993.
39. Drummond M. Evaluation of health technology: economic issues for health policy and policy issues for economic appraisal. *Soc Sci Med* 1994;**38**:1593–600.
40. McDonald R. *Using health economics in health services: rationing rationally?* Buckingham: Open University Press; 2002.
41. Prosser L, Koplan J, Neumann P, Weinstein MC. Barriers to using cost-effectiveness analysis in managed care decision-making. *Am J Managed Care* 2000;**6**:173–9.
42. von der Schulenburg JMG. *The influence of economic evaluation studies on health care decision-making*. Oxford: IOS Press; 2000.
43. Hoffmann C, Stoykova BA, Nixon J, Glanville JM, Misso K, Drummond MF. Do health-care decision makers find economic evaluations useful? The findings of Focus Group Research in UK Health Authorities. *Value Health* 2002;**5**:71–8.
44. Odedina FT, Sullivan J, Nash R. Use of pharmacoeconomic data in making hospital formulary decisions. *Am J Health Syst Pharm* 2002;**59**:1441–4.
45. Nixon J, Phipps K, Glanville J, Mugford M, Drummond M. Using economic evidence to support decision-making: a case study of assertive community treatment within the UK National Service Framework for Mental Health. *Appl Health Econ Health Policy* 2002;**1**:179–90.
46. Walley T, Barton S, Cooke J, Drummond M. Economic evaluations of drug therapy: attitudes of primary care prescribing advisors in Great Britain. *Health Policy* 1997;**41**:61–2.
47. Motheral BR, Grizzle AJ, Armstrong EP, Cox ER, Fairman K. Role of pharmacoeconomics in drug benefit decision-making: results of a survey. *Formulary* 2000;**35**:412–21.
48. Bergthold LA, Singer SS, Huang A, Gemperli M, Garber A, Osterhoff R. Using evidence and cost in managed care decision-making. 2002. Center for Health Policy/Center for Primary Care & Outcomes Research; 2002. Available at: <http://content.healthaffairs.org/cgi/content/full/hlthaff.w4.284v1/DC2>. 2002.
49. Kulsomboon V, Palumbo FB, Mullins CD. Criteria to request pharmacoeconomic data and data sources for hospital formulary decisions. *Drug Inf J* 2001;**35**:231–40.
50. Evans C, Dukes EM, Crawford B. The role of pharmacoeconomic information in the formulary decision-making process. *J Managed Care Pharm* 2000;**6**:108–21.
51. Lyles A, Luce RB, Rentz AM. Managed care pharmacy, socioeconomic assessments and drug adoption decisions. *Soc Sci Med* 1997;**45**:511–21.
52. Sloan FA, Whetten-Goldstein K, Wilson A. Hospital pharmacy decisions, cost containment and the use of cost effectiveness analysis. *Soc Sci Med* 1997;**45**:523–33.
53. Drummond M, Cooke J, Walley T. Economic evaluation under managed competition: evidence from the UK. *Soc Sci Med* 1997;**45**:583–95.
54. Ludbrook A, Mooney G. *Economic appraisal in the NHS: problems and challenges*. Northern Health Economics Publication. Aberdeen: University of Aberdeen, 1984.
55. West R, Borden EK, Collet J-P, Rawson NSB, Tonks RS. "Cost-effectiveness" estimates result in flawed decision-making in listing drugs for reimbursement. *Can J Public Health* 2002;**93**:421–5.
56. Williams I, Bryan S. Understanding the limited impact of economic evaluation in health care resource allocation: a conceptual framework. *Health Policy* 2007;**80**:135–43.

57. Milewa T, Barry C. Health policy and the politics of evidence. *Soc Policy Admin* 2005;**39**:498–512.
58. Teutsch SM, Berger ML. Evidence synthesis and evidence-based decision making: related but distinct processes. *Med Decis Making* 2005;**25**:487–9.
59. Dowie J. Why cost-effectiveness should trump (clinical) effectiveness: the ethical economics of the south west quadrant. *Health Econ* 2004;**13**:453–9.
60. Coast J. Is economic evaluation in touch with society's health values? *BMJ* 2004;**329**:1233–6.
61. Maynard A, Bloor K, Freemantle N. Challenges for the National Institute for Clinical Excellence. *BMJ* 2004;**329**:227–9.
62. Rawlins MD, Culyer AJ. National Institute for Clinical Excellence and its value judgments. *BMJ* 2004;**329**:224–7.
63. Marshall C, Rossman GB. *Designing qualitative research*. 2nd ed. Thousand Oaks, CA: Sage; 1995.
64. Yin RK. *Case study research: design and methods*. Thousand Oaks, CA: Sage; 1994.
65. Tellis W. Introduction to case study. *The Qualitative Report* 1997;**3**(2). www.nova.edu/ssss/QR/QR3-2/tellis1.html.
66. Pope C, Mays N. Qualitative research: reaching the parts other methods cannot reach: an introduction to qualitative methods in health and health services research. *BMJ* 1995;**311**: 42–5.
67. Duke K. Getting beyond the 'official line': reflections on dilemmas of access, knowledge and power in researching policy networks. *J Soc Policy* 2002;**31**:39–59.
68. Ostrander S. Surely you're not in this just to be helpful: access, rapport and interviews in three studies of elites. In Hertz R, Imber JB, editors. *Studying elites using qualitative methods*. London: Sage; 1995.
69. Holstein JA, Gubrium JF. *The active interview*. London: Sage; 1995.
70. Daniels N, Sabin JE. *Setting limits fairly*. New York: Oxford University Press; 2002.

Appendix I

Letters used in surveys of primary and secondary care organisations

Initial letter

Dear

We are writing to you in relation to a research project commissioned by the Department of Health that is exploring *The Use of Economic Evaluation in NHS Decision-making*.

At a national level our focus is on the NICE Appraisal Committee. At the local level we wish to study the decisions made by Primary Care Trusts and Local Health Groups regarding the entry of new medicines and other technologies. As part of the research we wish to review and collate the types of information that are routinely drawn upon, for example by Drugs and Therapeutics Committees, for these decisions. Given this, we would be most grateful if you could send to us (using the enclosed pre-paid envelope) any relevant information sheets and/or pro formas that detail the information required for such decisions in your PCT/Local Health area. If no such system currently exists, please indicate so on the attached reply form.

The information you provide will be treated as confidential and will not be used as an assessment or audit of committee performance. The research is an academic enquiry into the impact of economic analyses on current NHS decision-making. Reported findings from this research will not refer to named organisations.

We may have sent this request to another individual within your organisation. However we would be grateful if you would respond to this request, unless you are certain that someone else has already done so. If you would like further information about the project and/or are willing to be further involved in the research please additionally complete and return the enclosed form.

Thank you for your time and co-operation

Kind regards

Yours sincerely

Ron Pate
Pharmaceutical Adviser
West Midlands Strategic Health
Authorities

Stirling Bryan
Professor of Health Economics
HSMC
University of Birmingham

Reminder letter

Dear

We are writing to remind you of a request for information sent to you on If you have already responded please ignore this letter.

We are currently conducting a research project commissioned by the Department of Health that is exploring 'The Use of Economic Evaluation in NHS Decision-making'. At a national level our focus is on the NICE Appraisal Committee. At the local level we wish to study the decisions made by Drugs and Therapeutics Committees, Medicines Management Committees etc. regarding the adoption and/or introduction of new medicines and other technologies. As part of the research we wish to review and collate the types of information that are routinely drawn upon by such committees. Given this, we would be most grateful if you could send to us (using the enclosed pre-paid envelope) any relevant information sheets and/or pro formas that detail the information required by such committees in your health economy area.

The information you provide will be treated as confidential and will not be used as an assessment or audit of committee performance. The research is an academic enquiry into the impact of economic analyses on current NHS decision-making. Reported findings from this research will not refer to named organisations.

If you would like further information about the project and/or are willing to be further involved in the research please additionally complete and return the enclosed form.

Thank you for your time and co-operation

Kind regards

Yours sincerely

Ron Pate
Pharmaceutical Adviser
(Secondary Care), West
Midlands Strategic Health Authorities

Stirling Bryan
Professor of Health Economics
HSMC
University of Birmingham

Appendix 2

Interview schedule for interviews with representatives of local decision-making bodies

(A) Questions about the committee

1. What do you consider to be the main functions of the committee?
2. What are your own main roles/activities as committee member?
3. What sorts of decisions does the committee make?
4. In general, how do you contribute to the decision-making process?
5. What information is most useful to you personally in making these decisions?
6. What information do you think is most important to the committee in making decisions?

(B) Economic Evaluation questions (i)

7. What types of Economic Evaluation are made available to the committee?

8. In your opinion, how important is Economic Evaluation in the decision-making process?
9. Are different committee members more or less concerned with Economic Evaluation?

(C) Economic Evaluation questions (ii)

10. Do you feel you understand the Economic Evaluation presented to the committee?
11. What are the strengths and weaknesses of the Economic Evaluation accessible to the committee?
12. As a committee member, would you like to see more/less Economic Evaluation as an aid to decision-making?
13. In what ways could the use of Economic Evaluation be improved?

Appendix 3

Interview schedule for interviews with NICE Appraisal Committee members

Venue:	Date/time of interview
Interviewer:	Interviewee:
Designation:	Organisation:
Technology:	1st appraisal date:
Interviewee role in appraisal:	

(A) Decision questions

1. What considerations led to you reaching the decision?
2. How important was the economic evidence in your own thinking?
3. In your opinion, how important was the economic evidence in the committee's thinking?

(B) Economic Evaluation questions

1. What is your interpretation of the results of the economic analysis?
2. Did you feel the committee reached a satisfactory consensus regarding the economic data?
3. Would you have liked to see more/less economic evidence?
4. Did you feel you (the team) understood the economic evidence presented?
5. Would you have liked further clarification?
6. What were the strengths of the analysis?
7. What were the strengths of its presentation?
8. What were the weaknesses of the analysis?
9. What were the weaknesses of its presentation?
10. In what other ways could evaluation of economic data be improved?

(C) General questions

1. How did the appraisal differ from ones you've been involved in previously?
2. Do you feel economic evaluation has become more/less important to the appraisal process?
3. Are different committee members more or less concerned with health economics data?
4. How are other considerations (such as equity, patient choice, etc.) weighed against economic evidence/analysis?

Appendix 4

Programme of workshops held for local decision-makers

The use of economic evaluation in NHS decision-making Workshop Programme

Health Services Management Centre, University of Birmingham

Park House, Garden Room March 4 2004

12.30	Lunch	
1.00	Introductions	
1.10	Presentation	The role of economic evaluation in decision-making
1.30	Group discussion	Barriers to use of economic evaluation
2.00	Feedback	
2.15	Group discussion	Overcoming barriers to use of economic evaluation
2.45	Feedback	
3.00	Whole group discussion	
3.30	Close	

Appendix 5

Summary of independent economic analyses for each NICE appraisal topic studied

Results are given in *Tables 7–13*.

TABLE 7 Summary of economic analysis – capecitabine and tegafur with uracil for colorectal cancer

Aspect of economic evaluation		
<i>Decision problem addressed</i>		Interventions: tegafur with uracil (UFT/LV) and capecitabine Population: patients with metastatic colorectal cancer Comparator: intravenous 5-fluorouracil (5-FU/LV) regimen (Mayo Clinic)
<i>Analytic methods</i>	Type of economic evaluation	Cost-minimisation analysis and cost-effectiveness analysis (i.e. cost per progression-free year of survival gained)
	Modelling methods	No model developed
	Time horizon of analysis	12 months
	Perspective on costs	NHS and PSS only
	Discounting	Not relevant given the time horizon
	Measure of health benefits	Progression-free survival
	Source of quality of life and utility data	Not relevant
	Probabilistic sensitivity analysis	Not performed
	Subgroup analyses	None
	Equity considerations	None explicitly referred to
	Assessment of future research needs	No formal valuation of information analysis undertaken
<i>Presentation of results</i>	Expected CE results	Reported
	Parameter uncertainty	CE plane scatters not reported CEACs not reported
	Other forms of uncertainty	One-way sensitivity analyses undertaken
<i>Synthesis of evidence on outcomes</i>		Systematic review, using data from RCTs
<i>Assessment of NHS impact</i>		Budget impact calculated using prevalence and incidence information

CE, cost-effectiveness; PSS, Personal Social Services; RCT, randomised controlled trial.

TABLE 8 Summary of economic analysis – capecitabine for breast cancer

Aspect of economic evaluation		
<i>Decision problem addressed</i>		Interventions: capecitabine monotherapy or capecitabine in combination with docetaxel Population: women with locally advanced and/or metastatic breast cancer Comparator: vinorelbine and best supportive care
<i>Analytic methods</i>	Type of economic evaluation Modelling methods	Cost–utility analysis (i.e. cost per QALY) No formal modelling undertaken – using trial-based estimates reported in the company submission a Monte Carlo simulation was undertaken
	Time horizon of analysis	Not stated
	Perspective on costs	NHS only
	Discounting	“No discounting was undertaken due to the limited expected life span of patients in this setting”
	Measure of health benefits	QALYs
	Source of quality of life and utility data	Utility data taken from published sources and based on samples of nurses undertaking standard gamble exercises
	Probabilistic sensitivity analysis	Not undertaken
	Subgroup analyses	None
	Equity considerations	None explicitly referred to
	Assessment of future research needs	No formal valuation of information analysis undertaken
<i>Presentation of results</i>	Expected CE results Parameter uncertainty	Reported CE plane scatters reported CEACs reported
	Other forms of uncertainty	None
<i>Synthesis of evidence on outcomes</i>		Systematic review, using only information from RCTs
<i>Assessment of NHS impact</i>		Budget impact assessment presented

TABLE 9 Summary of economic analysis – olanzapine and valproate semisodium for the manic phase of bipolar I disorder

Aspect of economic evaluation		
<i>Decision problem addressed (from Scope)</i>		Interventions: quetiapine, olanzapine and valproate semisodium Population: patients experiencing mania associated with bipolar disorder Comparators: lithium or haloperidol
<i>Analytic methods</i>	Type of economic evaluation	Cost-effectiveness analysis (i.e. cost per additional responder to treatment)
	Modelling methods	Modelling approach not stated in report – model simply referred to as “probabilistic”. The Guidance document refers to it as “a hierarchical Bayesian model simulated using a Markov chain Monte Carlo technique”.
	Time horizon of analysis	3 weeks (since the focus was on the use of the drugs in the acute phase and not in the maintenance phase)
	Perspective on costs	NHS only
	Discounting	Not relevant, given the short time horizon considered
	Measure of health benefits	Response (typically measured as $\geq 50\%$ response on Young Mania Rating Scale)
	Source of quality of life and utility data	Not relevant
	Probabilistic sensitivity analysis	Performed on response rate (distribution not stated)
	Subgroup analyses	None
	Equity considerations	None explicitly referred to
Assessment of future research needs	No formal valuation of information analysis undertaken	
<i>Presentation of results</i>	Expected CE results	Reported
	Parameter uncertainty	CE plane scatters not reported CEACs reported
	Other forms of uncertainty	One-way sensitivity analyses undertaken
<i>Synthesis of evidence on outcomes</i>		Systematic review – mean response rates for each strategy estimated using a multiparameter synthesis model
<i>Assessment of NHS impact</i>		Budget impact assessment not presented

TABLE 10 Summary of economic analysis – fluid-filled thermal balloon and microwave endometrial ablation techniques for heavy menstrual bleeding

Aspect economic evaluation		
<i>Decision problem addressed (from Scope)</i>		Interventions: 4 alternative endometrial ablation procedures, i.e. thermal balloon, microwave, transcervical resection of the endometrium (TCRE) and rollerball Population: women with heavy menstrual bleeding Comparators: hysterectomy
<i>Analytic methods</i>	Type of economic evaluation Modelling methods Time horizon of analysis Perspective on costs Discounting Measure of health benefits Source of quality of life and utility data Probabilistic sensitivity analysis Subgroup analyses Equity considerations Assessment of future research needs	Cost-utility analysis Two Markov models developed – the endometrial ablation model had 8 states and the hysterectomy model had 6 states 10 years NHS and PSS only Benefits at 1.5% and costs at 6% QALYs Published estimates where available or assumption Not performed None None explicitly referred to No formal valuation of information analysis undertaken
<i>Presentation of results</i>	Expected CE results Parameter uncertainty Other forms of uncertainty	Reported CE plane scatters not reported CEACs not reported One-way sensitivity analyses undertaken
<i>Synthesis of evidence on outcomes</i>		Systematic review, using data from RCTs and large observational studies
<i>Assessment of NHS impact</i>		Budget impact calculated using prevalence and incidence information

TABLE 11 Summary of economic analysis – rituximab in the treatment of aggressive non-Hodgkinson's lymphoma

Aspect of economic evaluation		
<i>Decision problem addressed (from Scope)</i>		Intervention: rituximab in combination with CHOP chemotherapy Population: patients with diffuse large B-cell lymphoma in whom CHOP chemotherapy is not contraindicated Comparator: CHOP chemotherapy regimen (cyclophosphamide, doxorubicin, vincristine and prednisolone)
<i>Analytic methods</i>	Type of economic evaluation	Cost-utility analysis
	Modelling methods	Markov model with 3 states (academic team revised model submitted by the manufacturer)
	Time horizon of analysis	15 years
	Perspective on costs	NHS and PSS only
	Discounting	Benefits at 1.5% and costs at 6%
	Measure of health benefits	Life-years and QALYs
	Source of quality of life and utility data	Unpublished study sponsored by the manufacturer
	Probabilistic sensitivity analysis	Performed on relative risk information (log-normal distribution), utilities (uniform distribution), cost components (normal distributions) and proportion using other services (uniform distribution)
	Subgroup analyses	Analyses conducted separately for patients under the age of 60 and patients over 60 years
	Equity considerations	None explicitly referred to
	Assessment of future research needs	Formal valuation of information analysis undertaken
<i>Presentation of results</i>	Expected CE results	Reported
	Parameter uncertainty	CE plane scatter or ellipses not reported CEACs reported
	Other forms of uncertainty	One-way sensitivity analysis and threshold analysis undertaken
<i>Synthesis of evidence on outcomes</i>		Systematic review but estimates of relative treatment effect taken from single (only available) trial
<i>Assessment of NHS impact</i>		Budget impact calculated using prevalence and incidence information

TABLE 12 Summary of economic analysis – imatinib for chromosome-positive chronic myeloid leukaemia (CML)

Aspect of economic evaluation		
<i>Decision problem addressed (from Scope)</i>		Intervention: imatinib Population: patients with chronic phase CML Comparators: hydroxyurea (HU) or interferon-alpha (INF- α)
<i>Analytic methods</i>	Type of economic evaluation Modelling methods Time horizon of analysis Perspective on costs Discounting Measure of health benefits Source of quality of life and utility data Probabilistic sensitivity analysis Sub-group analyses Equity considerations Assessment of future research needs	Cost-utility analysis Two Markov models developed – the HU model had 4 states and the imatinib/INF- α model had 6 states 20 years NHS and PSS only Benefits at 1.5% and costs at 6% Life-years and QALYs Unpublished study sponsored by the manufacturer Performed on relative risk information (log-normal distribution), and utilities (beta distribution) Separate analyses reported for low- and high-risk patient groups None explicitly referred to No formal valuation of information analysis undertaken
<i>Presentation of results</i>	Expected CE results Parameter uncertainty Other forms of uncertainty	Reported CE plane scatters reported CEACs reported One-way sensitivity analyses undertaken
<i>Synthesis of evidence on outcomes</i>		Systematic review but estimates of relative treatment effect of imatinib taken from single (only available) trial and for HU taken from Benelux observational study
<i>Assessment of NHS impact</i>		Budget impact calculated using prevalence and incidence information

TABLE 13 Summary of economic analysis – myocardial perfusion scintigraphy for the diagnosis and management of angina and myocardial infarction

Aspect of economic evaluation		
<i>Decision problem addressed</i>		Interventions: single photon emission computed tomography (SPECT) myocardial perfusion scintigraphy Population: patients with suspected coronary artery disease (CAD) Comparator: stress electrocardiography (ECG) and/or coronary angiography (CA)
<i>Analytic methods</i>	Type of economic evaluation Modelling methods	Cost–utility analysis A decision tree model for the diagnosis decision and a 10-state Markov model for the management of suspected CAD
	Time horizon of analysis	25 years
	Perspective on costs	NHS only
	Discounting	Benefits at 1.5% and costs at 6%
	Measure of health benefits	QALYs
	Source of quality of life and utility data	Published estimates
	Probabilistic sensitivity analysis	Not performed
	Subgroup analyses	Subgroup analysis performed using females only
	Equity considerations	The issue of patient access to SPECT (because it is only available in specialist centres) was raised but not as part of the analysis
	Assessment of future research needs	No formal valuation of information analysis undertaken
<i>Presentation of results</i>	Expected CE results Parameter uncertainty	Reported CE plane scatters not reported CEACs not reported
	Other forms of uncertainty	A series of one-way sensitivity analyses undertaken
<i>Synthesis of evidence on outcomes</i>		Systematic review
<i>Assessment of NHS impact</i>		Budget impact not reported

Appendix 6

Data categories defined for analysis of information pro formas

Product/therapy details	Indications/reason for use of drug/therapy
Add-on or replacement	Evidence of effectiveness/benefits/efficacy
'Advantages'/'justification' for new technology	Licence information
Number of patients to receive treatment	Length of treatment course
Details on guidelines for use/treatment	Implications for primary/secondary care
Judgement on whether a 'therapeutic advance'	Restrictions on who should prescribe
Discussion with/support of colleagues	Clinical experience locally
Other information	Other respondent comments
Previous appraisal by NICE/national guidance	Annual savings
Conflicts of interest	Adverse effects
Cost information:	
• Price	
• Cost impact	
• Savings	
• Comparison with alternatives/current treatment	
Evidence on cost-effectiveness:	
• General details	
• Evidence	
• Usage/cost information	
• Declarations	

Appendix 7

Questions on new drug request pro forma where reference is made to cost-effectiveness information – secondary care organisations

ID number	Questions/comments
5	Are there any published pharmacoeconomic evaluations to support your request? Yes..... No..... If yes, please provide details:
14	The committee requires clear evidence of efficacy, safety, relative efficacy and cost-effectiveness before it can approve the introduction of a new agent
20	Does this drug provide good value for money? Please enclose any supporting information What is the evidence for cost-effectiveness?
24	What will be the cost benefit (£ spent vs £ saved) Cost-effectiveness (£ per unit of health outcome) Cost-utility (£ per QALY) Opportunity cost of using this drug (what could have done instead?)
29	Are there any published pharmacoeconomic evaluations to support your request? Yes..... No..... If yes, please provide details
33	Please indicate how this new drug differs from alternatives already on the formulary Cost-effectiveness
34	Is there evidence that this proposed new treatment is more cost-effective than standard treatment already in use? Yes..... No..... (If yes, please provide supporting references)
39	Give your evaluation of the literature, i.e., a detailed statement of case for including benefits and costs relative to existing treatments available in the trusts. If there is a major cost to the new treatment, please state how this will be funded, if known
40	What evidence in the literature is there to support its: Cost-effectiveness? References:
41	The Panel is interested in the comparative effectiveness and cost-effectiveness of drugs
47	Is there evidence that this proposed new treatment is more cost-effective than standard treatment already in use? Yes.... No.....
52	What are the likely benefits of this product over existing therapy, including any cost-benefit data available
81 & 82	Categorise the perceived cost-effectiveness of the drug: Category: <ul style="list-style-type: none"> • No proven evidence of effectiveness • Proven evidence of effectiveness but other drugs with a better cost-benefit available • Some evidence of effectiveness but not proven – more evidence required • Proven effective, no other drug of similar efficacy, but very high cost • Proven effective, no other drug of similar efficacy, judged to be of marginal cost benefit • Effective, no other drugs of similar efficacy – judged to be cost beneficial

continued

ID number	Questions/comments
115	Indicate how the product proposed for inclusion differs from the alternative(s) by ticking the appropriate boxes and providing additional relevant details. Cost or cost-effectiveness
118	Are there any published pharmacoeconomic evaluations to support your request? Yes.... No.... If yes, please provide details
141	Is there evidence that this proposed new treatment is more cost-effective than standard treatment already in use? Yes.... No.... If yes, please provide supporting references
145	Cost-effectiveness: Is the requested drug regarded as being cost-effective in terms of: (a) a decreased need for supplementary therapy? (b) duration of therapy Also, will adoption of the requested drug permit deletion or reduced use of any other stock drugs?
155/156	New drug application Pharmacoeconomics:
162	Does this drug provide good value for money? Please enclose any supporting information

Appendix 8

Questions on new drug request pro forma where reference is made to cost-effectiveness information – primary care organisations

ID number	Questions/comments
142	Financial considerations Please attach any relevant health economics studies Summarise the financial implications of this drug, where possible linking cost to benefit (for example, £ per life-year gained)
163	Managed entry of new drug framework Cost-utility
181	Financial considerations: Please attach any relevant health economics studies Summarise the financial implications of this drug, where possible linking cost to benefit (for example, £ per life year gained)
201	Pharmacoeconomic data, if any
228	Does this drug provide good value for money? Is there any good-quality evidence that it is more cost-effective than other available interventions? Are the benefits from this drug worth the costs involved?
237	Financial considerations Please attach any relevant health economics studies Summarise the financial implications of this drug, where possible linking cost to benefit (for example, £ per life-year gained, £ per event prevented)
241	Does this drug provide good value for money? Is there any good-quality evidence that it is more cost-effective than other available interventions? Are the benefits from this drug worth the costs involved? What impact would this drug have on the prescribing budget?
249	Does this drug provide good value for money? Is there any good-quality evidence that it is more cost-effective than other available interventions? Are the benefits from this drug worth the costs involved?
264	Financial considerations Please attach any relevant health economics Summarise the financial implications of this drug, where possible linking cost to benefit (for example, £ per life-year gained)
265	Clinical and cost-effectiveness The trust aims to promote both clinically effective and cost-effective prescribing. An economic assessment (e.g. cost-utility, cost-benefit) should be provided where available
269	New product assessment request Financial considerations Please attach any relevant health economics studies Summarise the financial implications of this drug, where possible linking cost to benefit (for example, £ per life-year gained, £ per event possible)
284	Use of resources What will be the: <ul style="list-style-type: none"> • cost-benefit (£ spent vs £ saved) • cost-effectiveness (£ per unit of health outcome) • cost-utility (£ per QALY) • opportunity cost of using this drug (what could have done instead?)

continued

ID number	Questions/comments
288	The aim will be to reach a consensus based on available evidence regarding: the affordability of drug therapies having considered their effectiveness and cost-effectiveness
289	Cost-effectiveness: what is the monthly cost and how does it compare with similar preparations used for the same conditions? (Please attach data from economic evaluations including NNT data and cost per QALY data where available)
308	When looking at new drugs, NICE guidance, etc., the following template is used: cost-effectiveness over existing treatments
320	Does this drug provide good value for money? Is there any good-quality evidence that it is more cost-effective than other available interventions? Are the benefits from this drug worth the costs involved?
NNT, number-needed-to-treat.	

Appendix 9

Reports of local case studies

This appendix reports findings from case studies of local decision-making bodies. The objectives in conducting these case studies were to:

1. investigate the extent to which economic evaluation influences decision-making
2. identify potential barriers to its use
3. explore ways in which these barriers could be overcome.

For each case study, there is a report of research activity and findings. These include:

1. a description of the committee and its place within the local health economy
2. a description of its terms of reference, composition and decision-making responsibilities
3. a report of case study findings, including interviewee perceptions as to the main functions of the committee and the role of members in its decision-making process, and researcher observations and interviewee reflections on:
 - (a) the importance of economic evaluation
 - (b) the barriers to effective use of economic evaluation
 - (c) suggestions as to how these might be overcome.

It is important to emphasise that an appraisal or review of a committee's overall performance was not the intention of the research but rather the part played by economic evaluation or cost-effectiveness information in the decisions each committee takes.

Case study one: County Priorities Committee (South Central England)

Case study one was selected as an example of a priorities network that was specifically concerned with prioritisation of spending on new technologies. In total six meetings were attended by members of the research team, five of which were formally observed. Interviews were conducted with nine committee members.

The committee was established in July 1999 as a mechanism for the rational prioritisation of expenditure on health technologies and treatments within its health economy, and meets monthly. Members of the committee include senior representatives of each NHS Trust and PCT in the area, and other stakeholder organisations such as Community Health Councils (CHCs) (until abolished in 2004) and academic departments. The committee reports directly to each member NHS Trust and PCT. In addition to making recommendations on the introduction of new technologies to the area, the committee has been delegated responsibility for a budget to cover the cost of implementing guidance from NICE. Decisions taken by the committee are returned via their representatives to trust boards which have the freedom to choose whether or not to adopt these, within the constraints of national guidance. New treatments and services will not be commissioned until sufficient funds to implement the policy have been identified. Where the committee recommends a drug or therapy and additional resources have not been identified for the provision of the intervention, the recommendation is passed to one of two Partnership Boards for consideration.

According to its stated terms of reference the committee was set up to support the health system in making priority decisions about what healthcare should be provided in the area, given that resources are limited and services are under increasing pressure. In this pursuit it considers:

- alterations in the priorities of healthcare provision associated with changing patterns of investment or disinvestment
- introduction of new forms of care (including technologies) or reduction of existing forms of care
- specific funding requests where the form of care is unusual and expensive, and where the decision to fund such care may set a precedent for future funding.

(Source: committee policies and procedures document)

In addition to making policy decisions, the committee also decides whether to make

de-prioritised treatments available to individual patients where unusual circumstances pertain.

Topics for consideration by the committee are tabled by all healthcare organisations within the area served. Other committees operating in the area – such as the Priority Case Review Committee and Drug Therapy Committees – may also request that a new technology be considered. Increasingly it was felt by interviewees that the committee’s agenda is influenced by guidance and guidelines published by NICE. Once a topic has been selected, a working group undertakes an appraisal of its evidence base. This group typically comprises relevant primary and secondary care clinicians with support from a public health network. Alternatively, this review is sometimes commissioned externally. This process was summarised by interviewees:

“The standard format has been: a topic will be raised, a small group will be assembled to look at the evidence and to produce a paper, hopefully with recommendations, possibly a draft policy statement to the committee who will then discuss it and then either a second draft or a first draft depending how the original presentation has been made will be written and brought back to the committee for final approval before dissemination.”

(CA 8)

“We will not take any decisions on a paper which has not gone to the committee, either with the minutes or very shortly afterwards, so there’s been a long period to enable people to read and digest it. For example, today we had a paper that was tabled at the meeting, and some discussion was taken but no decisions were allowed.”

(CA 3)

The committee considers the proposed technology in the light of its ethical framework and, through discussion, attempts to achieve a consensus decision. Where consensus is not reached voting can be employed. The key principles of the ethical framework are:

- effectiveness – measured in terms of impact on health outcomes
- fairness – measured in terms of the need for, and capacity to benefit from, healthcare
- patient choice – a commitment to prioritise measures of health outcome considered most important to the recipients of healthcare.

(Source: committee policies and procedures document)

For the purposes of this research, it is important to note that the committee’s key principle of

‘effectiveness’ requires taking into consideration evidence of cost-effectiveness and that where necessary an appropriate cost analysis is performed. Another area where cost-effectiveness data are explicitly requested is the committee’s written guidance to presenters/applicants. According to this document, the presentation should include:

- An introduction to the new technology/new use of a technology.
- Information on current practice within the area, with respect to the technology, including number of patients currently treated and the criteria for treatment.
- An outline of its proposed use, including any staffing or service implication.
- Information on whether the technology is subject to national guidance/priority setting.
- Information on whether the technology will substitute another technology, and its priority within the specific clinical area in the locality, including the extent to which its use could be funded within the current envelope of resource.
- Evidence of effectiveness, including how many, and which categories of, patients will benefit.
- **Cost-effectiveness** of the technology. The guidelines request data from economic evaluations and a cost per QALY estimate where available.
- An equity comparison with treatments from other clinical areas.
- Information on patient choice – the views of individual patients and patient groups.
- Implications of not using the treatment and alternative approaches.
- A financial impact assessment – to be provided by the organisation’s finance department.

Functions of the committee and role of committee members

Committee members were asked, in interview, to state what they considered to be the committee’s main functions. They confirmed that these were to look at the claims and evidence base of new drugs that come onto the market, apply the ethical framework to these and produce guidance notes to PCTs and trusts. This was seen as part of a process of ranking the demands placed on finite resources and advising the county’s health economy on priorities. The committee was also seen as being charged with disinvesting in existing treatments via application of the same criteria. Interviewees highlighted the role of allocating the fixed budget devolved to the committee as well as looking at local implementation of national guidance and the reduction of geographical variation in provision.

Interviewees identified the placing of constraints on the introduction of a new technology – for example, through phased implementation – as a further function of the committee.

Although new treatments in the area of oncology had recently been delegated to the Cancer National Services Framework network, the committee's typical focus was on the appraisal of high-cost pharmacological interventions in the specific locality served. Interview responses made clear that the committee was as concerned with **implementation** of policy as it was with the **evaluation** of new treatments. This meant that decisions had to reflect complex interfaces between primary and secondary care as well as differences between geographical locations within the health economy. Interviewees agreed that despite being charged with evaluating **existing** technologies with a view to disinvestment, this was rarely if ever achieved. The reasons for this were the difficulty in achieving consensus on what to disinvest in and related political difficulties and time and capacity constraints leading to a focus on new technologies and as a result the 'margins' of healthcare expenditure.

Some interviewees expressed concern at the committee's dual functions of making general recommendations to commissioners, and allocating a fixed budget. These interviewees felt that this latter addition to the committee's brief had led to the perception within the county that it was a place to bid for, or a 'distribution network' for, NICE money.

Interviewees were asked what they considered to be their role within the committee. Clinicians – both primary and secondary – identified three aspects to their role:

- representing their trust or PCT
- considering the needs of the health economy as a whole
- providing clinical expertise.

CHC representatives felt that their role was to represent patients and/or to witness that the committee's deliberations were discharged accountably and openly. Other individual committee members also provided specialist advice – for example, on finance and on legal implications of decisions. The Chair of the committee – a position that rotated among PCTs – felt that their role was to ensure that proper and adequate discussion and agreement were achieved.

Information used in decision-making

In the meetings observed by the research team, the committee considered four suggested new treatments and interventions. Three of these were pharmacological agents and the fourth was a request for a more general increase in treatment provision in a specific clinical area.

Written applications attached to the technologies under consideration averaged approximately 10 pages in length and were prepared by clinical consultants and/or other clinical specialists. Committee members expressed concern that one 25-page document did not conform to the requirements of the committee's guidance for applicants. The following information was most commonly included in written applications:

- definition of the problem/condition
- current national policy [National Service Framework (NSF)/NICE]
- current clinical practice
- evidence of clinical benefit of treatment
- assessment of cost of implementation to the local area.

The following was also included, although less routinely:

- information on epidemiology of the disease
- costs – derived from NICE guidance
- predicted cost savings.

We asked interviewees to explain the considerations that most influenced them personally, when considering any given technology. Although responses varied in emphasis, common themes emerged – for example, the key elements of the ethical framework were cited by some. Of these, the most frequently cited factor was evidence of clinical effect. The second most cited factor related to the cost of introducing the product. References to cost varied from the cost of the technology, to its cost-effectiveness and to the cost impact for the health economy area. Some clinicians interviewed preferred to concentrate on clinical evidence. This reflected a reliance on their areas of expertise and a wish to defer to experts in matters of cost and cost-effectiveness. CHC representatives also paid less attention to issues of cost/cost-effectiveness, preferring to concentrate on "patients" or on "the relief of suffering".

Evidence of effectiveness. That's the first thing that one looks at. And then cost-effectiveness.

(CA 8)

We need some clinical evidence that shows us that we as a body should use it ... The second thing we need

is information about the costs and the effectiveness. So we need a lot of information which has in it numbers which are about people, the take up, the cost, the possibility of phasing, the alternatives, all these things. We effectively need a sort of cost model for what we're trying to do."

(CA 3)

"It does include the clinical: what is the clinical data on its impact? What are the likely costs going to be per whatever you use for assessing it? So whether you use cost per QALY or more commonly, what would the cost be for [the committee's entire area] or for a health economy or for a PCT area?"

(CA 5)

"The ethical framework was intended to be applied as a series of filters . . . Having decided whether something is clinically effective and whether it is cost-effective and, we have to be honest, affordable in the health care economy, we also then need to look at whether it's being used in a way that addresses health inequalities, or at the very least treats people with like need fairly."

(CA 9)

Interviewees were then asked to reflect on their perceptions regarding the extent to which different committee members would share their ranking of considerations. Responses again reflect the twin concerns of evidence of clinical effect and cost.

"The first thing that the committee would look at is 'is this an effective treatment?' Because if it's not an effective treatment there's no need to really take the discussion any further, there's no point funding it. If it is an effective treatment then you have to then consider, is this treatment more effective than alternative treatments? Does it cost more or less than other effective treatments and is it therefore cost-effective and good value for money?"

(CA 8)

"I'd like to think I'm as interested in the clinical as the money but obviously my background would mean that I would understand the financial issues much better than the clinical issues. . . . I guess the clinicians would probably have the same two dimensions in their decision-making but probably the clinical would be slightly more prominent for them because obviously they're looking at it from a clinician's perspective."

(CA 1)

A further factor regularly cited as influencing the committee's deliberations was the guidance produced by NICE.

"I just feel we're just looking at things that bring their head above the parapet either because they're NICE

generated or they're something that the providers have a particular issue with. And it's getting into the whole mass of things below that really . . . but it's quite difficult with the workload we've got."

(CA 1)

"We will come to a stage when the cost of NICE absorbs so much of the fixed prescribing budget in any one health authority, that its discretion for the remainder will have become increasing compacted . . . and that means for all its perceptions of clinical needs in the community [the committee] will have increasingly less freedom to do what it thinks is right."

(CA 2)

The committee was seen as increasingly dealing with NICE guidance and how to implement this within the area. The distribution of funds allocated to the implementation of NICE guidance was seen as an expanding aspect of the committee's work.

Through observation of committee meetings, the research team was able to compare these responses with actual instances of committee decision-making. Typically, technologies under consideration were the subject of verbal presentations which varied in length. These presentations offered further information. Most commonly this included:

- further information derived from NICE guidance, including QALY estimates in two instances
- details of baseline costs of the technology
- further clinical data
- estimates of likely patient numbers
- further issues in delivery of proposed intervention.

In one case, the product manufacturer had conducted an economic evaluation for the area including projected savings to the economy.

Presentations were followed by questions and discussion. The most commonly raised issues here included:

- specific implications of NICE guidance and how this would be implemented
- implementation issues regarding the interface between primary and secondary care
- affordability issues and budget limits.

Other questions raised concerned the shortage of data and concerns with regard to potential bias in sources of data.

In one case, it was decided that the committee was in a position to recommend that the application be approved. In two cases, the decision was deferred pending the generation of further analysis. In one of these cases, this specifically required the input of health economics expertise. The committee agreed to set up a working group to look more closely at the fourth application. In this small sample, the most common outcome of the committee's first consideration of a new application was to defer the decision until more information and analysis were available.

The committee clearly received substantive amounts of information on the technologies that it was considering. This information ranged from current national guidance, through evidence of clinical effect, to a variety of cost data including cost of implementation for the area. Presentations and discussion re-established these areas of focus and reflected the specific concerns of representatives of different sectors and areas within the health economy. Interviewee responses reflected the committee's ethical framework, with evidence of clinical effect the first and most important 'filter' followed by other factors such as cost and issues in implementation of decisions.

Use of economic evaluation

As we have seen, the committee requests information on the cost-effectiveness of an intervention from presenters and includes cost-effectiveness within its key principle of effectiveness. Members of the committee who were interviewed were asked to reflect on the types of economic evaluation they received. One recently recruited committee member indicated that cost-effectiveness measures were regularly included and that QALY estimates were attached to the majority of applications she had seen. However, another interviewee felt that cost data received tended to be restricted to the price of the product in question. Most interviewees felt that cost analyses presented to the committee tended to focus more on a cost impact assessment for the larger area. Responses from interviewees seemed to suggest a lack of consistency in the types of economic evaluations accessed, possibly reflecting in part interviewees' differing definitions of what constitutes 'economic evaluation'.

"You get (information) presented all the way from extremely specific – which is based on epidemiological data for our area and take-up which comes from patient lists, so we know that it's going to be very specifically for our particular areas, and what the consequences are going to be for us – right the way through the spectrum to data which is based on

national figures and looks very vaguely at QALYs and those sort of things. You just have to accept you're going to get this very broad range."

(CA 3)

"I think the economic evaluation model comes as part of the package. So rather than 'we're now going to do an economic evaluation', it's something I'd expect to just pick up on by saying 'what are the benefits of this?' and I'd want to see that expressed in some kind of model. Could be QALYs, could be life saved per whatever. It could be whatever modelling you might want to use."

(CA 5)

"A weakness I think is that it's bottom line cost, not total cost. It's purely the cost of the drugs that we're looking at. We don't even look at the cost of the delivery systems."

(CA 6)

"Essentially we're usually looking at a cost-benefit calculation in terms of events prevented per pound. We very rarely look at cost-utility calculations, mostly because they're not available, and they're quite often very difficult to do. Occasionally we may get QALY-type stuff, but it's usually straight numbers of lives saved per pounds spent, or numbers of admissions avoided per pound spent."

(CA 9)

Where full economic evaluations – for example with a cost per QALY calculation included – were accessed, the primary sources of these were reported as being the manufacturers of the product and NICE guidance. Interviewees also pointed to the activities of a previous committee member who had some health economics expertise and who had accessed or generated evaluations whilst on the committee.

Having earlier detailed the considerations that most influenced them, interviewees were questioned specifically on the **importance** they attached to economic evaluation information when considering an application. Interviewees, on the whole, reiterated that cost and/or cost-effectiveness was an important consideration. Apart from one interviewee, none saw this as important enough to override evidence of clinical effect or the ethical principle of the rule of rescue. Although responses were influenced by differing definitions of cost-effectiveness, a small number of interviewees identified situations in which economic evaluation takes on increased importance – for example, when comparing across technologies and disease groups. In these situations economic evaluation was seen as providing a currency – for example QALYs – with which to make broad comparisons. Overall, it could be said that economic evaluation

– or more accurately the principles of cost-effectiveness – were seen as important in the committee’s deliberations but by no means the primary, or in some cases even a major, driver of decisions.

“The thing is, I think everybody’s concerned with the costs, but I suspect we have slightly different views of what constitutes economic evaluation. But we are all concerned with money, everyone in the health service is, and we are all concerned with clinical effectiveness, and we’re being told to be concerned with patient choice.”

(CA 9)

Levels of understanding of health economics

Responses to the question, ‘do you feel you understand the economic evaluation presented to the committee?’ seemed to suggest a lack of expertise in this area. Although a small number of interviewees expressed concern at their subsequent difficulty in critiquing economic evaluations – especially those provided by sponsors of the technology – the majority were happy for critiques to be carried out by experts.

“I’ve not done enough research into where a QALY comes from to understand the econometrics behind that but I’m quite comfortable with the fact there is a measure ... the fact that I know that it has been modelled in some way and we’re consistently modelling all of the processes then I feel that I don’t need to understand it any more than that really.”

(CA 1)

“Could I sit and describe to you precisely what modelling went into a QALY? No I couldn’t. Could I sit and say that I have an appreciation of what a QALY means? Yes I could. It’s a bit like yes, I can tell the time, but I’ve no interest in knowing how a watch works.”

(CA 5)

“I understand the general principles but I am not an economist, and I am very glad for advice from those who have better understanding than I.”

(CA 9)

At the time of the case study, committee members with skills in this area were not attending meetings. Observations of meetings seemed to suggest that this presented the committee with difficulties when processing economic evaluation information.

Barriers to use of economic evaluation

Research findings suggest that the committee’s use of economic evaluation in the meetings observed was patchy. Much of the economic evaluation used

derived from NICE guidance and the manufacturers of technologies. Although interviewees were aware of previous instances where analyses had been commissioned externally, the facility for pursuing this approach seemed to be limited at the time of the case study. This may have been an effect of the committee losing a key member of its information-providing team shortly before the case study was started. This appeared to have the two-fold effect of reducing the committee’s ability to **access** extant published evaluations, and reducing its capacity to **interpret critically** the analyses they did receive. These two aspects of the accessibility of economic evaluation – its availability at the time of need, and the capacity to understand and apply its recommendations – represented the initial barriers to its impact on decision-making.

Do we have a structured approach to looking at how we model these things? I think the answer is ‘no’. What we tend to rely on is the other organisations that have done this analysis, so very often what we’re using is that analysis ... We may not have postcode prescribing anymore, we actually have postcode analysis.”

(CA 5)

I think sometimes the figures are not as robust as they might be ... I think a weakness is that sometimes the underlying assumptions on which that presentation is made may not be very robust, often because the figures aren’t available.”

(CA 8)

A number of further barriers pertaining to the acceptability of economic evaluation emerged from the research. These revolved around the extent to which interviewees felt able or inclined to follow recommendations of economic evaluations. As we have seen, some economic analysis was made available to the committee via the sponsors and manufacturers of technologies. However, committee members were less inclined to accept the recommendations of these as valid. This was a result of concerns about the assumed inclination to present the product in a positive light. These concerns over potential bias were commonly cited by interviewees. Other factors affecting the ‘acceptability’ of economic evaluations included excessive variation in health economics methodologies, concerns about the robustness of analyses, or appropriateness of the comparators used, problems relating to the inability to actually realise savings identified in analyses and, finally, ethical objections to the perceived underlying values of health economics.

Improving use of economic evaluation

Despite reported limits to levels of understanding of health economics, committee members were asked for their views on whether they would like to see more or less economic evaluation information made available to aid the decisions they make. Responses were split between those who felt what the committee received currently was sufficient and those who saw room for more. No interviewee expressed a wish for a reduction in economic information. The need for greater levels of disinvestment was seen as a major reason for increased use of economic evaluation, although one interviewee speculated on the potential loss of freedom for decision-makers should recommendations of economic evaluations be followed in decision-making.

“I am generally happy with the level that there is. I mean there are one or two cases where we didn't have enough but generally it seems to be the right balance. I think usually the benefits are very self evident and most people are happy to support it. It's if it needs a lot of digging because it's very marginal. Those are the ones that we have a bit of difficulty and refer back a few times.”

(CA 1)

“I think overall, it's not bad. I don't think there's a lot more that I would want to see. It would be useful to have more information just occasionally in some specific areas but that's usually the hard to get information that's missing and it may just not be possible.”

(CA 8)

“I think the committee on the whole would like more economic evaluation, and a bit of understanding, a little bit of training around it.”

(CA 9)

Some interviewees also pointed to mechanisms for improving the committee's use of economic evaluation. These tended to centre on the need for an enhanced process of production and consumption of analyses.

“It would be very helpful to have a standard way of doing it and if there are going to be variations let us know what the variations are going to be. If you could develop something of that sort, a framework.”

(CA 2)

“We need some way of getting behind evaluations to be able to say 'although the drugs company says A, B, C, D and E, actually what this means in particular is this'. So we do need some kind of independent rigour, but the key bit is that that gets presented in the way that the committee can understand.”

(CA 5)

“[We need] a very early involvement, where a particular prioritisation question warrants it of somebody who has got sufficient economic background to say: 'If we really want to compare X and Y, what are the robust ways of doing it?'”

(CA 9)

As indicated earlier, a number of interviewee reflections on the committee emerged that were not exclusively within the remit of the research question. In particular these were: the difficulty and rarity of disinvestment in existing technologies; concerns about confusion in the committee's primary role, as a result of restructuring of the local health economy, and devolvement to the committee of a NICE implementation budget; and the restriction of operating on a county basis and the subsequent need to pool resources on a wider scale – to have a 'common engine room'. This would reduce 'postcode analysis' and increase capacity in production of economic evaluations.

Summary

1. The committee was established in 1999 as a mechanism for the rational prioritisation of expenditure on health technologies and treatments within its health economy and works with an ethical framework to make its decisions.
2. In addition to applying decision criteria, issues regarding implementation of its decision, including budgetary aspects, are reviewed.
3. The primary factors influencing the decisions are evidence of a technology's clinical benefit to patients and the cost implications of its introduction.
4. Main sources of written health economics are the manufacturers of technologies under consideration, and guidance produced by NICE.
5. The committee has previously contained members with health economics expertise although not at the time of research.
6. Barriers to use of economic evaluation include:
 - (a) Limited access to economic evaluation – including its availability at the time of need and the committee's capacity to understand and apply its recommendations. This was the most cited barrier to its use in decision-making.
 - (b) Concerns regarding the potential for biased analyses.
 - (c) Excessive variation in health economics methodologies.
 - (d) Concerns about the robustness of analyses, or appropriateness of the comparators used.

- (e) Problems relating to the inability to realise savings identified in analyses.
 - (f) Ethical objections to the perceived underlying values of health economics.
7. Strategies for improving or maximising the use of economic evaluation suggested by committee members include:
- (a) The need for a clear, standardised and generally accepted format for the presentation of economic analysis.
 - (b) Training for committee members (although this was not unanimously supported).
 - (c) The co-opting on to the committee of health economics expertise in cases where this was required.

Case study two: hospital Medicines Management Committee (North West England)

Case study two was selected as an example of a Medicines Management Committee (MMC) in a large, urban teaching hospital. In total three meetings were attended by members of the research team, two of which were formally observed. Interviews were conducted with eight committee members.

This case study was of an MMC in a large NHS Teaching Trust in an urban area of the UK. At the time of research the committee made decisions on behalf of the entire trust, which was in the early stages of merging two formularies. From within the trust, committee membership consisted of hospital pharmacists, a small medicines management team and a representative of each clinical directorate. The committee decided what technologies were introduced on to the trust formularies but did not control the budget for new technologies – this authority resided with individual directorates. Membership from outside of the trust included academic and primary care representatives. The committee liaised with individual PCT prescribing groups and with a prescribing strategy group that addressed issues of prescribing across a broader area. Meetings of the MMC took place monthly and lasted for approximately 2 hours.

The process followed by the committee has a number of stages. Currently, applications for the introduction of a technology are made by consultants within the trust. A form is completed by the applicant detailing the proposed formulary addition or other therapy. This needs to include the signature of the appropriate directorate

accountant indicating that money for the new technology is available within the directorate budget. This information is passed to the Medicines Information Manager, who is a member of the MMC.

The trust is involved in a large number of trials and as a result the committee will be aware in advance of some technologies that are likely to be coming before the committee. If the proposed formulary addition represents a new therapeutic area this will have to be presented to the trust in the form of a business case and may go before a separate clinical practice committee before coming to the MMC. At this stage inclusion on the formulary requires an application to the MMC. Before an application is considered, the Medicines Information Manager carries out a short literature search and review of evidence. These two documents are then circulated to committee members. The application is tabled at the next committee meeting where the applicant makes a short presentation that is followed by questions. A policy is in place for the regular reviewing of decisions after their implementation.

The application form attached to each proposed addition to the formulary is one page in length, although work was under way to develop a more detailed replacement. The form required information on:

- details of the new technology
- judgement as to whether it constitutes a minor or major therapeutic advance
- whether it replaces another treatment
- the drug's advantages (with references where possible)
- the grading and strength of supporting evidence
- the cost of treatment (per day)
- the estimated duration of treatment
- the estimated number of patients to be treated per year
- the likely impact of the introduction on primary care
- declarations of interests from the applicant.

The subsequent review conducted by the Medicines Information Manager draws data from any available sources, for example, existing published guidance and assessments. The review highlights factors such as:

- the quality of the published evidence
- the number of patients/centres involved in trials

- whether the trial was sponsored by the manufacturer of the drug
- what costs attached to the technology.

This information is then made available to committee members to inform their deliberations.

Functions of the committee and role of committee members

Interviewees specified the following functions of the committee:

1. Managing the introduction of new drugs/medicines.
This was seen as involving assessment of new drugs for addition onto the trust's formularies, and reviewing existing technologies. The committee provided a 'rational' approach to the introduction of new treatments and medicines.
2. Controlling prescribing within and across the trust.
The committee was seen as having a crucial role in 'maintaining a handle' on and 'regulating' the prescription and use of medicines within the hospital. This involved the ratification of guidelines and prescribing policies across the trust.
3. Influencing prescribing within primary care.
The committee was seen as playing a role in 'advising on prescribing generally', including taking account of the impact on primary care prescribing. This involved liaising with both PCTs and a local mental health trust as part of 'making sure prescribing policies become more congruent across the interface', for example through the use of shared care policies.

Other functions mentioned less often by interviewees included: looking at re-evaluation of, and where appropriate, disinvestment in older treatments and 'drug families', allowing 'clinical practice development', and discussing the implications of NICE guidance.

In discharging these duties the committee were seen as routinely deciding on the following:

- whether or not to include medicines on the formularies, and therefore to 'pass things for use within the trust'
- how to include new treatments and medicines: for example, whether to restrict its use to a single consultant, clinic or team, or alternatively to allow its use across the whole trust

- whether to produce or adopt guidelines for use of new drugs
- whether to develop strategies for contingencies – for example, in cases where drugs are not licensed or licensed for other purpose
- whether to develop algorithms of how new treatments fit in with others.

Committee members were asked to describe what they considered to be their particular role on the committee. Clinicians reported their primary contribution as being to analyse and test the validity of new applications. This role was informed by their clinical expertise. Other members – such as the academic representative – also saw their primary role as testing the validity of applications, albeit not from a clinical perspective. The self-reported role of the primary care representative was to raise awareness of repercussions of decisions for primary care. Members of the medicines management team reported specific duties such as conducting the review and liaising with applicants.

Information used in decision-making

The completed application form is frequently supplemented by information identified in searches carried out by the Medicines Information Manager. This may concentrate on issues such as clinical efficacy and safety, cost and cost-effectiveness.

Interviewees were asked what considerations most influenced them and the committee when assessing an application. Interviewees unanimously cited the importance of the review carried out by the Medicines Information Manager when considering a new drug in order for decisions taken to be evidence based. Within this, data relating to clinical effect were considered most influential and cost was the second most frequently cited factor.

"For me it's about the clinical benefits of a drug: are they really demonstrated as being much better than what we've got already? What is the quality of the evidence?"

(CB 4)

"Well basically the quality of the published evidence. The published trials: the number of patients involved, the number of centres involved, preferably fewer rather than greater, whether the trial was sponsored by the manufacturer of the drug. Cost is obviously something that needs to be considered these days."

(CB 2)

"Ultimately we are asked to judge a product based on the evidence that it is a product that is efficacious,

and in balance with the cost – that always comes into it unfortunately To tell you the truth I tend to switch off when it comes to the cost side. If there's good data on a drug then I'll listen to that and then the cost side of things is to me irrelevant if there is true efficacy.”

(CB 3)

Clinicians on the committee were most likely to cite the value of discussion and the input of clinical experts – especially those clinical consultants making the presentations. In some cases this was granted weight equivalent to the written evidence.

“We have the initial written application to read before we actually go to committee and a chance to look at background literature that comes round with it But I actually find it more useful to be in the meeting setting and hear from the clinician who wants to use the preparation. the rationale for using. I have respect for their clinical judgement within their own area of expertise and I put a lot of emphasis on that.”

(CB 6)

The main area of differential emphasis amongst committee members that interviewees identified concerned the relative importance attached to cost and clinical effect. This was attributed to the different priorities of hospital clinicians and other committee members.

“Other committee members, some of my colleagues in general practice, will have a much greater slant on the economic impact than myself. I and a lot of the other practising clinicians who are hospital-based consultants have very much a view that if it's a drug that is going to benefit the patient then I don't really care what it costs. And I want it to be used.”

(CB 3)

“I am not a clinical pharmacist so I would tend to look to my clinical medicines information colleagues to be really putting the argument about the clinical benefits.”

(CB 4)

“I think most of the clinicians – I mean it's a huge generalisation because they're not all the same – but quite a lot of the clinicians only look at the clinical effectiveness data So I would say that a lot of them don't take into account cost.”

(CB 7)

Interviewees cited other factors that at times influenced decisions taken. These included data on implications for primary care, the prevalence of a condition within the population of the area and practical implications of introducing a new

technology. It was suggested that NICE guidance was influential where this existed. However, as the committee did not make decisions in the area of oncology, NICE guidance on cancer treatments was not used.

Interview responses seemed to suggest that the approach to decision-making adopted by the committee did not permit the development of precedent or case law to inform prospective recommendations. Therefore, each application was considered on its merits, effectively from a 'blank slate' position. In this context, it was felt that the committee was more susceptible than it otherwise would be to powerful personalities on, or attending, the committee. Similarly, some interviewees felt that the requirement to avoid conflict with senior hospital staff influenced the decision-making process.

Through observation of committee meetings, the research team were able to compare these responses to actual instances of committee decision-making. A member of the research team attended two consecutive MMC meetings and was given access to the papers distributed to committee members. A total of 12 applications were discussed over the course of the two meetings. These were mainly for new drugs, or new uses of drugs, but also included a small number of devices. Concerns were expressed at the sheer volume of new applications – especially drugs – presented to the committee and the limited time left for its other duties.

Presentations from applicants usually lasted between 3 and 5 minutes. These were followed by questions from committee members. In general, presentations focused on the clinical benefits of the new treatment and its proposed use within the trust. Questions most commonly asked concerned:

- Whether the new technology would replace an existing technology, enabling dis-investment. In every instance where this was asked, except one, the applicant preferred to retain all existing treatment options.
- The implications of introducing the technology for primary care practitioners and primary care budgets.
- Whether the new drug had an established place within a treatment protocol or algorithm.
- The limits to, or dearth of, data on clinical effect.
- The cost of the treatment – for example, compared with current therapies.

Other issues raised included whether money had been made available for the new technology, issues of drug interaction and the influence of drug companies on applications and costs.

Of 12 applications put to the committee, two – pertaining to the same drug – were refused. The other 10 were approved subject to conditions and constraints imposed by the committee. These restrictions included:

- locating the new technology within a treatment algorithm for prescribers
- agreeing to review the decision when more data become available including as a result of a proposed RCT
- restricting prescribing rights to a clinical specialty within the trust.

Data derived from both interviews and observation suggest that the committee took an interest in the cost of any proposed technology, but that for many committee members this was considered less important than evidence of clinical effect. Cost data available to the committee included cost per patient figures and an estimation of likely patient numbers. Committee discussion frequently focused on the implications of decisions for primary care budgets. Committee members were aware that their decisions would have implications for the price setting of the manufacturers of technologies and took this into consideration when making those decisions.

The most frequent outcome of the committee's decision-making process was a qualified 'yes'. The committee employed guidelines and treatment algorithms as a mechanism to control prescribing. These were the primary mechanisms through which the committee strove to manage rationally the introduction of new drugs, control prescribing and manage the interface with primary care. There was no evidence that these caveats routinely included information on cost or cost-effectiveness.

Use of economic evaluation/levels of understanding of health economics

Findings indicate that the committee accessed cost data and took account of the budgetary implications of their decisions, for both secondary and primary care. As we have seen, the committee explicitly required applicants to supply information on the cost of a new treatment. They also sought to forecast the possible cost impact of introducing a new treatment by estimating the likely number of patients and prescribers. The Medicines Information Manager attempted to

supply this information where it had not already been provided. Interviewees also confirmed that discussion of a new drug would cover the issue of cost implications for primary care services. However, the primary focus of the research was the extent to which the committee used **economic evaluation**, as defined in the introduction. In interview, committee members were questioned about the extent to which health economics information was accessed, used and understood by the committee. Where appropriate, committee members were asked to reflect on strengths and weakness of economic evaluation and barriers to its use.

Despite the limits of using QALYs as a proxy for health economics, interviewee responses seem to indicate that most committee members had had little or no exposure to, and understanding of, economic evaluation. Responses suggested that all of the interviewees had at least 'heard of' QALYs. However, only two respondents reported a familiarity with them, and of these only one felt they had a detailed appreciation of how they are constructed.

The application form completed for new treatments did not specifically request evidence of **cost-effectiveness**. Interviews with committee members suggested that economic evaluations on new technologies were rarely if ever made available to the committee. Of the two interviewees with an understanding of health economics, neither could recall an instance where the committee had access to a relevant, published evaluation that had influenced a decision.

"I've not actually come across many situations where I've thought 'well actually there's a really good economic evaluation here which we should apply to this particular decision'. That doesn't happen that often ... I think we would just use what was out there, if there's an up to date published trial and economic evaluation and I'm just racking my brain to try and think of a situation where we've had one and I don't think we have actually, to be honest."

(CB 7)

For reasons of resource capacity, the committee were not able to commission *de novo* economic evaluations of the technologies they were considering. As a result, their use of economic evaluation would necessarily be restricted to accessing pre-existing literature. Interview responses suggested that such studies were not routinely identified and accessed. The Medicines Information Manager was aware of pharmacoeconomic journals, and interviewees

were aware that NICE guidance on new technologies included an appraisal of their cost-effectiveness. Manufacturers of new drugs were also seen as increasingly promoting the ‘economic’ benefits of their products:

“Increasingly drug companies are taking a more global picture in the formulary packs that they provide. They try and show the global advantage of using their particular product in terms of reducing knock-on costs, perhaps bed occupancy, length of hospital stay, getting them out of intensive care a day or two earlier.”

(CB 2)

Despite these actual and potential sources of economic evaluation, evidence of usage by the committee remained negligible. Both interviews and observations of committee meetings suggest a limited recourse to use of health economics in committee decision-making. References to published cost-effectiveness analyses were rare in committee discussion, and actual accessing of these did not occur in the course of the observed meetings.

Health economics input into decision-making appeared to be mainly restricted to the interventions of the committee’s academic representative, who attempted to address the combination of clinical effect and cost, and thereby to understand the incremental effectiveness of the technology and the degree of uncertainty around this. This application of the principles of health economics was, however, rarely supported with formal analyses. The academic representative was not present at the two observed meetings.

Barriers to use of economic evaluation

As we have seen, research findings suggested that the committee’s use of economic evaluation was hindered, in part, by problems of **access**. The data made available to committee members did not include a full assessment of cost and effect.

“Quite often the only costs that they get would be the clinician’s estimation of the cost per year and the clinician’s estimation of the number of patients per year. So that will be it for the cost and it won’t be integrated with any effectiveness data. And sometimes effectiveness data isn’t particularly well characterised.”

(CB 7)

It is unrealistic for committees of this type to expend the time and resources required to generate economic evaluation for every application they receive and as we have seen,

interviewees felt that relevant published material was rarely available. The problem of access was compounded by strict timelines to which the organisation was subject:

“The big problem is that most of the applications we get for drugs are at the time they are first launched and such data really doesn’t exist at that point other than guesstimates from the drug companies.”

(CB 2)

“They need to be available at the time when new drugs are being applied for. They’re not timely enough. You might have an economic evaluation two years after a drug’s launched but for teaching hospitals where we’re presumably early initiators, they’re not there quick enough.”

(CB 4)

The ‘accessibility’ of health economics studies was further reduced as committee members in general reported only a minimal awareness and understanding of the subject. These two aspects of the accessibility of economic evaluation – its availability at the time of need, and the capacity to understand and apply its recommendations – represented the initial barriers to its impact on decision-making.

A number of further barriers pertaining to the acceptability of economic evaluation emerged from the research. These revolved around the extent to which interviewees felt able or inclined to **implement** recommendations of economic evaluations. As we have seen, some economic analysis was made available to the committee via the sponsors and manufacturers of technologies. However, committee members were less inclined to accept the recommendations of these as valid. This was a result of concerns about the assumed inclination to present the product in a positive light. This was underwritten by a concern to ‘protect’ the trust and the committee from targeted sales techniques of pharmaceutical company representatives. This had already led the committee to impose restrictions on the process of applying for committee approval. Therefore, perceptions of the objectivity of economic evaluations were important in determining the extent to which they influenced the committee’s deliberations.

Where interviewees had accessed economic evaluations, further difficulties of implementation of recommendations were identified.

“I would say we probably don’t use economic data enough but the clinical application of using economic

data is a difficult concept to introduce because a lot of the economic data looks at savings which can't be realised. ... And the fact also that some of the ones that I've seen tend to produce benefits twenty years downstream which okay can be costed back to how much that will save us on a yearly basis but budgets don't work in twenty year cycles. We are in annual or, at best, three-year cycles so it needs to realise benefits within that very short time-scale."

(CB 4)

The perception that economic evaluation is driven by the imperative of reducing spending was also seen as a potential barrier to its use:

"I am sure it would be useful to have more economic information. The problem I think is going to be one of perception by the consultants that sometimes they're a bit like boys with a new toy. They want something new to play with and they don't, in some circumstances, want to be confused by too many facts. And if it were perceived that the committee was putting a very heavy emphasis on cost rather than effectiveness or innovation, then I think that would be viewed in a negative light."

(CB 2)

"To be realistic I almost think the term needs to be from talking about economics. A lot of clinicians think that pharmacy's all about money, that's really all we're concerned about, and if you say 'economics' well that's money really. So it's difficult to actually try and get away from looking at benefits to the patient without tying those to a financial element."

(CB 4)

This second order of barriers to the **acceptability** of economic evaluation featured less prominently in interviews. This could be a result of barriers to its **accessibility** that arise chronologically earlier in the decision-making process.

Improving the committee's use

Respondents were asked whether they would like to see more economic evaluation. Although, in general, this suggestion was greeted positively, clearly this was difficult for them to assess given the lack of exposure to health economics hitherto.

"I feel it would be useful to be sent out to give you a good background for going into discussion. I think perhaps it may be a little too difficult to have at the meeting but it would nice to have something behind the meeting to be sent out. I think it would be very useful to have as sort of pre-reading."

(CB 5)

"I don't really know to be honest. I don't know enough about health economics to know if it would influence us within that setting."

(CB 6)

Committee members pointed to the need for recommendations that were understandable and/or assistance in processing these.

"It's got to be clear and quite simple. I'm not saying that we're thick because we're not but it would be nice to have something that you could look at straight away and say 'that means that'. I suppose to have an element in the pre-reading and maybe to have somebody as a representative at the meeting would be useful. To actually have somebody there to give the global economic picture that is seen from both primary and secondary care would probably be quite powerful."

(CB 5)

"We have actually talked about providing [the committee] with training in how to interpret systematic reviews and clinical trials and to explain to them how to understand economic evaluation. ... I know there have been discussions about having training sessions for all the committee members, so that's one way that we could go forward. ... basically to say 'Look this is what you've got to do in order to make these decisions. You've got to have these skills. You've got to understand these techniques'."

(CB 7)

Summary

1. The primary factor influencing decisions is evidence of a technology's clinical benefit to patients.
2. Cost implications and a range of other considerations also affect decisions taken.
3. The main sources of written health economics are the manufacturers of technologies under consideration and guidance produced by NICE.
4. The committee has a member with some health economics expertise.
5. Reasons for the current limited impact of economic evaluation on decisions are:
 - (a) difficulties experienced by the committee in accessing studies, especially within the time-frame of the decision-making process
 - (b) difficulties with interpreting the analyses performed in economic evaluations
 - (c) barriers to implementation of savings identified in economic evaluations
 - (d) other objections to the approaches adopted by health economics
 - (e) concerns regarding bias in economic evaluation.
6. Suggested strategies for improving or maximising the use of economic evaluation included:
 - (a) the need for the provision of clear, timely and relevant studies, and
 - (b) the need for training of committee members.

Case study three: primary care area Medicines Management Committee (Midlands, England)

Case study three was selected as an example of a recently formed decision-making committee operating primarily within primary care. In total three meetings were attended by members of the research team, two of which were formally observed. Interviews were conducted with nine committee members.

This committee was established in 2002 “to provide strategic leadership and advice on the safe, effective and efficient management of medicines, taking into account the impact on the entire health economy ... and its stakeholders” (source: committee constitution). The committee meets bimonthly and seeks to draw members from all key stakeholder organisations within the health economy, including pharmacists, PCT prescribing leads, secondary care consultants and specialists in pharmaceutical public health.

According to its stated terms of reference the committee was set up with the following key responsibilities:

1. The production and maintenance of an integrated medicines management strategy for the ... Economy which is responsive to local and national policy and which will support the PCTs and trust in meeting relevant targets.
2. The management of the ‘... Recommended Drugs and Medicines Management Policy’, including the new products application process (except those which are hospital only and will be considered by the hospital Drugs and Therapeutics Committee).
3. To provide a local consensus on the place in treatment of new products or changes in product licence for medicines that could be used across the ... health economy.
4. Horizon scanning for products in development or current research which may influence the use of medicines and advise on the local implications and management of such developments.
5. To support the PCTs and trust in prioritising investment in new drug technologies, taking into account the impact on the health of the ... population and associated costs.
6. To produce and/or approve guidelines and protocols, including medicines management aspects of NSF, to facilitate the sharing of

good practice, including Patient Group Directions and the provision of expert advice in the development of organisation specific guidelines and protocols when requested.

7. Provision of an effective forum for resolving problems in prescribing and medicines management at the primary–secondary care interface, e.g. Essential Shared Care Arrangements.
8. Provision of advice on the management of risks associated with medicines use and the systems for reporting errors, identifying trends and learning from mistakes.
9. Provision of advice on the content of elements of contracts/service level agreements which are relevant to medicines management.
10. Communication of recommendations and decisions to stakeholders in a timely fashion.

(Source: committee constitution)

The committee reports to the PCT Professional Executive Committees (PECs) and the hospital Clinical Governance Committee on a quarterly basis. The committee’s role is advisory and “it is the responsibility of the clinical directorate or the PCT to consider the clinical and financial implications of adopting a new drug treatment, following the provision of advice from the case study committee. In certain cases, this may necessitate a business case for funding or the Directorate/PCT may decide against making the medicine available.”

(Source: committee guidance)

Applicants are required to submit a five-page summary of the evidence. This should include:

1. general information on the technology in question
2. its intended use and licence information
3. information on potential to replace an existing technology
4. the proposed place of the new technology within current treatment
5. information on who will prescribe the technology
6. the number of expected patients to receive the treatment in primary and secondary care
7. the advantages over current treatment
8. evidence of efficacy (including grading of this evidence)
9. information on numbers-needed-to-treat
10. evidence for safety and tolerability, including numbers-needed-to-harm
11. conflicts of interest
12. the signature of the appropriate clinical director/PCT prescribing lead

13. Financial considerations including:
- cost of the product per year
 - cost of existing treatments per year.
 - estimated additional annual cost to primary care drugs budgets
 - estimated additional cost to secondary care drugs budgets.

In addition, it is requested that 'relevant health economics studies' be attached and that details of non-drug costs (for example, other health resources such as pathology, outpatients department or wider considerations such as ability to work) are included. This is followed by an explicit requirement to summarise the financial implications of this drug, where possible linking cost to benefit (for example, cost per life-year gained, cost per event prevented). Potential applicants are provided with in-depth guidance notes on how to complete the form. In the guidance, applicants are asked to "where possible provide an indication of cost-benefit (all financial terms), cost-effectiveness (cost per impact, e.g. life-year saved) or cost-utility (e.g. cost per QALY)."

Functions of the committee and role of committee members

Committee members were asked, in interview, to state what they considered to be the committee's main functions. Respondents unanimously emphasised the primary function of adopting a **health economy**-wide perspective on the use of medicines. This was seen as the primary area of difference from other committees operating with more specific terms of reference within local health economy.

Functions commonly cited by interviewees include:

- Medicines management across the local health economy including both primary and secondary care. This was seen as involving the development, where appropriate, of guidelines, protocols and procedures in relation to prescribing, and reviewing both new and current therapeutic practice.
- Making decisions on new product requests from a health-economy perspective. This was seen to involve new product assessment and some management of formularies. Interviewees emphasised the responsibility of ensuring the managed entry of a new drug and establishing whether there is both a sufficiently robust evidence base and a safe and effective ladder of treatment.
- The reviewing of 'essential shared-care agreements'. This was frequently cited as a key function of the committee.

Functions less frequently cited included horizon scanning, standardising care for patients in the stakeholder area, trouble-shooting in situations where inappropriate practices in relation to prescribing are taking place and exercising general control over prescribing.

Interviewees were asked what they considered to be their role within the committee. The Secretary and Chair – both pharmaceutical public health specialists – saw their role as ensuring the required process is followed. The Secretary oversees the agenda and minutes and, in particular, leads on communication with interested parties within primary care. The Chair sought to enable full and fair discussion and to ensure that a decision was reached. Other interviewees pointed to areas of specific expertise and input – for example, generating and sharing information, and raising prescribing issues relating to nurses. Each of the clinicians interviewed described a similar, dual role which combined input on behalf of the whole health economy with a specific brief to represent their organisation and healthcare sector.

Committee members felt they had areas of expertise that they brought to bear on decisions taken. One GP considered their primary role to be that of feeding the committee's recommendations to other practitioners within primary care.

Information used in decision-making

In the meetings observed by the research team, the committee considered two 'new products', both pharmacological agents. Other activities undertaken – for example, reviewing previous guidance and developing policies – were not included within the research focus.

Written applications attached to the technologies under consideration were 29 and 17 pages in length, including attached papers, and in each case were presented by a hospital consultant. The longer document consisted of the five-page application form, a two-page summary statement from the applicant and then published papers with attached summaries and a scoring/grading of evidence. The other document used an apparently older two-page hospital drugs and therapeutics committee form followed by a page of information from a pharmacist, which in turn was followed by a 'protocol for use', some 'medication interactions' information and a shared care agreement. Studies were again attached, although no attempt at quality rating had been undertaken.

In both cases the submissions included some data on clinical effect and side-effects. Both submissions

also offered some cost information, including the cost of the treatment (although only in one case was this presented as a comparison with current practice) and some attempt to predict cost pressure. A calculation of numbers-needed-to-treat was included in one of the applications. No reference was made to any cost–utility or cost-effectiveness data or analyses. However, for the first technology the committee received some further written information which had been emailed to the Chair by the Secretary, who was unable to attend the meeting. This contained reflections on the cost-effectiveness of the new drug.

Although interviewees were not asked specifically about these two applications, they were asked to reflect more generally on the considerations that most influenced them personally, when considering any given technology. All committee members stated that an important consideration was the evidence supplied in the application, although one saw this as secondary to the evidence derived from ‘key clinical trials’. Within this evidence base, respondents were unanimous in referring to the importance of data on efficacy of the treatment. In most cases this was seen as the most important consideration. The next most commonly referred to consideration was evidence of ‘cost-effectiveness’ with five interviewees referring to this. This was referred to as the first consideration by only one interviewee who measured cost-effectiveness in terms of numbers-needed-to-treat. Four interviewees mentioned ‘safety’ as an important consideration. Three referred to the cost of the product and a further three made general reference to the ‘robustness of the data’ as an important consideration. Two interviewees referred to the number of patients requiring the treatment. Considerations referred to once by interviewees included its ‘likely impact’ on the local health economy and how it would be implemented.

“With decisions to do with new products I look at the information on the new area medicines management form that we have now for new products. It’s a very extensive form, and that I find very useful in helping to, myself, make a decision. I’ve usually made a decision before I attend the meeting by reading the data and the evidence behind products, on efficacy and also on adverse effects, safety and also cost-effectiveness of every product.”

(CC 1)

“I need a summary of the product characteristics which is generally available. That’s a useful starting point because that gives you a lot information about the product. You need to know something about

obviously the cost of the product, its safety and efficacy profile, the latest evidence about it, projected costs if they are available, what the impact is going to be on our local economy, those sorts of things we’d be after really. Things really that would help us arrive at a decision as to whether we’re going to support the product actively, passively or not at all.”

(CC 3)

Interviewees were asked to reflect on their perceptions regarding the extent to which different committee members would share their ranking of considerations. In general, it was felt that there was a reasonable degree of shared emphasis amongst committee members. Two issues were raised more than once by interviewees. These were that:

- Primary care representatives are more likely to be conscious of limits to the prescribing budget and therefore would pay more attention to cost of treatments than secondary care clinicians.
- Prescribers from all sectors are more likely than the committee members to be influenced by the practical implications on services and prescribers of introducing a new technology into the health economy.

Through observation of committee meetings, the research team were able to compare these responses with actual instances of committee decision-making. In both instances where the committee considered a new product, the Chair led a discussion based on the written submissions to the committee. Discussion of the first technology covered the following areas:

- Efficacy data – with committee members questioning its effectiveness compared with current practice.
- Safety – the drug currently had ‘black triangle’ status, a source of concern to a number of contributors to the discussion.
- Licence restrictions.
- Cost – it was noted that the drug was cheaper than alternatives and therefore offered ‘cost benefits’. However, this was not seen as outweighing or counterbalancing the prior factors.

This application was rejected, apparently on the basis of the evidence of efficacy, licence restrictions and safety.

Discussion of the second application was more extensive and covered the following areas:

- Evidence of efficacy – perceived weaknesses in this.

- Clinical issues – including concerns about contraindications and drug interactions.
- Practical difficulties – with regard to controlling who can and should prescribe the drug and the need for a protocol. Primary care prescribers present were particularly reluctant to endorse the technology because of the potential implications for practice.
- The possibility of a restricted pilot introduction of the drug.

The decision was made to defer consideration until the next meeting and the relevant clinical experts would be asked for more information and input into a protocol.

Use of economic evaluation

Interviewees were asked to reflect on the types of economic evaluation they received. Responses were unanimous in suggesting that access to published cost-effectiveness analyses was rare and not a feature of most new product assessments. Interviewees pointed to the economic information supplied by the manufacturers of new products as the main source. Beyond this, it was felt that, for example, QALY data were infrequently available to the committee. Such information as was received was usually identified and accessed by the committee's pharmacists.

“Applicants provide information to go with their application, supporting evidence, and some of that could be QALYs, but not necessarily, there's other evidence as well other than just QALYs. ... I think the way we've gone about it gives us adequate economic analysis. If we feel that we need more for a particular decision then we can always ask for it and give that to the applicant. So I don't think we actually need raw analysis for every application, because that's not necessary and it's just extra work for the applicant and for ourselves, when the decision could actually be quite easily made around other measures for that product.”

(CC 3)

“We take most of our information from the UK medicines information service, and we take that source if they've got it as much as possible. Or the national prescribing centre, they do some horizon scanning on new drugs. Those would be our gold standard sources. If we couldn't find anything there we'd do an independent literature search. And we would look at the information that the companies give us.”

(CC 8)

Having earlier detailed the considerations that most influenced them, interviewees were questioned specifically on the **importance** they

attached to economic evaluation information when considering an application. Responses were difficult to interpret at times as some interviewees reflected on the importance of 'cost' or 'financial considerations', as distinct from cost-**effectiveness**.

All respondents believed cost or cost-effectiveness concerns to be an important consideration for the committee, but none saw it as an overriding factor in the committee's decisions. It was seen as secondary to clinical efficacy data and/or other, less routinely identified factors, such as safety and patient well-being. It was referred to as 'one strand' of the information considered by the committee. Two interviewees believed economic evaluation increases in importance in informing decisions on 'me too' drugs.

“If I was looking to put one product above another, with a me-too drug I would need more economic data to decide. Because if the outcome data and the safety were the same that would be the main factor on which you'd be choosing one or the other.”

(CC 1)

“I think it's very important. I think it's becoming more important. I think we're managing to steer people away from the bottom line costs from the 'this drug costs this much and this drug costs this much, so, we'll use the cheaper of the two'. And I think we're managing to persuade people now that it's a bigger issue than that. And people are becoming more familiar with that way of working.”

(CC 8)

Levels of understanding of health economics

Of nine interviewees, three felt they had little or no understanding of the discipline and would not feel able to interpret an economic evaluation. Four interviewees felt they understood the economic information provided to the committee although, of these, two were unaware of, for example, what QALY measures represent. Two more interviewees reported having had some health economics training. One of these had taken on primary responsibility for interpreting economic analyses accessed by the committee. Some interviewees felt the general level of understanding of the committee was low, although the majority felt there was sufficient expertise 'around the table' to process information received.

“There's a lot of jargon in health economics. If you said at the committee 'the health economics was done by a Markov model', people wouldn't know whether that was good or bad. And if you started talking about a Monte Carlo analysis or bootstrapping or anything like that, people would say, 'I don't know what the

bloody hell that means'. But if you said, 'it's a randomised, double-blind cross-over trial', then most people would have a good understanding of that."

(CC 4)

Barriers to use of economic evaluation

Six interviewees felt economic evaluations provided by the manufacturer of the technology being considered were treated sceptically by the committee out of a concern at possible bias. This was the most frequently cited barrier to use of health economics information.

"Quite often this sort of information is available from the actual drug companies themselves, isn't it? I see that as a weakness with it. Because if a drug company is driving a product there may be the risk of bias."

(CC 1)

Two interviewees felt that there was often a shortage of robust data to inform evaluations and that this lessened their value for the committee. Others expressed concern about how evaluations are conducted: not taking into account all the relevant costs, wrongly adopting a narrow focus on NHS costs and excluding work, pensions and social care, and making questionable assumptions. One interviewee was concerned that economic evaluations, in focusing on efficiency, can have a detrimental effect for the care of patients with rare conditions requiring expensive treatment. A barrier reported by two interviewees concerned the difficulty of accessing studies within the time constraints of the decision-making process. The difficulty in interpreting evaluations was also cited as a barrier to its use. Other interviewees felt that budget holders would have difficulty in implementing the types of savings identified in health economics analyses.

"Do the health economics work in real life? It's okay to model things on say, reduced bed occupancy or whatever, but can you translate it into savings or costs or whatever in the real delivery of health services? ... You're talking about disinvesting in bed days but actually, if that patient gets discharged early, then we get another patient coming into that bed. So we're not saving any money. And so if we're spending a thousand pounds a year more on drugs, we're not going to recuperate two thousand pounds back into our drug budget for spending less on hotel costs! So how do we actually know the economics does really, really work?"

(CC 4)

What sometimes muddies the picture is the NHS never takes a long-term view. Only recently they started taking three-yearly reviews, previously it was

year-to-year. Sometimes short-term losses can make long-term gains. So you spend more in the beginning to recoup the benefit afterwards. ... That's why, the PCT can't put preventative medicines into place; prevention will take five years to recoup back. But I don't think that's the fault of the economic evaluation as such. It's if the government directs the PCT to take a short-term view, a long-term view or a medium-term view."

(CC 6)

Improving use of economic evaluation

The majority of interviewees expressed the view that it would benefit the committee to have more economic evaluation available to them. Three felt there was sufficient health economics available in most instances and one felt there was currently an over-emphasis on economics.

Some interviewees also pointed to strategies for improving the committee's use of economic evaluation. These tended to centre around the need for an enhanced process of production and consumption of analyses. From the point of view of the producers of evaluations, it was felt that a standard, generally accepted and well-presented presentation of economic analysis would be welcome.

"I think the industry has strived to produce a template for health economic studies and has failed. There isn't a common framework for every product that you can say, 'this is the way to do a health economic study' that will support payers in making decisions."

(CC 4)

"I think it should be kept simple. I think many of these economic evaluations are too woolly. So we ought to aim a bit more for simplicity and then get consistency. It just makes it easier to use as a tool."

(CC 9)

From the point of view of consumption, it was felt by some that training for committee members was required. Others argued that additional expertise – especially in specific circumstances – should be made available to the committee when interpreting economic evaluations.

"I think we need to improve how we present it but we also need to improve the committee's understanding of it. I think that's the bit I'd like to build on quite a lot, is their skills."

(CC 8)

Summary

1. The committee was established in 2002 to guide the safe and effective use of medicines

within the local health economy, including the introduction of new technologies, and to manage the impact of prescribing costs on its stakeholders.

2. The primary factor influencing its decisions on whether to recommend a technology is evidence of clinical benefit, followed by information on its cost and/or cost-effectiveness.
3. Main reported sources of written health economics are the manufacturers of technologies under consideration.
4. The committee has some health economics expertise within its membership.
5. Committee members expressed concerns about the objectivity of analyses conducted by drug companies. Variable levels of access to sources of economic evaluation other than from manufacturers were noted, as was variation in committee members' capacity to understand health economics analyses.
6. Respondents identified a number of perceived weaknesses in economic evaluations reviewed such as:
 - (a) excessive variation in health economics methodologies
 - (b) concerns about the robustness of analyses, or appropriateness of the comparators used
 - (c) problems relating to the inability to realise savings identified in analyses.
7. Suggested strategies for improving or maximising the use of economic evaluation included:
 - (a) the need for a clear, standardised and generally accepted format for the presentation of economic analysis
 - (b) training for committee members
 - (c) the co-opting on to the committee of health economics expertise in cases where this was required.

Case study four: interface Medicines Management Committee (West England)

Case study four was selected as an example of a recently formed decision-making committee operating across the interface between primary and secondary care. In total three meetings were attended by a member of the research team, two of which were formally observed. Interviews were conducted with five committee members.

This committee was established in 2002. Its aims are: "to act as a countywide, clinical strategic advisory forum on medicines' management issues, particularly those affecting the interface between

primary and secondary care, applying the central principles of rational prescribing in medicine use (i.e. clinical and cost-effectiveness, appropriateness and safety) to inform the clinical network."

(Source: committee's Annual Report).

The committee meets bimonthly. Members of the committee include:

- clinician and Prescribing Pharmacy Adviser from each PCT
- Chair of Drugs and Therapeutics Partnership Trust, Senior Pharmacist, Partnership Trust,
- Medical Director/Director of Clinical Strategy, Pharmacy Director and Chair of Medical Directorate Drugs and Therapeutics, from the Hospital Trust
- local Medical Committee representative
- local Pharmaceutical Committee representative
- Service and Financial Framework Finance representative.

According to its stated terms of reference the committee was set up:

- To provide evidence-based advice on the place of new medicines or existing medicines with new indications. It is expected that medicines' management groups within trusts will deal with local issues, but that with some medicines, particularly of high cost, committee advice will be necessary.
- To provide advice on NICE guidelines' implementation, audit and monitoring, particularly when across organisational boundaries.
- To forecast developments which involve medicines and provide advice on local implications of such developments and their management. Working within the SAFF process to advise on forecasting and monitoring prescribing spend and collaborative commissioning for prescribing issues, ensuring a countywide approach to prescribing.
- To advise on the formation, development and implementation of medicines' management policies and guidelines, coordinated across primary and secondary care.
- To make recommendations to assist in the resolution of problems relating to prescribing at the interface between primary, secondary, tertiary and social care. To develop the traffic light system and shared care guidance to clarify prescribing responsibilities.
- To develop effective communication with the strategic health authority and other medicines' management groups, to enable sharing of advice and developments.

- To advise on further developments to enhance a whole system countywide approach to medicines' management.

(Source: committee's Annual Report)

The committee reports to the boards of the trusts in the area through their representatives sitting on the committee. Topics for consideration by the committee are tabled by representatives of member organisations. They are deemed suitable for consideration only if they have a potential impact on both primary and secondary care. The committee links with decision-making bodies with a specific secondary or primary care brief (for example, hospital drugs and therapeutics committees). There is no prior requirement for applicants to have identified funding for the new technology's introduction. Recommendations must therefore be fed back into the relevant commissioning and financial planning processes. Interviewees expressed reservations about how 'joined up' this process was at the time of the research.

"I think one of the things that we've still not addressed is those links between this committee as a medicines management county-wide committee, and the whole planning process and how that relates to some of the financial and priorities that the health community has. And I don't think that link has actually been made by a cross-membership, shall we say, of either finance or on a planning basis, and I think those two ingredients are definitely needed to make it an effective, cost-effective group."

(CD 5)

It became clear during the case study that there was some uncertainty surrounding the future role and responsibilities of the committee.

Functions of the committee and role of committee members

Committee members were asked, in interview, to state what they considered to be the committee's main functions. Interviewees agreed that the committee's main functions were to:

- provide an interface between primary and secondary care (for example, developing policies on discharge and outpatient prescribing)
- manage and generate county-wide agreement on the introduction of new or expensive drugs
- develop shared care guidelines (linked to a traffic light system for the county).

Individual committee members cited further functions of the committee, including to reduce

postcode prescribing and to problem solve at the 'coalface' where necessary.

Interviewees were asked what they considered to be their role within the committee. The Chair's role was to oversee the decision-making process and to agree the agenda for the committee. Other committee members saw their individual roles from varying standpoints. A GP saw their role as being to advise the committee from a primary care prescriber's perspective and to represent the PCT's interests. A hospital pharmacist saw their role as involving the provision of medicines information to the committee. A more senior pharmacist saw their role as representing the main hospital trust but also representing pharmacy for the county generally and linking in with the acute trust medicines committee.

Information used in decision-making

In the two meetings observed by the research team, the committee did not consider any new treatments or interventions. Other matters were discussed such as shared care guidelines and the traffic light system for new technologies in the area. However, with regard to the information used by the committee when deciding on new technologies, we are reliant on data derived from interviews with committee members.

Interviewees were asked to explain the considerations that most influenced them personally when considering any given technology. Although responses varied in emphasis, common themes emerged. Evidence of clinical benefit was universally cited as the primary consideration. Information on the cost of the product was most frequently cited as a second-order consideration. Other influencing factors identified were the likely patient group, safety issues and local clinical opinion. Two interviewees mentioned 'health economic information' as a consideration in their thinking.

"I would consider that the safety and the therapeutic indication, and the benefit of it, that those would be the critical issues. The cost is of secondary importance, but is there. The critical issues are who is it going to help, by how much, and what are the risks in doing it?"

(CD 1)

"First of all, the evidence behind it, and how strong and robust that evidence is. Secondly, local clinical opinion, because evidence will only go so far. It's what all our consultants think of the evidence, their experience, and whatever else they know in their specialities. The third consideration is the costs associated with it."

(CD 2)

“The cost-effective agenda, which for me includes a county-wide formulary approach, as well as getting very involved with horizon scanning, as well as getting involved with review of current high cost medicines is not well developed.”

(CD 5)

Interviewees were also asked to reflect on their perceptions regarding the extent to which different committee members would share their ranking of considerations. In general, interviewees felt there was a broadly shared approach.

“I think probably most committee members will be pretty similar. We all have to be mindful of the cost but none of us would want to block a drug on cost basis. We need to take it into account and plan for it, but what we wouldn't do is say yes or no purely on the basis of cost. Whereas you might say yes or no purely on the basis of safety. I don't know anybody on the committee who would be different from that.”

(CD 1)

Use of economic evaluation

Members of the committee who were interviewed were asked to reflect on the types of economic evaluation they received. Three interviewees referred to the companies manufacturing new technologies as the primary source of economic analyses and two interviewees referred to the cost-effectiveness information that accompanies NICE guidance. Apart from these sources, all interviewees agreed that cost-effectiveness data were rarely available to inform a committee decision on a new product. Respondents could think of very few instances where, for example, QALY data had been accessed. Cost data used by the committee was seen as limited to narrow costs associated with the product.

“Ideally we would like cost data as NICE uses with QALYs etc. to look at comparative costs within the bigger picture of healthcare intervention costs, across the health economy. But it's unusual for independent quality data and health economic data to be around at the time we look at the drugs and we don't have the local capacity to generate it ourselves.”

(CD 2)

Having earlier detailed the considerations that most influenced them, interviewees were questioned specifically on the **importance** they attached to economic evaluation information when considering an application. Interviewees were unanimous in their assessment that health economic information was not currently a crucial factor in the committee's decisions. A number of reasons for this were suggested, relating to capacity, access and implementation issues.

“I think it's an important aspect of it but it's not critical. It's possible that if we have better information on QALYs and on the cost-benefit ratios and perhaps on opportunity costs then we may attach more importance to economic evaluation.”

(CD 1)

“A lot of NICE guidance has an element of health economic data but I think many commissioning managers look at the additional financial cost implications of NICE guidance rather than the health economics data. So even when it is available in that local commissioning kind of environment it probably isn't used as much as it should be.”

(CD 2)

“My guess would be that, if we ask more people locally about this, then because of their current level of understanding of health economics, they'd probably see this as an initial complication and be unclear of the practical benefits, in real terms, compared to the additional time involved in digesting and understanding the data.”

(CD 2)

“Health economics is going to be an interesting part of our discussions but is not going to be a major part unless everybody can see savings which are tangible and extractable and which they can spend on something else.”

(CD 5)

Levels of understanding of health economics

Responses to the question, ‘do you feel you understand the economic evaluation presented to the committee?’ indicate significant variation in committee members' familiarity with economic evaluation. Overall, interviewees demonstrated a working knowledge of cost-effectiveness analysis although none had specific health economics expertise. Two interviewees had received some training in this area. Two interviewees reported only a ‘very basic’ understanding of economic evaluation. Interviewees felt that clinicians and commissioning managers would be less likely than other committee members to understand fully health economics analyses.

“I think I do understand them in some cases. I think generally I'd feel happier if I went back and just refreshed my memory on certain aspects. I wouldn't claim to be able to pick up a paper at any point and fully understand it, because obviously, at the moment, we're not using them day in and day out, and so the concepts become a bit blurry.”

(CD 3)

“I understand QALYs enough to know that they are a measure of the cost-effectiveness and affordability rate of a particular product. I don't know enough about

the influencing factors within the model to be able to make a reasoned approach to it.”

(CD 5)

Barriers to use of economic evaluation

Respondents displayed a detailed grasp of the barriers facing the committee with regard to use of economic evaluation. Four out of five interviewees cited as a major barrier the issue of the committee’s resources and capacity to generate or locate evaluations.

“I think that what would be critical is having the information available. What we don’t have as a committee is the resources to be able to go and find the information and put it together, assess it to make sure that it’s robust and then deliver it to the committee. We don’t have the team to be able to do that sort of work.”

(CD 1)

Concerns about the subsequent reliance on economic analyses conducted by the manufacturer of the product was also cited by four interviewees as a barrier to its use.

Three interviewees detailed the difficulties in implementing some of the potential savings identified in analyses. The problem of the committee’s levels of expertise in health economics was cited as a barrier by two interviewees. The unavailability of timely economic evaluations for new drugs and complaints about presentational styles of the latter were also cited by individual interviewees.

“If more health economics was available and therefore there was more of an onus for us to use it, I guess we’d have to then develop more of a wider educational package so that some of the clinicians and commissioning managers could understand the implications of it a bit more. Having said that I think also taking that next step infers that the health economy can move funds across for different interventions easily. But in reality that isn’t the case. Not in the short to medium term.”

(CD 2)

“I think we haven’t got to that degree of sophistication basically because we still struggle with some of the more basic concepts of where we’re actually going for funding. I think if you’ve got a new product, it’s difficult because you can try and influence what’s going to happen in the health economy, but you can’t say, ‘well if we introduce this one you can’t use that one’.”

(CD 3)

“I think it is a weakness that there are often a lot of technicalities associated with economic evaluation and

I don’t think it should be presented in a summary format. I think a weakness is that it doesn’t put it into my context: how will it be releasing resources associated with the acute trusts?”

(CD 5)

“A lot of the models that I’ve seen come out with a bottom line cost which is difficult to extract in cash terms. Saving beds is not, at this moment in time with the pressures on the NHS, going to realise any savings at all, because that bed will be used for the next patient that’s coming in.”

(CD 5)

Improving use of economic evaluation

Despite reported limits to levels of understanding of health economics, those committee members who expressed a view indicated that they would like to see more economic evaluation information made available to aid the decisions they make as long as the information was from a reliable source and was easy to interpret.

“I think it would be good to have more information provided, yes. The only difficulty is where does it come from? What’s the provenance of it? And the difficulty would be, how reliable is this information going to be? And if it was good and reliable information that was consistent and it was generally accepted to be sort of the industry standard of how good you’re going to get, then I think that would be good.”

(CD 1)

“Going back to the NICE process. Obviously, the concepts and the ideas are there so I think we should be trying to sort of mesh into that and doing that on a more local basis. I just don’t think it’s got quite that sophisticated yet but I think it is something that we should aspire to do.”

(CD 3)

“As long as we all had a common understanding of it, so we could all interpret it in the way it’s meant to be interpreted, I would like to have more information. If I have a guide as to how to interpret it. Because it’s no good giving me something if I haven’t got a clue how to interpret it. So we all have a common understanding of what it means.”

(CD 4)

Some interviewees also pointed to mechanisms for improving the committee’s use of economic evaluation. In the main these centred around improving the accessibility of economic evaluations. The most commonly cited area for improvement was in access to relevant, timely analyses. It was suggested that the committee needs either its own enhanced information-generating capacity (for example, a full-time pharmacist) or increased opportunities to ‘tap

into' the activities of organisations with a greater capacity, either at a regional or national level. The latter approach would require 'fast track reviews' to be made available to the committee in a time-frame not currently adhered to, for example, by NICE. Although it was acknowledged that committee members' levels of expertise could usefully be increased, this was seen as conditional on improving the availability of economic evaluations. One interviewee felt that a written guide to interpreting evaluations would be welcome. Interviewees also felt that economic evaluations currently do not always address the specific local circumstances and do not reflect the structural constraints facing budget holders.

"Well, for us I think it's simple. It's basically having more independent, credible health economic data available at the time we're making local decisions on the managed entry of new drugs. It's as simple as that. If more of that was available, then that would be a prompt for us to look at it more, incorporate it more, use it more, and more people would become aware of what that means."

(CD 2)

"Across the country there are other committees, like ours, doing similar amounts of work, some probably more effectively, others not. And for me a lot of it depends on how well they're supported. We have one or two days a week of a pharmacist's time to do reviews but ideally you probably need a full-time pharmacist to do this properly, linked to a drug information centre with critical appraisal skills. We don't have that, and couldn't make the case to have that. Therefore, if there was some national coordinating centre doing that who bring in more health economics data, because they've got health economics expertise then that'd be much more useful for us. Because the expectation that that would be done locally is unreal and it won't happen."

(CD 2)

Summary

1. The committee was established to advise, on a county-wide basis, on the strategic clinical management of medicines issues.
2. Primary considerations influencing decisions are evidence of clinical efficacy, followed by the cost of the intervention and its impact on the interface between primary and secondary care.
3. Main sources of written health economics are the manufacturers of technologies under consideration, and guidance produced by the NICE, with only limited access to other sources of economic evaluation.
4. According to interviewees, economic evaluation – as understood within the academic discipline of health economics – has a minor impact on the committee's deliberations.
5. Limited resources and capacity to generate or locate evaluations was the most cited barrier to better usage of health economics.
6. Other barriers include:
 - (a) concerns regarding bias in evaluations
 - (b) problems relating to the inability to realise savings identified in analyses
 - (c) objections to the presentational format of evaluations
 - (d) difficulties in understanding and interpreting economic evaluations.
7. Suggested strategies for improving or maximising the use of economic evaluation include:
 - (a) improving the information-generating capacity of the committee or linking it to organisations with greater capacity
 - (b) increasing the expertise of the committee in understanding evaluations
 - (c) vision of a guide to reading and appraising economic analyses.

Appendix 10

Information on the seven NICE appraisals observed as part of the case study of the Technology Appraisal Committee

Introduction

This appendix presents findings from the national case study which focused on the Technology Appraisal Committee of NICE. It begins with a description of NICE and its technology appraisal process and goes on to present results from interviews, observations and documentary analysis relating to the seven technology appraisals that were considered in detail. Our focus is on the process followed by the Appraisal Committee and the apparent place of economic information in this process.

The National Institute for Health and Clinical Excellence: an introduction

NICE is a Special Health Authority in the National Health Service of England and Wales. It was set up in 1999 and currently has four functions:

- to appraise new and existing health technologies
- to develop and disseminate clinical guidelines
- to appraise interventional procedures used for diagnosis or treatment
- to identify ways of improving the quality of care (confidential enquiries).

The first of these functions – producing guidance on new and established medicines and treatments – is performed via the Institute’s appraisal process. The key decision-making element of this process is carried out by the Appraisal Committee, which consists of experts appointed by NICE. For each technology appraised, NICE receives an independent assessment of evidence, which includes an economic evaluation. The committee also takes submissions from interested parties ranging from the sponsor of the technology to patient representative and expert bodies (www.nice.org.uk).

The committee meets to discuss the evidence and listen to further testimony from clinical and patient representatives before producing a provisional determination (the ACD) as to the technology’s clinical and cost-effectiveness. This is made publicly available for consultation and typically forms the basis of the committee’s FAD. At its most definitive, this guidance will either recommend the routine use of the technology in all appropriate clinical situations, or will recommend the NHS not to adopt the technology. Alternatively, guidance will recommend restricted use, for example, in certain patient categories only or as part of ongoing research.

Interviews with the Appraisal Programme Director at NICE and other members of the appraisal team were used to obtain information on the process.

On the issue of selection of people to serve as members of the Appraisal Committee:

“The selection of the members initially was determined by discussion between us at NICE about the kinds of background for individuals we would want ... as well as taking advice from professional societies, the colleges and so on. We came up with a list of individual names, and selected them from that list as opposed to the present process which of course requires advertisement and CVs and so on.”
(Chair)

On the selection of topics that are considered by NICE:

“That is done via the Department of Health. They essentially send us what we term the ‘remit’ for the appraisals ... so NICE doesn’t actually select the technologies themselves, that’s outside of our remit.”
(NICE PD)

Once topics have been selected, two members of the committee are appointed as the ‘lead team’ and have responsibility for verbally presenting the evidence and analyses from the appraisal reports to the rest of the committee.

“... we have one member of the lead team who concentrates on the economic issues and another one who concentrates on either the clinical or the clinical effectiveness issues and then both of them concentrate on those other issues that impinge on both the information and the decision that needs to be made The lead team will receive absolutely everything The rest of the committee will receive the assessment report, the summaries of manufacturers’ submissions and the professional and patient submissions. They don’t automatically receive the full copy of the manufacturers’ submissions but these are available on request.”

(NICE PD)

Another committee member described the process of preparing the ACD and FAD as follows:

“The ACD is part drafted before the meeting. It’s a twenty-page document that’s derived from the factual material. The thing that has to be added is the final decision. Then immediately after the committee meeting there is a period of two or three days when the ACD is re-written, by the Chairman and by the technical leads (i.e. the secretariat). Much more happens because the decision is not as it were written off until after (a) the ACD, (b) the email discussion on the draft ACD, (c) the submissions of all the complainants about what the ACD said, (d) the FAD meeting, and (e) the discussion by email around the FAD meeting. The FAD meeting itself is a complex procedure which could have another iteration with TAR [Technology Assessment Report] teams and further calculations being made and then finally of course the appeal.”

(NICE 1)

The seven technology appraisal topics

The seven technologies selected for consideration are listed in *Table 14*, along with the dates of the first and second Appraisal Committee meetings.

TABLE 14 *The seven selected technology appraisals*

Technology	Date of first Appraisal Committee meeting	Date of second Appraisal Committee meeting
Capecitabine and tegafur with uracil for colorectal cancer	13.11.02	11.02.03
Capecitabine for breast cancer	13.11.02	11.02.03
Olanzapine and valproate semisodium for the manic phase of bipolar I disorder	25.02.03	29.05.03
Fluid-filled thermal balloon and microwave endometrial ablation techniques for heavy menstrual bleeding	12.03.03	15.05.03
Rituximab in the treatment of aggressive non-Hodgkinson’s lymphoma	24.04.03	01.07.03
Imatinib for chromosome-positive chronic myeloid leukaemia (CML)	15.05.03	10.07.03
Myocardial perfusion scintigraphy for the diagnosis and management of angina and myocardial infarction	01.07.03	27.08.03

Each technology will be considered in turn below. For each of the technologies we provide:

- a summary of the economic analysis reported to the committee as part of the Technology Assessment Review
- notes from observations of committee meetings by the research team where the technology was considered
- a summary of findings from interviews with committee members on the particular appraisal topic
- a summary of the final guidance issued by NICE on each technology.

Capecitabine and tegafur with uracil for colorectal cancer

Observation of the economic evaluation for this appraisal was undertaken by the University of Sheffield – a summary of the analysis is given in *Table 15*. The analysis presented was a cost-minimisation analysis (CMA), given no evidence of survival gains, and an illustrative cost-effectiveness analysis (cost per progression-free year of survival gain). Some of the complexities in the economic analyses seen in other appraisal reports (e.g. model-based analyses, probabilistic sensitivity analyses, value of information considerations) were not seen as being necessary and so were not included as part of this report. In addition, it is worthy of note that, given that a cost–utility analysis was not undertaken, the committee was not presented with QALYs.

The observation of the appraisal meeting

Two members of the research team observed the first meeting (IW and SM) and one team member (IW) observed the second meeting. A single health economist committee member was present for the first appraisal meeting. The lead team presentation on cost-effectiveness was by a

TABLE 15 Summary of economic analysis – capecitabine and tegafur with uracil for colorectal cancer

Aspect of economic evaluation		
Decision problem addressed		Interventions: tegafur with uracil (UFT/LV) and capecitabine Population: patients with metastatic colorectal cancer Comparator: intravenous 5-fluorouracil (5-FU/LV) regimen (Mayo Clinic)
Analytic methods	Type of economic evaluation	Cost-minimisation analysis and cost-effectiveness analysis (i.e. cost per progression-free year of survival gained)
	Modelling methods	No model developed
	Time horizon of analysis	12 months
	Perspective on costs	NHS and PSS only
	Discounting	Not relevant given the time horizon
	Measure of health benefits	Progression-free survival
	Source of quality of life and utility data	Not relevant
	Probabilistic sensitivity analysis	Not performed
	Subgroup analyses	None
	Equity considerations	None explicitly referred to
Assessment of future research needs	No formal valuation of information analysis undertaken	
Presentation of results	Expected CE results	Reported
	Parameter uncertainty	CE plane scatters not reported CEACs not reported
	Other forms of uncertainty	One-way sensitivity analyses undertaken
Synthesis of evidence on outcomes		Systematic review, using data from RCTs
Assessment of NHS impact		Budget impact calculated using prevalence and incidence information

CE, cost-effectiveness; PSS, Personal Social Services; RCT, randomised controlled trial.

committee member with expertise in statistics. The lead team presentation, in general, focused on issues such as the epidemiology of the disease, the impact of new drugs on secondary and primary care, patient compliance issues and the place of this appraisal within the context of previous NICE guidance. The presentation of the cost-effectiveness analysis supported the use of CMA as the preferred form of economic evaluation on this occasion. It was noted that the economic analysis was weakened by data limitations, notably by the shortage of relevant head-to-head clinical trials.

There was some discussion on the scope of the appraisal, particularly the choice of the appropriate comparator, with one committee member questioning whether a technology not included within the scope might outperform both the new treatments and current practice. In addition, clarification was sought on the issue of discounts being offered by the pharmaceutical companies which varied and were known to be substantial. This issue was particularly important

for this topic because of the CMA approach to the economic analysis.

The issue of oral therapy and patient preference was discussed at length, with one committee member observing that oral versions of the new treatment are not available in all centres. Further exchanges centred on issues such as patient preference and monitoring arrangements and this was followed by discussion about the implications of recommending oral therapy. It was felt that the quality of life benefits of oral regimens were not adequately assessed in the trials. Later in the meeting this line of argument continued with one committee member suggesting that the clinical and economic evaluations revealed so little disparity between new technologies that other considerations such as patient preference should come to the fore. For example, individual patients may prefer an orally administered treatment on quality of life grounds. Another committee member agreed that patient preference issues become important only when cost-effectiveness is 'not crucial'. There was, therefore, lengthy

discussion as to the broader benefits to patients of an orally administered treatment.

In conclusion, the Chair proposed that the new technologies were effective and cost-effective, and explored whether there was any evidence to indicate that one was superior to the other. Despite some differences in toxicity and cost, it was felt there was insufficient evidence to separate them.

Post-ACD meeting interviews

In the days following the first appraisal meeting, the research team conducted separate interviews with two committee members (a clinician and a statistician) who were asked to reflect on the specific appraisal in question.

Both interviewees considered that the demonstration of cost-effectiveness was critical to recommending this or any technology. One interviewee commented on the fact that there were more data for capecitabine than for tegafur uracil and that the clinical evidence was limited.

There were no head-to-heads between the two drugs that were of any consequence, and so the comparative cost-effectiveness data wasn't really there.

(NICE 29)

The other interviewee reflected on the CMA approach to the economic analysis adopted by the review team.

"It is reasonable to do a cost-minimisation approach. In other words it is reasonable to say that these preparations – capecitabine and tegafur – are as good as or no worse clinically than 5-FU and therefore to go for a cost-minimisation approach which showed them to be cost-saving."

(NICE 25)

However, this interviewee went on to state that in most other circumstances he would prefer to see a stochastic rather than a deterministic approach to the analysis.

As the economic evaluation had involved a relatively simple CMA approach, both interviewees indicated that the committee would have had no difficulty in understanding it. One interviewee felt the appraisal had been unusual in how 'straightforward' the results of the health economics analysis had appeared to be. A sense of confidence in the decision was reinforced by the apparent robustness of the analysis to uncertainty, demonstrated through the sensitivity analysis. The interviewee also remarked that there was an

unusual level of attention paid to patient choice considerations. However, it was also made clear that such considerations remained secondary to the assessment of a technology's clinical and cost-effectiveness in shaping the committee's decision.

"I think overall the complexity wasn't as great as some of the technologies are. Technically it was a fairly straightforward area, and in terms of health economics it was relatively straightforward. And the gaps were probably not significant, whereas in other appraisals, the gaps that we have or the assumptions that have to be made to fill those gaps are sometimes too significant to faithfully rely on the economic analysis that comes out of it."

(NICE 29)

The second interviewee also identified the focus on patient choice as an unusual feature of the deliberations, and also raised the issue of the indirect comparisons made necessary by the appraisal remit and the limited clinical evidence base.

"It would be very difficult to hang your hat on saying one was definitely clinically better than the other and it would be very difficult to hang your hat on saying one is cost-effective or, the equivalent, one is definitely cheaper than the other for the same clinical effectiveness. So it's difficult to prove that they were the same; it's difficult to prove that they weren't the same, clinically, and it would have been difficult to justify throwing one out and saying that's all we're going to use in the UK. That would have been extremely difficult to justify. So it did come down to wider issues such as patient choice."

(NICE 25)

The guidance

Following the second appraisal meeting, the committee issued its FAD, which contained the following guidance:

"Oral therapy with either capecitabine or tegafur with uracil (in combination with folinic acid) is recommended as an option for the first-line treatment of metastatic colorectal cancer.

"The choice of regimen (intravenous fluorouracil/folinic acid [5-FU/FA] or one of the oral therapies) should be made jointly by the individual and the clinician(s) responsible for treatment. The decision should be made after an informed discussion between the clinician(s) and the patient; this discussion should take into account contraindications and the side-effect profile of the agents as well as the clinical condition and preferences of the individual.

"The use of capecitabine or tegafur with uracil to treat metastatic colorectal cancer should be supervised by oncologists who specialise in colorectal cancer."

In the ‘consideration of the evidence’ section of the guidance, the absence of data on patient preferences is emphasised:

“In the absence of patient preference data from adequately designed studies, the Committee took particular note of the opinions of both the professional and patient representatives regarding the advantages of oral compared with intravenous administration of chemotherapy, and of the potential problems of concordance with oral treatments. The patient representatives particularly emphasised that the vast majority of individuals expressed a strong preference for oral drugs provided that effectiveness was not compromised, because they reduce the disruptive impact of chemotherapy on individuals’ lives and give them greater control over the management of their disease.”

The guidance reiterates the point that there was a lack of compelling evidence for a difference in effectiveness between the alternatives being considered and therefore, the committee was happy to consider the CMA only. The final judgement is, therefore, based on which option was associated with the lower expected cost.

Overall, it seems that the guidance reflected a number of factors which emerged in both the observations and interviews with the committee. These included the weakness in clinical and quality of life data and, therefore, the difficulty in separating the treatment alternatives on cost-effectiveness grounds. The economic analysis performed was generally understood and accepted as valid by the committee and as such this appraisal was seen as unusually straightforward. Although interviewees emphasised the importance of establishing the cost-effectiveness of any recommended technology, it was felt that in this case the economic analysis generated few areas of particular concern or debate and, therefore, committee discussion focused, to a greater extent than is usual, on issues of patient preference and choice.

Capecitabine for breast cancer

The second appraisal topic included within our sample had strong links to the first inasmuch as it was also concerned with the use of capecitabine – but for a different indication. The NHS Centre for Reviews and Dissemination and the Centre for Health Economics at the University of York prepared the Technology Assessment Report for this topic. A summary of the main components of the economic analysis is given in *Table 16*. A cost–utility analysis was reported and so this topic provided an opportunity to see how the committee

made use of QALYs. Although no model-based analysis was undertaken by the review team, there was a Monte Carlo simulation using trial-based data and, thus, the committee had results from the economic analysis reported using cost-effectiveness plane scatters and CEACs.

The observation of the appraisal meeting

Two members of the research team observed the first meeting (IW and SM) and one team member (IW) observed the second meeting. Two health economists were present for the first appraisal meeting. The lead team presentation was relatively brief (because the committee had heard about capecitabine for a different condition earlier on the same day) and summarised the evidence of the technology’s clinical effectiveness followed by its cost-effectiveness. The presenter noted that, as in the earlier capecitabine appraisal, the cost-effectiveness analyses were constrained by the limited evidence base.

Committee discussion explored the strength of the clinical evidence and toxicity of the drugs. Areas of weakness in the evidence were considered at length. These included:

- poor quality of life data
- the poor quality of the evidence base generally and the need for head-to-head trials between technologies
- limited data on the adverse effects of treatments.

There was discussion about the appropriate comparator and the pathway of care. The point was made that a technology not included within the scope of the appraisal (vlnorelbine) was currently being appraised by another branch of the Appraisal Committee. The outcome of the vlnorelbine appraisal was discussed – subject to appeal, it has been recommended for use. Without any direct comparison between capecitabine and vlnorelbine, it was felt that the committee had no alternative other than to accept an indirect comparison which suggested that capecitabine is cost-saving versus vlnorelbine.

The Chair indicated that the committee is not required to limit the availability either of combination therapy (capecitabine and docetaxel) or either drug as monotherapy. However, one health economist argued that retaining all options should not stop the committee indicating a preference for the option that appeared to be most cost-effective, emphasising that the committee should do more than simply leave the

TABLE 16 Summary of economic analysis – capecitabine for breast cancer

Aspect of economic evaluation		
<i>Decision problem addressed</i>		Interventions: capecitabine monotherapy or capecitabine in combination with docetaxel Population: women with locally advanced and/or metastatic breast cancer Comparator: vinorelbine and best supportive care
<i>Analytic methods</i>	Type of economic evaluation	Cost–utility analysis (i.e. cost per QALY)
	Modelling methods	No formal modelling undertaken – using trial-based estimates reported in the company submission a Monte Carlo simulation was undertaken
	Time horizon of analysis	Not stated
	Perspective on costs	NHS only
	Discounting	“No discounting was undertaken due to the limited expected life span of patients in this setting”
	Measure of health benefits	QALYs
	Source of quality of life and utility data	Utility data taken from published sources and based on samples of nurses undertaking standard gamble exercises
	Probabilistic sensitivity analysis	Not undertaken
	Subgroup analyses	None
	Equity considerations	None explicitly referred to
	Assessment of future research needs	No formal valuation of information analysis undertaken
<i>Presentation of results</i>	Expected CE results	Reported
	Parameter uncertainty	CE plane scatters reported CEACs reported
	Other forms of uncertainty	None
<i>Synthesis of evidence on outcomes</i>		Systematic review, using only information from RCTs
<i>Assessment of NHS impact</i>		Budget impact assessment presented

choice to clinicians. Overall, it was felt the cost-effectiveness evidence presented in this appraisal was not a source of difficulty for the majority of the committee.

At the second meeting, the committee agreed that the importance of individual patient choice should be emphasised in the guidance as, at a population level, the two treatment options appeared to be equivalent. One of the health economists argued that this aspect of the guidance should not be justified using cost-effectiveness criteria.

Post-ACD meeting interviews

Following the first appraisal meeting, the research team conducted separate interviews with two committee members, a health economist and a surgeon. (The health economist interviewed made the point that the research team had left too long a period between the appraisal meeting and the interview and that this had diminished his recall of the committee’s deliberations. The research team accepted this point and ensured that subsequent interviews were all within 1 week of the first

appraisal meeting. As a result of the period between the first appraisal meeting and the interview, the interview with the health economist was broader and more generic than other interviews.) The health economist interviewee remarked on the committee’s consideration of the evidence base.

“For the combined therapy there was an analysis that was based on one trial but the analysis for monotherapy was only based on case-controlled studies. This led the committee to take different views on the two. In my view that link is much more fuzzy than they think it is. I don’t see the trial evidence being so conclusive as most other members of the committee ... They give much greater weight to cost-effectiveness analyses for which you can find some sort of clinical trial data than to ones where you can only find case control data and while I would generally see some case for that principle, it’s not as clear cut as I think many of the committee feel.”

(NICE 26)

The non-economist interviewee provided some support for this view and generally felt that the appraisal had offered an “easy, clear-cut decision”.

“The combination therapy was easier because there was at least one good RCT showing distinct benefit for combination and what really clinched it was the economic analysis that it was cost-saving. And that was very straightforward. The monotherapy was much more difficult and the evidence wasn’t very good for it. It may well be good and may be effective but we don’t know for sure. But I think we took a more pragmatic approach in that there was a feeling from the clinicians there, those who came to give evidence, that it was a useful drug and there were circumstances where it might be useful as a monotherapy rather than in combination. And I think the feeling was that, actually, in the long run, most people would go to the combination and then would avoid the monotherapy. So it became less of a concern really as to what we did with that.”

(NICE 30)

This interviewee accepted the conclusion of the committee discussions that patient and clinician options had to be kept open due to the complex and varied profiles of the patient group. However, this interviewee did feel that the economic analysis had been an important consideration in the committee’s deliberations.

“Well, before I got to it, it sounded as if the combination was something that should be supported, and it made it much easier once I’d read the economic analysis because there seemed to be no question about it after that really. So it did play a part. If it had come out at, sort of £100,000 for the treatment, then it would have been more difficult to argue it.”

(NICE 30)

The non-economist interviewee was unable to comment further on the economic analysis as a result of being relatively ‘new’, both to NICE in general and to economic evaluation in particular.

Both interviewees felt the committee had achieved consensus as to whether or not to recommend the technology. As with the previous appraisal topic, interviewees emphasised that the analysis had been clear and unusually non-contentious.

The guidance

Following the second appraisal meeting, the committee issued its FAD, which contained the following guidance.

“In the treatment of locally advanced or metastatic breast cancer, capecitabine in combination with docetaxel is recommended in preference to single-agent docetaxel in people for whom anthracycline-containing regimens are unsuitable or have failed.

“Capecitabine monotherapy is recommended as an option for people with locally advanced or metastatic

breast cancer who have not previously received capecitabine in combination therapy and for whom anthracycline and taxane-containing regimens have failed or further anthracycline therapy is contraindicated.

“The decision regarding treatment should be made jointly by the individual and the clinician(s) responsible for treatment. The decision should be made after an informed discussion between the clinician(s) and the patient; this discussion should take into account contraindications and the side-effect profile of the agents, alternative treatments for locally advanced or metastatic breast cancer, and the clinical condition and preferences of the individual.

“The use of capecitabine to treat locally advanced or metastatic breast cancer should be supervised by oncologists who specialise in breast cancer.”

Overall, capecitabine plus docetaxel was judged by the committee to be cost-effective against comparators, with the following qualifications:

“The Committee considered that evidence from the RCT demonstrated that capecitabine combination therapy is likely to be more effective than docetaxel monotherapy in terms of several outcomes, including overall survival. However, the side-effect profile of combination therapy may be less acceptable, and the final choice of therapy may be influenced by factors such as contraindication to the different regimens and the clinical condition and preference of individuals. The Committee was also mindful that, although over time the increased use of capecitabine/docetaxel combination therapy will result in fewer individuals being eligible for subsequent capecitabine monotherapy, there will still be a group for whom it should be considered.”

As with the prior appraisal of treatments for colorectal cancer, this appraisal guidance relies heavily on patient and clinicians to exercise choice as to the appropriate treatment – albeit within constraints. Key issues arising from this appraisal appeared to echo the previous appraisal: limits to the clinical evidence base, a non-controversial cost-effectiveness profile for the new technologies, and a recourse to patient preference in the absence of evidence of superiority between the new technologies.

Olanzapine and valproate semisodium for the manic phase of bipolar I disorder

The topic of new drugs for the treatment of manic phase bipolar disorder was selected as it appeared to constitute a complex decision scenario with a range of comparators. The University of York prepared the Technology Assessment Report for

this topic. A summary of the main components of the economic analysis is given in *Table 17*. A cost-effectiveness analysis was undertaken (i.e. cost per additional treatment responder) given that QALYs are difficult to utilise in the mental health area. Modelling was used, giving results for a probabilistic analysis that were reported using CEACs. The time horizon of the analysis was unusually short (i.e. 3 weeks) and only considered the acute phase of the condition.

The observation of the appraisal meeting

Two members of the research team (IW and SB) observed most of the first meeting (transport difficulties prevented IW and SB arriving for the start of the meeting; they missed the initial presentations and the early discussion). The second appraisal meeting was not observed but an account of the discussions was obtained through an interview with the committee Vice-Chair. Two health economists were present for the first appraisal meeting. The lead team for this topic

summarised the evidence on clinical effectiveness and cost-effectiveness – the latter being presented by one of the health economists on the committee.

An important point of discussion was the scope of the benefit assessment in the economic analysis. Clinical experts, patient representatives and committee members all accepted that the side-effect profile issue was very important and were, therefore, concerned by the omission of drug-related side-effects from the economic analysis. The explanation given for the exclusion of side-effect issues was the paucity of good data.

Several committee members also questioned the validity of the 3-week time-frame used in the economic analysis. It was suggested that this did not relate to the average length of acute phase bipolar disorder – the time-frame was apparently set on the basis of the evidence base that had informed the economic analysis. The Chair asked whether the time-frame should be extended,

TABLE 17 Summary of economic analysis – olanzapine and valproate semisodium for the manic phase of bipolar I disorder

Aspect of economic evaluation		
	<i>Decision problem addressed (from Scope)</i>	Interventions: quetiapine, olanzapine and valproate semisodium Population: patients experiencing mania associated with bipolar disorder Comparators: lithium or haloperidol
<i>Analytic methods</i>	Type of economic evaluation	Cost-effectiveness analysis (i.e. cost per additional responder to treatment)
	Modelling methods	Modelling approach not stated in report – model simply referred to as “probabilistic”. The Guidance document refers to it as “a hierarchical Bayesian model simulated using a Markov chain Monte Carlo technique”.
	Time horizon of analysis	3 weeks (since the focus was on the use of the drugs in the acute phase and not in the maintenance phase)
	Perspective on costs	NHS only
	Discounting	Not relevant, given the short time horizon considered
	Measure of health benefits	Response (typically measured as $\geq 50\%$ response on Young Mania Rating Scale)
	Source of quality of life and utility data	Not relevant
	Probabilistic sensitivity analysis	Performed on response rate (distribution not stated)
	Subgroup analyses	None
	Equity considerations	None explicitly referred to
	Assessment of future research needs	No formal valuation of information analysis undertaken
<i>Presentation of results</i>	Expected CE results	Reported
	Parameter uncertainty	CE plane scatters not reported CEACs reported
	Other forms of uncertainty	One-way sensitivity analyses undertaken
	<i>Synthesis of evidence on outcomes</i>	Systematic review – mean response rates for each strategy estimated using a multiparameter synthesis model
	<i>Assessment of NHS impact</i>	Budget impact assessment not presented

possibly to 6 months – the response focused on the lack of good evidence on the maintenance use of these drugs and the licensing restrictions for use beyond the acute phase. In support of the short time horizon, the point was made that extending the economic analysis to consider costs and benefits beyond the acute phase would necessitate that analysis being based on further extrapolation and supposition. However, as a counter to this, some members of the committee felt that hospitalisation rates should be a key driver of the cost-effectiveness analysis but this was not allowed for in the analysis since, as a consequence of the relatively short 3-week time horizon, hospitalisation was assumed to be the same for all drugs being compared.

Some members of the committee expressed frustration at the lack of information on quality of life and QALYs in this appraisal. This was dealt with robustly by the Chair, who felt that quality of life assessment was highly problematic in this context because of the difficulties of measurement in patients with this condition. The assessment team, along with one of the health economists on the committee, was called upon to explain the CEAC approach to presenting results of the probabilistic analysis. It was noted that this was one of the first occasions when the committee had received analyses presented in this way.

The committee felt that it was unable to differentiate between the drugs in question on cost-effectiveness grounds and so patient choice again was put forward as an appropriate consideration. At a later meeting, the committee revisited this appraisal in the light of consultee comments on the ACD – no significant alterations to the ACD were made.

Post-ACD meeting interviews

In the days following the first appraisal meeting, the research team conducted interviews with three committee members: a health economist, a physician and a patient representative. Two interviewees expressed the view that the cost-effectiveness analysis conducted by the assessment team had been important in steering the committee, whereas one interviewee felt this importance had been eroded by data shortages:

“The questions really surrounded comparative effectiveness and there the data was fairly weak and as a result of that weakness the cost-effectiveness data dissolved into whether people’s length of stay in hospital was longer or not. And we just didn’t have the evidence on that so it all fell a bit flat. But don’t

let’s assume that this is the way things always happen.”

(NICE 18)

The health economist interviewee felt that the economic analysis had been very important in making the committee aware that effectiveness, measured in terms of reduced hospitalisation rates, was the main driver of new technologies’ cost-effectiveness. One interviewee felt that the cost-effectiveness analysis helped in identifying that the new drugs were cost-effective when compared with older technologies but was unable to provide grounds to recommend one over the other. The health economist interviewee summed up the economic analysis as follows:

“Basically I was arguing that effectiveness was all and that if you had something that was effective in a subgroup of patients then the chances were that that would also be cost-effective because it would keep people out of hospital. So that was at a very general sort of level. It had no numbers associated with it but I thought that was a clear implication of several of the bits of economic analysis that had been done.”

(NICE 21)

The health economist interviewee also re-emphasised the gap between the question faced by the committee and the evidence provided to it.

“The mismatch between the analysis that was done and the question that really needed to be answered was unusually large. Most of the time we do get a reasonably good match.”

(NICE 21)

Interviewees were unanimous in the perception that consensus had been achieved within the committee. The two non-economists agreed that the committee had appeared to understand the economic analysis. Both emphasised the importance of the lead team presentation on the cost-effectiveness analysis in helping committee members understand. By contrast, the health economist felt there was probably some variation among committee members in their level of understanding.

One interviewee noted that there was difficulty in comparing **between** the new drugs because of the 3-week time-frame employed in the analysis. This was viewed as an unsuitable time horizon as more data on hospital admissions in the medium term would have overwhelmed any differences in the drug acquisition costs. The second interviewee considered the lack of data on the side-effects of the treatments as a weakness of the evidence base. The health economist, in interview, returned to

many of the same themes highlighted in the appraisal discussion but the primary problem was seen as resulting from gaps in the evidence base.

“There’s probably insufficient evidence to rule anything out and sufficient evidence to make you think you should be giving all of them a chance. So my view is that we should not rule anything out. We should leave the clinicians to have all of those new technologies available but to push very strongly for some process of monitoring, so that by the time it comes round for review we won’t be in the same position as we’re in now.”

(NICE 21)

The economist interviewee also felt that more evidence on side-effects – for example, from patient group submissions – could have been incorporated into the economic analysis and that there was a need for further research on how cost-effectiveness varies across different patient subgroups.

“I think in this case the whole question we were looking at was unhelpful and rather misguided. The idea that it makes any sense to concentrate solely on the acute mania phase and not to have some cognisance of the fact that actually what we’re looking at is one slice in what is a chronic condition is, I just think not a very sensible way to approach it. I think the fact that the question was set up that way possibly reflects a misunderstanding on the part of those who are responsible for framing the scope of exactly what is involved.”

(NICE 21)

As with the first two observed appraisals, interviewees each felt it was an unusual appraisal in that the economic analysis was not discussed in great detail. One in particular felt that overall it was an unusually simple appraisal.

“I think it was a relatively straightforward appraisal in that there wasn’t the sort of evidence that would allow us to look very carefully at one drug versus another drug so in that sense it was more straightforward. There weren’t very good cost-effectiveness data or evidence there so in a sense we had to reach some fairly general sort of conclusions. You couldn’t get into nitty gritty on ‘well where does the cost per QALY lie?’ so in that sense it was kind of simpler I suppose.”

(NICE 10)

The guidance

NICE issued its guidance following the second appraisal meeting. This document states:

“Olanzapine and valproate semisodium, within their licensed indications, are recommended as options for

control of the acute symptoms associated with the manic phase of bipolar I disorder.

“Of the drugs available for the treatment of acute mania, the choice of which to prescribe should be made jointly by the individual and the clinician(s) responsible for treatment. The choice should be based on an informed discussion of the relative benefits and side-effect profiles of each drug, and should take into account the needs of the individual and the particular clinical situation.

“In all situations where informed discussion is not possible advance directives should be taken fully into account and the individual’s advocate and/or carer should be consulted when appropriate.”

The guidance document also described the methods and results of cost-effectiveness analyses conducted by both manufacturers and the independent academic team. In the ‘consideration of evidence’ section of the guidance, a number of influences on the committee are detailed:

“The Committee reviewed the evidence available on the clinical and cost-effectiveness of olanzapine and VSS to treat acute mania associated with bipolar I disorder, having considered evidence on the nature of the condition and the value placed by users on the benefits of these technologies from people with bipolar disorder, those who represent them, and clinical experts. It was also mindful of the need to ensure that its advice took account of the efficient use of NHS resources.

“In the absence of definitive evidence of superiority in clinical or cost-effectiveness, the choice of the most appropriate treatment regimen would usually depend on the clinical situation, individual circumstances, and the patient’s preference.”

This appraisal had a number of features that echoed previously observed decisions – limited data leading to an inconclusive cost-effectiveness analysis and ultimately to an inability to make differential recommendations for the alternative new drugs under review. The scope of the appraisal was felt, in retrospect, to be too narrow in terms of time-frames considered.

Fluid-filled thermal balloon and microwave endometrial ablation techniques for heavy menstrual bleeding

The fourth appraisal included within the sample was of endometrial ablation techniques for heavy menstrual bleeding which was selected for inclusion in particular as a non-pharmaceutical intervention. The Peninsula Technology

Assessment Group prepared the technology assessment report for this topic. A summary of the economic analysis is given in *Table 18*. A model-based cost–utility analysis was undertaken and so the committee had information on QALYs to consider. The model type was a Markov model which was presented in an accessible manner, using diagrams. Probabilistic sensitivity analysis and value of information analyses were not reported.

The observation of the appraisal meeting

Two members of the research team (IW and SB) observed both the first and second meetings. Four health economists were present for the first appraisal meeting. In line with committee convention, the lead team summarised the evidence of the technology’s clinical effectiveness and then its cost-effectiveness. However, a member of the NICE technical support team, with expertise in health economics, presented a further account of the cost-effectiveness component. The presentation provided a critique of the economic

evaluations submitted by product manufacturers and the academic review team.

At the outset, the Chair sought to clarify the issue of the questions being addressed and the appropriate comparators. The potential for being distracted by inappropriate comparators was recognised and the need to focus on the comparators included in the scope of the decision was emphasised. Although there was acknowledgement at the outset that this was a clinical area where individual preferences and choice were important – for example, it was noted that if a woman’s objective is amenorrhoea then hysterectomy is required and ablation is not an appropriate option – it was emphasised that the committee was not considering choice issues. The issue before the committee was reiterated as determining whether second-generation technologies (i.e. microwave and thermal balloon endometrial ablation) were more cost-effective than the first-generation approach (i.e. transcervical resection and rollerball ablation) and

TABLE 18 Summary of economic analysis – fluid-filled thermal balloon and microwave endometrial ablation techniques for heavy menstrual bleeding

Aspect of economic evaluation		
<i>Decision problem addressed (from Scope)</i>		Interventions: 4 alternative endometrial ablation procedures, i.e. thermal balloon, microwave, transcervical resection of the endometrium (TCRE) and rollerball Population: women with heavy menstrual bleeding Comparators: hysterectomy
<i>Analytic methods</i>	Type of economic evaluation	Cost–utility analysis
	Modelling methods	Two Markov models developed – the endometrial ablation model had 8 states and the hysterectomy model had 6 states
	Time horizon of analysis	10 years
	Perspective on costs	NHS and PSS only
	Discounting	Benefits at 1.5% and costs at 6%
	Measure of health benefits	QALYs
	Source of quality of life and utility data	Published estimates where available or assumption
	Probabilistic sensitivity analysis	Not performed
<i>Presentation of results</i>	Subgroup analyses	None
	Equity considerations	None explicitly referred to
	Assessment of future research needs	No formal valuation of information analysis undertaken
	Expected CE results	Reported
	Parameter uncertainty	CE plane scatters not reported CEACs not reported
<i>Synthesis of evidence on outcomes</i>	Other forms of uncertainty	One-way sensitivity analyses undertaken
		Systematic review, using data from RCTs and large observational studies
<i>Assessment of NHS impact</i>		Budget impact calculated using prevalence and incidence information

hysterectomy. One consequence of the initial steer was that early debate concerning the choice of comparators, in particular whether the new Marina coil technology should have been included in the scope, was drawn to a close.

The importance of patient preferences and choice was a recurring theme in this discussion. In the discussion, it was noted that a number of outcomes of treatment might be sought and that these would vary according to individual patient wishes. The committee explored with the experts what might constitute a successful treatment and the factors likely to influence this. The experts emphasised the importance of patient choice and quality of life. It was noted by one of the health economists that a recommendation for individual patient choice in these circumstances would potentially have resource implications.

The issue of choosing between new ablation techniques, given the closeness of the cost-effectiveness results for the first- and second-generation technologies, was an important discussion topic. Some committee members felt that the results of the cost-effectiveness analysis suggested that first- and second-generation techniques could not be separated. The policy conclusion on the basis of this observation was not, however, clear to all on the committee. One member argued that, if the new techniques are equivalent in cost-effectiveness terms, the committee should, therefore, not encourage their use. However, another member argued the exact opposite, indicating that evidence of no difference means that the committee is free to advocate the use of second-generation techniques.

The issue of the comprehensiveness of the assessment of benefits in the economic evaluation was also raised. It was suggested that there are some aspects of benefit for the second-generation technologies that were not been fully captured. The particular issue highlighted was the convenience aspect associated with their delivery in outpatient settings. Although it was agreed that second-generation ablation techniques have advantages and are not less cost-effective 'in general' than first-generation techniques, there might be circumstances under which the latter are preferred. However, one of the health economists agreed that the committee was attempting to run two conceptually incompatible ideas simultaneously: an overall average cost-effectiveness estimate for use in societal rationing decisions, and patient preferences relating to individual patient decisions.

A strict interpretation of the economic analysis could be that all presenting women are recommended to have hysterectomy, given that amenorrhoea was achieved. In response, it was noted that the reason for having experts present was to avoid such inappropriate conclusions. However, some of the health economists present argued that the decision had to relate to the cost-effectiveness analysis. A clinical committee member dismissed the favourable analysis of hysterectomy, arguing that the driving force for the decision should be patient and professional choice, and so viewed the economic analysis as irrelevant. Although there was some degree of sympathy for this view point, it was agreed that patient choice could not be the only consideration regardless of cost. The suggestion was, therefore, made that the new technologies be recommended but not on cost-effectiveness grounds.

Other issues relating to the health economics that were discussed included the likely budget impact. An argument put forward was that with all other measures showing equality between the two technologies, the total cost to the NHS would determine which was preferable. Some doubts were raised as to whether some of the savings identified in the economic analysis could actually be implemented by budget holders. It was acknowledged that this is an issue the committee have faced before although it is not a consideration that can alter the committee's recommendations. A health economist asked what the introduction of these new methods might do to the threshold of treatment. This was discussed, but no definitive answer was reached.

At a later meeting, the committee revisited this appraisal in the light of consultee comments on the ACD. In an unusually lengthy second discussion, many of the previous issues were revisited. The issue of choosing between the new techniques was raised with frustration expressed at the inability to recommend one over the other. Although it was pointed out that it was not sensible to make a decision between techniques with apparently little difference in terms of costs and effects, some committee members reiterated a frustration at not being able to recommend one of the two technologies. A point of broad agreement at the end was that the importance of 'patient choice' would have to be explicitly stated in the opening paragraph of the guidance.

Post-ACD meeting interviews

The research team conducted interviews with two committee members: one health economist and

one with a nursing background (unfortunately, parts of the recording of one interview were inaudible due to a technical recording failure). The non-economist interviewee reiterated concerns expressed on the day of the appraisal about the desired outcome of treatment for women and the need for this area to be reported accurately and clearly in the guidance issued. This interviewee also felt that the health economics information was less prominent in the appraisal discussion than it often was, for example, when looking at expensive cancer treatments. The non-economist interviewee explained that her focus had been on clinical dimensions to the appraisal as her view was that her expertise in health economics was insufficient to grasp some of the economic arguments.

The issue of the apparent cost-effectiveness of hysterectomy arose again in interview with the health economist.

“I think everybody around the table’s view is ‘well that’s just ridiculous so let’s just ignore it’. Whereas myself, and I guess some of the other health economists were struggling with ‘well how else would we do the analysis? There obviously is something fundamentally wrong here’, most people round the table just ignored it.”

(NICE 28)

The economist also summed up a number of other areas of concern in this appraisal. The first related to the comparators and the scope of the appraisal, with frustration at the limited discussion of the possible impact of the decision on referral thresholds.

“I think there was a strong feeling amongst the health economists and indeed quite a few other people around the table that actually these two techniques are as likely to affect the clinical threshold as much as anything. And indeed that may prove to be more important in the long-term. But that was ruled out of consideration. We also had to rule out the consideration of non-surgical alternatives and also the coil. Many of us felt a bit uncomfortable about that since it didn’t make sense to limit the comparators in that way.”

(NICE 28)

The second area of concern expressed related to the assessment of benefits.

“There was general agreement that actually objectives between patients varied in terms of end-points. And there was quite, I thought, quite a sophisticated discussion of the different objectives that patients have and how that may affect, may impact on, the way

you assess benefits. Now, the problem we had yesterday was that the way we were assessing benefits was using these average patient preference weights and we didn’t really have a proper analysis based on, if you like, individual patient preferences.”

(NICE 28)

The economist was concerned at the lack of a fuller consideration of uncertainties in the assessment team’s economic analysis.

“They had a model, a sort of Markov model, that I thought looked pretty reasonable. I think the difficulty with this was partly the problem of the extent of the uncertainty around the estimates. I didn’t think they’d really demonstrated that really well. I mean confidence intervals are obviously problematic anyway, but they didn’t really do any kind of proper stochastic analysis. And the sensitivity analysis that they did is all in the back, but I think the significance of it wasn’t really brought out in the document.”

(NICE 28)

The guidance

The subsequent guidance document contained the following decision statement.

“Fluid-filled thermal balloon endometrial ablation and microwave endometrial ablation are recommended as treatment options for women with heavy menstrual bleeding in cases where it has been decided (by the woman and the clinician responsible for her treatment) that surgical intervention is the appropriate next step in management of the condition.

“For heavy menstrual bleeding, the choice of surgical treatment should be made jointly by the woman and the clinician responsible for treatment. The decision should be made after an informed discussion taking into account the desired outcome of the treatment (such as normal menstrual bleeding [eumenorrhoea] or complete cessation of menstrual bleeding [amenorrhoea]), the relative benefits of all other treatment options and the adverse events associated with them, as well as the clinical condition, anatomical suitability and preferences of the woman.”

Three economic analyses were made available to the Institute as part of manufacturers’ submissions, in addition to the Assessment Group model. The guidance detailed methods and results of these analyses. The guidance states that a review of the evidence did not uncover grounds for differentiation between thermal balloon endometrial ablation and microwave endometrial ablation.

“it was not possible to draw conclusions on the relative clinical and cost-effectiveness of TBEA and MEA.”

“The Committee was persuaded that the relative merits of these techniques varied greatly for individual patients, and was highly dependent on the specific outcome that was appropriate for any particular patient. The Committee therefore considered that the issue of choice for the individual rendered differences in overall effectiveness between the techniques less relevant. It concluded that these techniques may separately be appropriate for specific subgroups of women, and the choice between them should be made by the woman and the clinician responsible for her treatment, following informed discussion.”

The final choice on treatment options, it was decided, should be left to the clinician and patient.

This appraisal raised similar issues to those that preceded it. First, it involved some discussion as to whether the appraisal scope had included all of the potentially relevant comparator technologies. Second, the cost-effectiveness analysis again did not permit a ranking of the new technologies, leading the committee to promote the importance of patient choice and dialogue between patient and clinician in the selection of appropriate treatment options. This was the first appraisal that saw significant disagreement between those who felt the committee should take more account of the results of the cost-effectiveness analysis, which in this case indicated the dominance of hysterectomy over other treatment options, and those on the committee who felt other factors were more important.

Rituximab in the treatment of aggressive non-Hodgkinson’s lymphoma

The fifth technology included within the case study was another intervention in the field of oncology. The technology assessment report was prepared by the University of Sheffield and is summarised in *Table 19*. The report contained a cost–utility analysis and so the committee again considered outcomes expressed as QALYs. A model-based analysis was undertaken whereby the assessment team further developed the model prepared by the manufacturer. The model was considered by the research team to be a reasonably simple Markov model (with only three states) that was reported in an accessible manner, using diagrams. The analysis in this report was more technical and extensive than in the other selected topics – it included a probabilistic sensitivity analysis, results reported using CEACs and a formal value of information analysis.

The observation of the appraisal meeting

Two members of the research team (IW, SB) observed the first meeting and one team member

(IW) observed the second meeting. Two health economists were present for the first appraisal meeting. In line with normal practice, the meeting began with presentations from the lead team, which included a summary of the evidence on clinical and cost-effectiveness presented in the submission from the academic review team and the submissions from the manufacturer and from other groups. The cost-effectiveness part of the presentation was delivered by a committee member with expertise in finance. The Markov model used by both the manufacturer and the review team was briefly introduced, although no detail of the model structure was presented. The focus for the presentation was on the results of the economic analysis rather than on the methods. The one exception to this was a concern expressed over the use of quality of life data from a study sponsored by the manufacturer which was unpublished. This issue was picked up in the general discussion where the concern was raised that the manufacturer of the technology had not submitted all the data that had fed into their analysis of its effectiveness and cost-effectiveness. This was particularly the case relating to the quality of life and utility data, where the economic analysis relied on unpublished and unseen data from a study sponsored by the manufacturer. The sensitivity analysis results were used in order to explore the importance of this issue, and the general view to emerge was that the analysis results were robust to reasonable variation in quality of life scores.

Emphasis was given in the discussion to the budget impact of the proposed new intervention and there was general acknowledgement that a positive recommendation from NICE would have a large financial impact on the NHS. The majority view appeared to be that the academic team were wrong to exclude the VAT component from the calculation.

There was much discussion of how the effectiveness and cost-effectiveness varied for different patient subgroups, defined by performance status and/or age. The focus on performance status was quickly dismissed by the clinical experts – the advice given was that this factor might influence the decision whether or not to initiate CHOP (cyclophosphamide, doxorubicin, vincristine and prednisolone) alone but not the decision regarding the move from CHOP to rituximab plus CHOP (R-CHOP). The suggestion was made by the clinical experts that CHOP alone is more effective in the under-60s, compared with its use in those over 60 years of

age. Concerns were then raised that R-CHOP may, therefore, be less effective, and less cost-effective, in the younger age group. Clarification was provided that the focus should be on considerations of ‘incremental effectiveness’ and there was no good data to say that the incremental effectiveness was any different in the younger age group.

There was some discussion of the extent to which introduction of rituximab for use in this condition would have capacity implications for oncology treatment services – for example, by requiring a large time commitment from pharmacists. However, although this point was generally accepted, it was felt by those present that it did not necessitate a significant adjustment to the analysis.

The need for consistency in the committee’s decisions was a further debate topic and a

reminder was given that NICE had previously decided on rituximab in earlier appraisals, when it was to be used in other patient groups. There was also repeated concern relating to the paucity of evidence in this appraisal, given the early stage of the use of the drug. On the basis of these concerns, the suggestion was made that the decision should be reviewed early in order to judge whether the estimated cost per QALY from the academic team’s analysis was about right. On this note, the point was made that NICE has to undertake an iterative process where some of the decisions taken will be ‘wrong’ because many of the technologies considered are very early in their life and so long-term data are unavailable.

Overall, it appeared that the committee was satisfied that rituximab plus CHOP provided some important clinical benefits when compared to CHOP alone and at an acceptable incremental

TABLE 19 Summary of economic analysis – rituximab in the treatment of aggressive non-Hodgkinson’s lymphoma)

Aspect of economic evaluation		
Decision problem addressed (from Scope)		Intervention: rituximab in combination with CHOP chemotherapy Population: patients with diffuse large B-cell lymphoma in whom CHOP chemotherapy is not contraindicated Comparator: CHOP chemotherapy regimen (cyclophosphamide, doxorubicin, vincristine and prednisolone)
Analytic methods	Type of economic evaluation	Cost–utility analysis
	Modelling methods	Markov model with 3 states (academic team revised model submitted by the manufacturer)
	Time horizon of analysis	15 years
	Perspective on costs	NHS and PSS only
	Discounting	Benefits at 1.5% and costs at 6%
	Measure of health benefits	Life-years and QALYs
	Source of quality of life and utility data	Unpublished study sponsored by the manufacturer
	Probabilistic sensitivity analysis	Performed on relative risk information (log-normal distribution), utilities (uniform distribution), cost components (normal distributions) and proportion using other services (uniform distribution)
	Subgroup analyses	Analyses conducted separately for patients under the age of 60 and patients over 60 years
	Equity considerations	None explicitly referred to
	Assessment of future research needs	Formal valuation of information analysis undertaken
Presentation of results	Expected CE results	Reported
	Parameter uncertainty	CE plane scatter or ellipses not reported CEACs reported
	Other forms of uncertainty	One-way sensitivity analysis and threshold analysis undertaken
Synthesis of evidence on outcomes		Systematic review but estimates of relative treatment effect taken from single (only available) trial
Assessment of NHS impact		Budget impact calculated using prevalence and incidence information

cost per QALY. There was little or no disagreement between committee members and overall the deliberations lasted for a shorter than average time. At the second meeting, the committee revisited this appraisal in the light of consultee comments on the ACD. After a short discussion, it was decided that no substantial changes to this document were required.

Post-ACD meeting interviews

Interviews were conducted with four committee members: an epidemiologist, an Association of British Pharmaceutical Industry (ABPI) representative, a health economist and someone from a nursing background. Each interviewee expressed the view that the clinical evidence base was both a strength and a weakness of the appraisal. It was a strength inasmuch as it derived from a high-quality clinical trial – unusual, particularly in the area of oncology. However, it was a weakness as only one such trial had been carried out. Nevertheless, interviewees agreed that there was good reason to believe that the technology in question delivered demonstrable clinical benefits.

In addition, individual interviewees expressed views on the following issues:

- A concern over the absence of some key quality of life data used by the manufacturer and the academic team in their analyses.
- That the severity of the medical conditions in question ‘focuses the mind’ of committee members.

The cost per QALY decision threshold was explicitly mentioned by three of the four interviewees and was clearly an important consideration in reaching a view on the adoption decision. However, there was also reference to the importance of flexibility in decision-making by the committee and that no absolute threshold exists.

“It was fairly costly but not above the magic £30,000 per QALY.”

(NICE 17)

“There was a lot of confidence that by approving rituximab ... we were going to be well within a threshold level of less than £30,000. I know we don’t use threshold levels in NICE but if you get below that level then usually we have a certain level of comfort.”

(NICE 27)

Each interviewee pointed to the fact that the review team analysis had upheld the industry model and its conclusion that rituximab appeared to be cost-effective in the treatment of this

condition. It was felt by all interviewees that the committee members were in broad agreement at the end of the deliberations.

One interviewee felt that her level of understanding of the economic information was limited. The health economist interviewed expressed the view that in general, levels of understanding within the committee were varied. However, interviewees agreed that overall there were no apparent problems with levels of understanding in this specific appraisal.

The health economist interviewed stated his satisfaction with the analytical approach adopted by the academic review team, including the decision to adopt the industry economic model and the testing of its robustness to changing assumptions. In general terms, the use of sensitivity analyses was highlighted as being of particular value to the committee. However, three of the four interviewees felt that there was room for more exploration of the impact on the NHS of recommending the technology. One referred to a general need to take into account the ‘overall pressure’ on health services. Another advocated a ‘net QALY benefit’ approach that simultaneously took into account cost-effectiveness and the total budget impact.

There was a unanimous view that this appraisal was more straightforward than is usual. One interviewee felt that appraisals where the evidence seems to point to a favourable recommendation are generally more straightforward for the committee. The economic analysis was thought to be particularly accessible.

“My own experience in health economics is limited so therefore I do rely on other experts on the committee for their input in that. But yesterday’s appraisal, unusually, was one I could follow and the economic analysis, I did feel, was well done.”

(NICE 13)

It was noted by three of the four interviewees that a key feature in determining the outcome of the appraisal was the overall agreement between the industry and academic economic analyses as to the technology’s cost-effectiveness. It was felt that such a level of accord was rare in appraisals.

“In this particular case the industry figure and the assessment report were very similar so we had quite a lot of confidence. And again there was very little uncertainty around that figure.”

(NICE 20)

“The fact that the economic analyses, both company and independent assessments, were very, very similar,

with no great dispute, made the decision relatively straightforward.”

(NICE 27)

The guidance

The guidance document produced by NICE following the committee’s deliberations concluded:

“Rituximab is recommended for use in combination with a regimen of cyclophosphamide, doxorubicin, vincristine and prednisolone (CHOP) for the first-line treatment of people with CD20-positive diffuse large-B-cell lymphoma at clinical stage II, III or IV (see Section 2.3). Rituximab is not recommended for use when CHOP is contraindicated.

“The clinical and cost-effectiveness of rituximab in patients with localised disease (stage I, see Section 2.3) has not been established. It is recommended that rituximab be used in these circumstances only as part of ongoing or new clinical studies.

“A specialist in the treatment of lymphomas should supervise the use of rituximab in combination with CHOP for the treatment of diffuse large-B-cell lymphoma.”

In describing the cost-effectiveness analyses considered by the committee, the guidance document mentioned that the Assessment Group incorporated a number of different assumptions into the framework of the manufacturer’s model as part of the review process. The Assessment Group’s version of the model differed from the manufacturers mainly in the interpretation of the survival curves for people receiving CHOP or R-CHOP and the inclusion of other costs associated with treatment failure (second-line therapies and palliative care costs). The results for people younger than 60 years were slightly less favourable than those from the manufacturer: approximately £8500 per life-year gained and £7500 per QALY gained. In people aged 60 years and older, the ICERs were less favourable: about £9700 per life-year gained and £10,500 per QALY gained. Both versions of the model suggested that Rituximab in combination with each of eight cycles of CHOP was cost-effective relative to CHOP used alone.

Despite some concerns over data shortages, there was widespread agreement within the committee that the technology was both clinically effective and cost-effective in first-line treatment. The level of accord between the economic analyses of the manufacturers and the academic review team was seen as an unusual feature of the appraisal. The issue of precedent arose with the committee made explicitly aware of the constraints of previous decisions taken in relation to this technology.

Imatinib for chromosome-positive chronic myeloid leukaemia (CML)

The committee’s consideration of imatinib for patients with CML was the sixth appraisal included within the case study. It was expected that the treatment would be relatively expensive and therefore might throw up previously unseen issues in the committee’s discussion of the economic information. The Peninsula Technology Assessment Group produced the assessment report for this appraisal. *Table 20* summarises the economic analysis. Model-based cost–utility analyses were reported with a time horizon of 20 years being considered. The models used had a Markov structure and were presented in what the research team considered to be a reasonably accessible manner. Probabilistic sensitivity analysis was undertaken with results reported using CEACs.

The observation of the appraisal meeting

Two members of the research team observed the first meeting (IW and SB) and one team member (IW) observed the second meeting. Four health economists were present for the first appraisal meeting. The lead team presentation on cost-effectiveness was from a committee member with expertise in statistics. The main focus for the presentation of the economic analyses was on the ICERs (cost per QALY), for all patients and for the subgroups defined as high and low risk. Some additional analyses (described as back-of-the-envelope calculations) were also presented and these included cost-effectiveness results (i.e. cost per life gained and cost per life-year gained). Brief mention was made of the CEACs but they were not presented.

The Chair opened the discussion by stating that the committee had established previously that cytogenetic response is an important surrogate measure for survival in this patient group. Given this, the point was made that the committee should not be concerned by the fact that the trial showed no gains in survival because it did reveal that imatinib generated improvements in cytogenetic response.

The committee questioned experts as to the place of imatinib within treatment pathways, and were particularly interested in whether imatinib outperformed interferon- α , the identified comparator for the appraisal, to the extent that the latter would be replaced. The issue of comparators came to dominate subsequent discussions. Committee members referred to a second possible comparator present in the academic review team’s economic analysis: HU.

TABLE 20 Summary of economic analysis – imatinib for chromosome-positive chronic myeloid leukaemia (CML)

Aspect of economic evaluation		
Decision problem addressed (from Scope)		Intervention: imatinib Population: patients with chronic phase CML Comparators: hydroxyurea (HU) or interferon-alpha (INF- α)
Analytic methods	Type of economic evaluation	Cost-utility analysis
	Modelling methods	Two Markov models developed – the HU model had 4 states and the imatinib/INF- α model had 6 states
	Time horizon of analysis	20 years
	Perspective on costs	NHS and PSS only
	Discounting	Benefits at 1.5% and costs at 6%
	Measure of health benefits	Life-years and QALYs
	Source of quality of life and utility data	Unpublished study sponsored by the manufacturer
	Probabilistic sensitivity analysis	Performed on relative risk information (log-normal distribution) and utilities (beta distribution)
	Subgroup analyses	Separate analyses reported for low- and high-risk patient groups
	Equity considerations	None explicitly referred to
	Assessment of future research needs	No formal valuation of information analysis undertaken
Presentation of results	Expected CE results	Reported
	Parameter uncertainty	CE plane scatters reported CEACs reported
	Other forms of uncertainty	One-way sensitivity analyses undertaken
Synthesis of evidence on outcomes		Systematic review but estimates of relative treatment effect of imatinib taken from single (only available) trial and for HU taken from Benelux observational study
Assessment of NHS impact		Budget impact calculated using prevalence and incidence information

Although imatinib was shown to be cost-effective when compared with interferon- α for this condition, it was markedly less so when compared with HU. This led some committee members to question the grounds for a recommendation of imatinib as cost-effective. Responses from those in favour of recommending imatinib fell into two broad camps. The first of these argued that interferon- α is superior to HU, the evidence for this being that use of interferon- α is currently the preferred option of clinicians working in this area. Therefore, if imatinib is superior to interferon- α , it follows that imatinib is superior to HU. The second camp argued that HU is not an appropriate comparator in this appraisal because, unlike both imatinib and interferon- α , it does not act on the progression of the disease and, therefore, does not extend life. The benefits of HU are, it was suggested, confined to symptom control and so it should be viewed as a very different type of therapy.

An argument made against the first of these points was that the NICE Appraisal Committee had

never been asked to consider the comparison between interferon- α and HU. Therefore, the superiority of the former could not be assumed. Some committee members felt that its status as preferred current practice was not sufficient grounds for asserting the supremacy of interferon- α over HU. For example, it was argued that ‘what doctors do’ does not have an independent status regardless of evidence and should, therefore, not affect ‘what we do at NICE’. In turn, some clinicians present felt that this position reflected a lack of understanding on the part of health economists of the realities of current NHS practice.

On the second point, concerning the effect of HU on disease progression, there appeared to be some uncertainty. It was broadly accepted that cytogenetic response was not a feature of HU, although some clinical experts stated that in clinical trials it had been shown to extend life when compared with placebo. Other committee members pointed out that the objective of the QALY measure was precisely to combine measurement of improvements in survival and quality of life, and

so they argued that HU had to be considered a legitimate comparator. The point was made that if the use of interferon- α is shown to be inefficient in comparison with HU, then to compare imatinib with interferon- α runs the risk of 'building inefficiency upon inefficiency' and that choosing an inappropriate comparator (interferon- α) could serve to exaggerate the apparent benefits of the new technology (imatinib). This led to some discussion about previous instances where the committee had had to make comparisons with 'inefficient' current practice.

These differences of opinion appeared to reflect a disagreement between those who were concerned with clinical effectiveness – in this case as measured by increased survival rates – and those who believed that the cost per QALY estimate was the most important factor. In the end, there was broad agreement that, for the purposes of this appraisal, HU was not the designated comparator. However, it was also decided that the very poor cost-effectiveness of imatinib against HU should be recorded in the ACD.

The issue of the company's pricing strategy was raised – on the whole, committee members felt the technology was unduly expensive. It was acknowledged, however, that these issues were beyond the committee's remit. The committee went on to discuss the possible implications of disinvestment in interferon- α , and whether these would result in poorer treatment for older patients. This point related to the side-effect profile of imatinib and the concern that older people might find the drug less acceptable, with the possibility that they would be offered only HU and denied access to interferon- α .

One committee member suggested that a decision to recommend imatinib would generate savings, given that current practice is to use interferon- α rather than HU. This view was challenged and it was pointed out that the committee member had not fully understood the health economics presented.

A final point was raised concerning the role of NICE to promote innovation. The suggestion was put forward that the approval of imatinib would give a positive message concerning innovation, and that the committee might be prepared to be more lenient in this case (and vary the threshold) in order to take this factor into account.

Having looked initially like a potentially straightforward appraisal, the committee

deliberations were in the end lengthy and apparently not completely conclusive. This was the longest discussion of a single technology observed within the study sample.

At a later meeting, the committee revisited this appraisal in the light of consultee comments on the ACD. In a short discussion, the importance of adopting a 'pragmatic' approach, which acknowledged the realities of current practice, was emphasised. Reference was also made to the importance of maintaining consistency with previous NICE guidance. Health economists present requested that treatments are not recommended on the basis of their 'cost-effectiveness' when there is no evidence to demonstrate that this is the case.

Post-ACD meeting interviews

Interviews were conducted with four committee members: an NHS manager, a patient representative, a radiologist and a health economist. Interviewees agreed that imatinib had demonstrable benefits in terms of life expectancy gains and quality of life improvement for patients with CML. Two interviewees indicated concern at the use of current practice as a starting point for the committee's deliberations and the view was expressed that the expected response of clinicians 'in the field' influenced the committee's thinking.

Two interviewees felt that the nature and perceived severity of the condition influenced the committee. One of these was the health economist for whom this, along with the relative lack of alternatives for this patient group, meant that benefits were more highly valued by the committee and that they were, therefore, willing to accept a higher cost per QALY threshold. One interviewee referred to this as an 'alpha' drug and suggested that the committee was more inclined to positively recommend drugs of this type. Another felt the committee's familiarity with imatinib and its benefits (from previous appraisals) led to a position of being more predisposed to recommending its use in this patient group.

Interviewees unanimously acknowledged the importance of the choice of comparator in determining the cost-effectiveness of imatinib in the treatment of this condition and that this had become the central consideration in deciding whether or not to recommend the treatment. Although all interviewees cited the issue of choosing the correct comparator as central to the cost-effectiveness analysis, they differed in their interpretation of the economic evaluation.

“My original stand-point was, though we don’t have a threshold, this looked like a promising new drug and the cost-effectiveness ratio seemed to be within what we would usually consider reasonable and that it was likely to go through. I did actually notice that all the data were there about the cost-effectiveness of imatinib and interferon against hydroxyurea and I had noticed that it looks jolly expensive compared to hydroxyurea but when I was reading it I thought that probably isn’t relevant in practice.”

(NICE 9)

In contrast, two interviewees, including the health economist, felt the evaluation showed Imatinib to have poor cost-effectiveness.

“For me it suggests that imatinib is not efficient according to strict economic criteria and according to the NICE framework which ultimately looks at value for money.”

(NICE 4)

The fourth interviewee was undecided as to the correct choice of comparator.

Two interviewees acknowledged a division within the committee deriving from the first appraisal meeting for this technology. One felt this organised around a split between ‘methodologists’ and ‘clinicians’, with some committee members placed between these two groups. Another felt that the majority of committee members were in favour of a positive recommendation of imatinib, as distinct from the minority who believe that ‘if the health economics say no, that’s the end of the discussion’. The other two interviewees did not express an opinion.

One interviewee believed that the distinction between whether or not the treatments ‘act on the disease’ was irrelevant. In reference to the distinction between life-extending and quality of life improving treatments, another respondent supported this view and stated that the committee:

“... were forgetting that the QALY is the proxy measure for these things.”

(NICE 9)

Two interviewees commented on the decision at the end of the first committee meeting to ask the review team to revisit the economic analysis in the light of committee discussions. One felt this was a necessary undertaking. The other felt it was typical of attempts to “fiddle with the model to bring the cost per QALY into an acceptable range”.

The guidance

Following the second appraisal meeting, the committee issued its FAD which contained the following guidance:

“Imatinib is recommended as first-line treatment for people with Philadelphia-chromosome-positive chronic myeloid leukaemia (CML) in the chronic phase.

“Imatinib is recommended as an option for the treatment of people with Philadelphia-chromosome-positive CML who initially present in the accelerated phase or with blast crisis. Additionally, imatinib is recommended as an option for people who present in the chronic phase and then progress to the accelerated phase or blast crisis if they have not received imatinib previously.

“There is currently no evidence on clinical cost-effectiveness on which to base guidance on the continued use of imatinib that has been initiated in the chronic phase of CML but has failed to stop disease progression to either the accelerated phase or blast crisis. Therefore, under these circumstances the use of imatinib is recommended only in the context of further clinical study. The data for this study should be collected systematically to allow aggregation and analysis at a national level in order to inform the appraisal review.

“For people in chronic-phase CML who are currently receiving interferon alpha (IFN- α) as first-line treatment, the decision about whether to change to imatinib should be informed by the response of the disease to current treatment and by the tolerance of the person to IFN- α . This decision should be made after informed discussion between the person with CML and the clinician responsible for treatment, taking full account of the evidence on the risks and benefits of imatinib and the wishes of the person.”

The guidance document stated that the committee received economic models from both the manufacturers and the academic assessment group, and reported the methods and results of each of their analyses. The guidance document went on to outline influences on the committee’s deliberations:

“The Committee reviewed the data available on the clinical and cost-effectiveness of imatinib for CML, having considered evidence on the nature of the condition and the value placed on the benefits of imatinib from people with CML, those who represent them, and clinical experts. It was also mindful of the need to take account of the efficient use of NHS resources.

“The Committee was mindful of the current licensed indications for the use of imatinib and the previous

guidance produced by the Institute regarding the use of imatinib in the circumstances of intolerance or resistance to first-line IFN- α treatment, which was based on evidence primarily from case series.”

On the particular issue of HU as a possible comparator, the guidance states:

“The Committee concluded that, although it was reasonable to regard HU as a comparator treatment in this context, current clinical practice (prior to the licensing of imatinib) uniformly considered IFN- α as the principal treatment of choice for people in the chronic phase of CML, provided it can be tolerated.

“The Committee was ... persuaded that, because IFN- α is currently accepted as a standard first-line treatment for people with CML (although it might not be considered cost-effective), it was appropriate to compare imatinib with IFN- α in terms of its ICER.”

This suggests that ‘current clinical practice’ was a strong influence on the guidance. The guidance reports further economic modelling undertaken as a result of committee discussions:

“The results from the independent model suggested ... that the cost-effectiveness of imatinib when compared with HU was not acceptable, with an ICER of around £87,000 per QALY. The ICER of IFN- α compared with HU was very much higher in excess of £1 million per QALY.

“In line with the considerations outlined in Section 4.3.5, the Committee asked the Assessment Team to test the impact of using per protocol values instead of intention-to-treat values on the cost-effectiveness results. The additional analysis using new assumptions, including the use of per protocol values, resulted in slightly improved ICERs for imatinib, to around £60,000 when compared with HU.”

This appraisal raised a number of interesting issues. First, it highlighted some differences within the committee in attitudes towards the economic evaluations they receive. Despite the importance of the cost-effectiveness information, there were clearly a range of other factors that predisposed sections of the committee to a positive recommendation of this drug. These included:

- the views of the clinical community in defining ‘appropriate’ current clinical practice
- the nature and perceived severity of the condition
- innovation and the ‘orphan’ status of the technology
- the committee’s prior familiarity with imatinib and its benefits through other appraisals of this drug.

Myocardial perfusion scintigraphy for the diagnosis and management of angina and myocardial infarction

The seventh and final appraisal included within the case study was of myocardial perfusion scintigraphy for the diagnosis and management of angina and myocardial infarction. The technology assessment report for this appraisal was prepared by the Health Services Research Unit at the University of Aberdeen. A summary of the main components of the economic analysis is given in *Table 21*. A cost–utility analysis was undertaken using a decision analytic model. The model was interesting in that it had a decision tree section (dealing with diagnosis issues) and a Markov component (for the management of suspected coronary artery disease). The time horizon considered was very long – 25 years. No probabilistic analysis was undertaken and so the results were reported as ICERs, in terms of incremental cost per QALY gained.

The observation of the appraisal meeting

Two members of the research team observed the first appraisal committee meeting (IW and SM). The second meeting was not observed. Two health economists were present for the first appraisal meeting. At the outset of the meeting the committee heard presentations from the lead team – the cost-effectiveness component was presented by a committee member with some experience in economic evaluation.

The experts present contended that single photon emission computed tomography (SPECT) is cost-effective and affordable as a first-line treatment but stated that healthcare providers were not currently equipped to deliver this. Some attention was paid to the training implications of introducing and rolling out SPECT. Experts were asked for their opinions as to why there has hitherto been a low uptake of this approach. It was felt the reasons were multiple and included resource scarcity and the capacity constraints that follow but also political influence – notably of cardiologists promoting the use of coronary angiography (CA). There was some discussion as to whether issues of resource capacity and implementation were within the committee’s remit. An employee of NICE present felt that the main finding was that the technology was cost-effective even if it could not be implemented immediately. One of the health economists felt that the model erroneously assumed in general that resources could be expanded in the short run to meet demand, pointing out that ‘people are a fixed resource’. In general, committee members

TABLE 21 Summary of economic analysis – myocardial perfusion scintigraphy for the diagnosis and management of angina and myocardial infarction

Aspect of economic evaluation		
<i>Decision problem addressed</i>		Interventions: single photon emission computed tomography (SPECT) myocardial perfusion scintigraphy Population: patients with suspected coronary artery disease (CAD) Comparator: stress electrocardiography (ECG) and/or coronary angiography (CA)
<i>Analytic methods</i>	Type of economic evaluation	Cost–utility analysis
	Modelling methods	A decision tree model for the diagnosis decision and a 10-state Markov model for the management of suspected CAD
	Time horizon of analysis	25 years
	Perspective on costs	NHS only
	Discounting	Benefits at 1.5% and costs at 6%
	Measure of health benefits	QALYs
	Source of quality of life and utility data	Published estimates
	Probabilistic sensitivity analysis	Not performed
	Subgroup analyses	Subgroup analysis performed using females only
	Equity considerations	The issue of patient access to SPECT (because it is only available in specialist centres) was raised but not as part of the analysis
	Assessment of future research needs	No formal valuation of information analysis undertaken
<i>Presentation of results</i>	Expected CE results	Reported
	Parameter uncertainty	CE plane scatters not reported CEACs not reported
	Other forms of uncertainty	A series of one-way sensitivity analyses undertaken
<i>Synthesis of evidence on outcomes</i>		Systematic review
<i>Assessment of NHS impact</i>		Budget impact not reported

expressed a preference to make a decision now and look at implementation issues afterwards.

One of the health economists sought to structure the discussion using the economic model and argued that, on face value, the economic analysis recommended going straight to CA as the most cost-effective option, in all patient groups except for low risk. His contention was that if the clinical experts were right then there must be an error in the analysis (either as underestimating the value of SPECT or not accounting for negative features of CA). He felt that the committee should explore the possible reasons for this. In response, discussion centred on aspects of CA that might not adequately be captured by the economic analysis: CA is an invasive procedure, it kills one in every 10,000 who receive it, and it requires a greater number of cardiologists than are currently available.

The experts were asked about prevalence issues and whether clinicians could actually use risk level indicators, as had been modelled in the academic

review team's economic analysis. It was confirmed that this was plausible. A committee member asked the academic review team about the 25-year time horizon and wanted to explore problems with discount rates for models that consider such long periods. However, it was agreed this was not a highly contentious aspect of the analysis. A number of subgroup analyses were discussed, including a focus on women only and people with diabetes.

The committee devoted time to considering the issue of risk/prevalence and sought some clarification of terms here. One of the health economists on the committee noted that, as prognostic information is more valuable the lower the baseline risk in the population, this suggested the model was plausible. However, he felt that it was important, given resource constraints, for the committee to be clear and specific in recommending for which groups SPECT would be cost-effective, and where the line should be drawn. There was some discussion as to what level of risk

supports the use of SPECT and some present felt that this should be explored further in the economic model. The possibility of commissioning the academic review team to look at these issues through further runs of the model was suggested by a health economist committee member. However, the committee agreed not to support the idea of further analysis – some present characterised the suggestion as an example of health economics purism. The Chair contended that the committee always wanted more information but that in this case he was not convinced it would help in what was characterised as a clinically pragmatic decision. A health economist committee member supported making a decision now but welcomed further work on the model to give the committee a better understanding for the future review of the technology.

In the discussion on the drafting of the guidance, and in particular on how the results of the cost-effectiveness analysis should be presented, a health economist committee member argued that the guidance document should make it clear that the judgement was not based on the findings of the economic analyses.

Post-ACD meeting interviews

The research team conducted separate interviews with four committee members: a health economist, a patient representative, a surgeon and a GP. The three non-economist interviewees all noted that the committee had looked in some detail at issues of capacity and the implications of a positive recommendation of this technology. Two interviewees felt this had exercised too great an influence on the committee's deliberations.

“The issue with this particular one was whether the infrastructure and resources in the NHS were able to deliver it. And I think people were probably trying quite hard for that not to influence how they interpreted it all.”

(NICE 2)

All of the non-economists interviewed felt that the committee had spent too long discussing the economic evaluation when the consensus was that the technology was both effective and cost-effective with complementary benefits to CA.

“I personally didn't think that it [the economic evaluation] was that important. The point was made several times during the discussion that even if the models were redone it was going to be very doubtful that it would make a great deal of difference. But the health economists kept saying that we should still be disciplined about the whole approach and do it

properly. But from a pragmatic point of view, and I'm a clinician, I don't think it makes much difference.

(NICE 16)

“I thought when I was preparing for this, that this was mainly cut and dried and it would just be a matter of perhaps looking at special subgroups in whom we might be able to jump one stage of the pathway to coronary angiography. But most of the discussion has been around the health economics which I find very difficult to understand because in fact it isn't as if we were sort of debating about something that was highly expensive.”

(NICE 16)

One interviewee argued that the economic analysis should not dictate the decision, and suggested that in this example there were clinical aspects not captured in the economic model.

“Just because something is possibly more cost-effective, it doesn't mean that you shouldn't be doing something else ... I think that was quite a good indication of where actual clinical practice varies from just a pure cost-effectiveness analysis and economic evaluation, because really what the clinicians were saying was that they get extra value from it.”

(NICE 24)

Interviewees discussed the concern that the economic analysis was suggesting something different from what was considered appropriate clinical practice. This produced different reactions in the interviewees. Some were happy to live with this discrepancy whereas others thought it was necessary to find out whether something important was being missed by the model.

“I ended up having to ask quite a lot of questions about that sensitivity analysis because the results of doing that seemed to me to be quite initially counter-intuitive.”

(NICE 12)

Two of the interviewees without a health economics background admitted that they struggled to follow the economic analysis and felt frustrated at this lack of understanding.

“What frustrates me is that I don't understand whether the point is significant or not. And if it's significant then yes it has got to be thrashed out but I think there are times when I just think 'well maybe it's just a fairly academic point'.”

(NICE 2)

It was also suggested that the presentation and use of terminology in the course of the discussion presumed too high a level of expertise amongst committee members.

One interviewee felt it was an unusual appraisal in that there was good clinical evidence and not that expensive a technology, also noting that there was very little by way of patient group representation. Another noted that it was unusual in the degree of polarisation between committee members over what was the appropriate policy stance to adopt on the basis of the economic evaluation.

The guidance

The guidance document published by NICE for this technology was drafted as follows:

“MPS using SPECT is recommended for the diagnosis of suspected coronary artery disease (CAD) in the following circumstances.

- As the initial diagnostic tool for people with suspected CAD for whom stress electrocardiography poses particular problems of poor sensitivity or difficulties in interpretation, including women, patients with cardiac conduction defects (for example, left bundle branch block), and people with diabetes, and for people for whom treadmill exercise is difficult or impossible.
- As part of an investigational strategy for the diagnosis of suspected CAD in people with lower likelihood of CAD and of future cardiac events. The likelihood of CAD will be based on the assessment of a number of risk factors including age, gender, ethnic group, family history, associated comorbidities, clinical presentation, physical examination, and results from other investigations (for example, blood cholesterol levels or resting electrocardiogram).

“MPS using SPECT is recommended as part of the investigational strategy in the management of established CAD in people who remain symptomatic following myocardial infarction or reperfusion interventions.”

In describing the cost-effectiveness analyses considered by the committee, the guidance document pointed out that the economic models provided by the Assessment Group and the manufacturer used similar designs in that decision tree models were constructed for the diagnostic performance of different strategies and Markov models were used to estimate the long-term costs and benefits. In the ‘consideration of evidence’ section of the guidance, it was reported that the committee appreciated that considerable uncertainty remained over the true values for sensitivity and specificity of SPECT.

Overall, this was the third of the seven appraisals where there was significant disagreement between

committee members regarding the implications of the economic information made available to them. As with the previous appraisal, the dispute appeared to derive from the extent to which other factors could be seen as legitimate modifiers of a strict or ‘purist’ health economics approach. In this case, these other factors appeared to be:

- current clinical practice and the need for guidance not to go directly counter to this
- capacity issues and the implementation of guidance.

Summary across the seven technologies

The case study involved a sample of seven technology appraisals. We have provided a detailed account of the research undertaken and findings deriving from this for each appraisal. There are a number of recurring themes that can be highlighted.

Several appraisals considered a number of new technologies that often had results (from the economic analyses) that were broadly similar. Clearly, this posed difficulties for the committee in seeking to recommend one new technology over another on cost-effectiveness grounds. In addition, frustration was repeatedly expressed by committee members at not being able to prioritise between new technologies due to data shortages, particularly in the areas of clinical and quality of life data. However, four of the seven technology appraisals studied appeared to have a broadly non-controversial economic analysis, and as a result the details of the cost-effectiveness analyses were not discussed extensively. When both sponsor and independent economic assessments found similar results, the decision was considered to be considerably easier and more straightforward.

A number of the appraisals were hampered by concerns regarding the scope of the decision. In some cases the view was expressed that a highly appropriate comparator had been excluded from consideration. In another case it was felt that the analyses received had adopted too short a time-frame in which to measure the full benefits of treatment options.

Three appraisals saw significant disagreement among committee members. In each case this revolved around the economic evaluation. Each time this involved the cost-effectiveness analysis favouring the use of a treatment option that was seen as undesirable by some committee members. Subsequent disputes focused on the issue of how to reconcile the ‘economic paradigm’ advocated by

NICE and the desire of those on the committee to reject as unhelpful the implications of the commissioned economic evaluation. One resolution to these disagreements was for guidance not to be explicitly supported with reference to cost-effectiveness analysis. This occurred predominantly when the results of the economic evaluation challenged current clinical practice. Other factors that appeared to influence the committee – although not to the same extent – ranged from the severity of the disease, the importance of promoting innovation, patient preferences and implementation issues.

The net effect of these other factors tended to be to incline the committee towards a positive recommendation.

A number of other interesting themes recurred throughout the case study. For instance, it appeared the committee were to some extent bound by decisions taken in previous appraisals and also practices considered legitimate in other appraisals such as the use of indirect comparisons. Also, final published guidance regularly recommended funding of the technology but restricted access to certain patient subgroups.

Appendix 11

Data deriving from interviews with NICE Appraisal Committee members

Introduction

This appendix draws on data from the interviews with committee members and from an interview with the NICE Technology Appraisal Programme Director. The focus is on interviewee reflections on the decision-making process. In particular, it reports on the issue of the importance of economic evaluation and its status within the range of factors influencing the outcome of technology appraisals. This appendix is structured under six broad headings:

- the information drawn upon by the committee
- committee procedures and processes
- committee composition and the roles of committee members
- how the information is processed in order to arrive at a judgement
- conceptual issues concerning economic analyses
- practical issues relating to the economic analyses received by the committee.

The information drawn upon by the committee

Interviewees unanimously emphasised the importance of the evidence base in the decision-making process.

“They [committee members] say ‘we ought to be absolutely sure that the way we’re making the decision is based on the evidence presented to us’ and they spend a lot of time checking and re-checking, going back to the evidence base.”

(NICE PD)

“The committee is looking for good evidence, robust evidence, evidence that will stand up to scrutiny, whether it’s statistical scrutiny or clinical.”

(NICE 10)

“Now it is much clearer that the quality of the audit trail needs to be at a legal level of quality whereas before we were just satisfied that we knew and we had the information. Now we need to prove it.”

(NICE 1)

Individual committee members, therefore, placed great weight on the written evidence.

“I try and take a balanced view across all of the evidence that’s presented and focus particularly on the written evidence that we receive, following that up then with my own questions and the questions of other committee members.”

(NICE 15)

Written submissions – the independent assessment report

Within the written evidence, the assessment report was generally considered to be of most importance. Several of the interviewees indicated that over time improvements had been made in the content and presentation of such reports.

“It’s the weight of evidence in the appraisal report that is fundamental.”

(NICE 9)

There has been a progressive move to define the assessment report as being fit for purpose for NICE as opposed to simply being that which is standard practice for the HTA [Health Technology Assessment] monograph. In my view that has improved it.”

(NICE 6)

“I’ve sat on the committee for three and a half years now and the reports are much clearer these days than they used to be. I think the lead team by and large gets a better grasp on it, probably because the NICE secretariat are very helpful. They lead us into understanding it really quite quickly.”

(NICE 10)

However, a small number of interviewees felt unable to digest fully the contents of the assessment report.

“I look at the assessment report which to be honest I usually find pretty impossible to understand. So I tend to focus on the sort of conclusions and discussion and the introduction which gives the background . . . I’ve actually stopped wading through the whole assessment report because I think I could spend days on it and still not properly understand it. I just don’t think that’s a terribly good use of my time.”

(NICE 2)

“Personally I don’t generally read the assessment reports. I read the summary of it. And that is for two reasons. One of them is I can guarantee that the assessment report will contain a section which is meaningless to me So in terms of do I need more information? Not more like the assessment report, no. That is already too much for me. Though it’s entirely right I think that different members of the committee should have access to everything and can read the bits they want.”

(NICE 8)

Although these quotations indicate a general emphasis on the importance of the evidence base in the committee’s work, they also begin to suggest some differences of emphasis amongst committee members in how they process that evidence.

Written submissions – the industry submission

Industry submissions were seen as a more contentious part of the evidence base. They appeared to be treated with differing degrees of scepticism by committee members.

I put relatively little heed by what the manufacturers submit . . . but having said that I have sympathy for the industry because it is a broader environment and a broader world that drives what they do. And I know they do their clinical trials to extremely stringent standards. It’s just that they’re not having to do clinical trials for the reasons that actually would be useful to the NICE committee. They’re doing them for regulatory reasons.”

(NICE 2)

“There is evidence that that stuff [the industry submission] is likely to be biased and it makes sense that it is likely to be biased. The fact that they always find their own sort of drug to be the best is interestingly suspicious”

(NICE 17)

These interviewees also reflected on how the usefulness of industry submissions might be increased.

“I personally feel that the manufacturers ought to have to deliver much more of the appropriate data. I also feel quite strongly that the trials ought to be carried out independently but the manufacturer should pay for it.”

(NICE 2)

“NICE should operate a collaborative modelling exercise saying to the manufacturers ‘If you want to submit a model join this group under independent auspices and produce a model. Don’t try to submit any commercial in confidence inputs into it either

because we’re not interested as a decision maker in trying to justify a decision publicly which is based on private information’.”

(NICE 26)

Despite these expressions of concern over the value and credibility of industry submissions, other interviewees appeared to treat the manufacturer’s assessment as a counterweight to the academic review team’s assessment and saw the final decision as involving some dialectic reconciling of the two.

“I think there have been occasions where we really just couldn’t understand why there was such a large difference between the independent academic analysis and the company analysis. From our point of view we want to look very closely at the transparency of the academic piece, understand the differences between the academic and the industry piece and then we can make a reasonable judgement.”

(NICE 27)

“You’ve got the assessment report at one end of the spectrum and you’ve got the manufacturer’s analysis at the other I think the committee does quite a good job of saying ‘well why are these two different and can we explain it and how do we marry it up?’ and I actually think that’s quite a big factor in how the committee reaches its decision.”

(NICE 2)

This approach, in which the analyses undertaken by the independent assessment team are viewed as something other than independent, was a source of concern to another interviewee.

“The independent assessors are our assessors – they’ve got no vested interests around this. You get people saying ‘well the industry submission says this, the other submission says that and where’s the truth of it?’ and my view is it would be much more sensible to have a view that the independent appraisal is our appraisal and then if we want to criticise it or critique it or anything like that we can work from there. We ought to start from the principle that it is our assessment. We don’t always do that.”

(NICE 9)

Written submissions and professional and patient group submissions

Few interviewees made direct reference to the submissions from bodies representing professional bodies (such as the Royal Colleges). One interviewee, however, commented that these were useful.

“To some extent the professionals are all out to push their own areas in exactly the same way as the patient groups are but I think because there’s the clinical

evidence as the baseline, it is done on a more objective basis The professional groups do seem to generally have their act together reasonably well to give their view and their interpretation and everything else. And they're quite good at picking up on work that has been done but isn't formally published.”

(NICE 2)

Others were unhappy with the way that patients' perspectives were presented to the committee, considering this information to be less scientific than other evidence presented:

“One has to be realistic. The patient organisations have a responsibility to push for and campaign for their particular area over and above any other so they're not putting an objective view so I think you've got to take that into consideration. And they do sometimes lack any real quantitative information or anything like that.”

(NICE 2)

“[The patients' perspective] can be very emotive, especially if they're talking about their first hand experiences. So therefore it is obviously very subjective and perhaps doesn't balance out against other expert opinion which does have research and evidence data to support it.”

(NICE 13)

“The stronger patient voice tends to come from the more minority disease areas, but then it's taken sceptically because it's seen as a group of paranoid patients pushing their own self interest.”

(NICE 2)

Expert witnesses – patients and professional experts

Interviewees reflected on how some value-based considerations can influence the committee's deliberations and these were frequently seen as being channelled through the testimony of stakeholders and experts who are invited to advise and answer questions on individual appraisal topics. Further, interviewee comments centred on the potential for bias in these contributions and whether or not patient and professional opinions expressed in this form do and/or should be allowed to shape committee decision-making.

“I think the committee does take the professional view quite seriously and it's only when they understand it will they either dismiss it or be guided by it.”

(NICE 2)

“There are always clinician experts. Patient groups are always represented. They are supposed to be there for factual information, not to guide the committee

although inevitably they do that to some extent. They can be quite influential.”

(NICE 1)

“Sometimes you're thinking 'yes we believe what they [the experts] are saying, they're giving us information' but in the back of our mind we're thinking they've got an agenda. It's like when you're cross examining a witness I suppose. You've got in the back of your mind, 'are these people telling the truth, what are they hiding?'”

(NICE 20)

“Patient preference gets a lot of questioning when the patients are in the room. The reality is that because patients who come always want the new drug, whatever it is, or whatever the cost per QALY, I think it gets less credence than perhaps it might. It's very difficult to try and pull that in.”

(NICE 9)

“[The committee] are very influenced by the experts and the patient representatives. I'm not sure whether I'm in favour of that or against it. I think they sometimes exert a disproportionate influence on the outcome of the decisions.”

(NICE 26)

“If you have a good clinician presenter who is articulate and biased towards the drugs – they always are but in a way that seems reflective, i.e. 'he or she seems a reasonable person' then that can be very influential in changing the clinical view of things.”

(NICE 9)

“What we want is a perspective of someone in the health service understanding the reality of care, and what isn't being funded. What we don't want is the special pleading from the patient group. And I think that's where we haven't got it right.”

(NICE 7)

These comments reflect a concern among interviewees as to what the best use of patient and professional experts should be so that a reasonable process of arriving at decisions can be followed.

“I would be asking experts about the inputs into the model and their view about particular parameters, not about their view about the options and that's what tends to happen: 'would you do this in your work?' rather than 'what's your estimate of the effectiveness of this drug in this particular category of patient as compared with that in the model?'”

(NICE 26)

The questioning of the role of experts who appear before the committee, and the need for experts to be informed about the model and economic analysis in order to play a supportive role, was also raised by another interviewee.

“I think there is a problem in kind of engaging the experts into the model, because it’s a bit difficult to see what they’re there for really. They’re meant to be there to answer questions of professional practice and things like that. But in practice, they start to argue against whatever conclusions the assessment group have come up with. And I think if they’re going to do that, they’ve got to buy in to and understand the model.”

(NICE 7)

Most interviewees considered that the patients’ perspective was taken seriously and was important to the committee, but there was some disagreement about the extent to which this perspective was or should be taken into consideration and in what way it should be presented. Some interviewees thought the patients’ perspective ought to be included in the economic analysis and so any additional information was unnecessary:

“If you had an analysis where the cost per QALY was particularly sensitive to the figures used and the figures weren’t derived from a very secure source, and there was at least descriptive evidence which came from say the patient groups which suggested that those QALY figures were misleading, that might be one circumstance in which you would see economic analysis being challenged.”

(NICE 21)

“The patient preference for oral medication rather than taking injections and so on, that should be built into the QALY.”

(NICE 25)

“I think one of the things that really does impress me about NICE is that people take the patient perspective hugely seriously and try to get data on quality of life and so on.”

(NICE 5)

“The purpose of arriving at clinical excellence, taking into account QALYs which reflect patient values is undermined if you then say ‘And by the way patients should have what they prefer’.”

(NICE 26)

Others expressed the view that health economic analysis was insufficient or that the patients’ perspective was not taken into account enough:

“Side-effects, adverse effects can be very important to patients and are often not modelled into the analysis well enough.”

(NICE 10)

“Certainly quality of life issues are not very well addressed either by manufacturers when they’re doing their phase four trials, or by subsequent trials that compare the technology to something else.”

(NICE 29)

Other information drawn upon

Interviewees were asked what other considerations influenced the committee. Some interviewees expressed the view that other factors, in addition to clinical and cost-effectiveness, do play an important if not a central role in driving the final decision.

“I think the economic evaluation is an integral and an important part in the process of the decision which probably has five or six key elements: clinical, patient experience, cost-effectiveness, impact on the NHS, equity ... those are all in there although I think probably clinical and cost-effectiveness continue to be the main drivers of decisions.”

(NICE 10)

Appraisal Committee procedures and processes

Overall, interviewees praised the processes employed by NICE and indicated, in general terms, that the appraisal process worked very well.

“The only issue I would raise about the committee more generally is just to say how impressed I’ve been by the way the committee works. And I think that the NICE process is incredibly efficient given the volume of data that is produced, that has to be brought to bear and analysed and so on. And also the large number of consultees, committee members and so on. I think that the processes deployed by NICE are actually extremely efficient at taking a large number of data, a large number of people, quite a lot of emotional heat, and within a time scale that is rarely exceeded, actually coming to a clear conclusion.”

(NICE 15)

Setting the policy question

Frustrations with the appraisal process were expressed in terms of the scope of the policy question sometimes being addressed. There was a repeated concern that the definition of the policy question, and the development of the appraisal scope, were not given sufficient time or resource and often lead to problems in the committee meetings themselves. The suggestion was made that an opportunity to clarify and clearly identify the relevant policy question should more formally be part of the appraisal process.

“One of the problems I think we have in the whole NICE process is that the stage at which the specific questions are framed is probably too early. It is too early in the sense that the people doing it aren’t sufficiently well informed and can’t be really, to really understand what the issues are.”

(NICE 21)

“Often we’re quite frustrated in the meeting because we have to disregard something because it wasn’t included in the scope.”

(NICE 3)

“It does cause problems that we look at an individual technology in isolation essentially. It can be frustrating looking at an individual technology and you’re thinking ‘well it depends what they’ve had before. It depends what the options are down the line, it depends what else might be available.’”

(NICE 25)

Some interviewees proposed a ‘two-stage’ process that could address difficulties in identifying appropriate appraisal questions:

“For a long time I’ve been arguing for a two-stage process where you actually do some work which is targeted primarily at framing the right question then you do the rest of the work.”

(NICE 21)

“It’s almost like we’ve got to have a mini-appraisal half-way through to tease these things [the relevant policy question] out and then go back into the modelling Ideally they would devote a lot more resources to the assessment ... that would actually build in some sort of modelling and then a period of reflection and then further modelling.”

(NICE 28)

The cost-effectiveness threshold

Virtually all interviewees who spoke about the notion of using a cost-effectiveness threshold indicated that the NICE committee did make use of some form of threshold but also expressed some concerns around both its basis (especially where the threshold in use currently might have come from) and its use as a basis for decision-making. The line put forward by most interviewees was that there was not a precise value to the threshold, but that when the ICER far exceeded £30,000 per QALY this began to signal that the technology was unlikely to be cost-effective.

“There is a feeling when we get beyond £30,000 per QALY we’re running into trouble.”

(NICE 19)

“There is no threshold and any threshold that has been derived is purely, if you like, case law rather than statute. The cost per QALY per se does not determine whether or not there is a ‘yes’ or ‘no’ guidance. It is conceivable that a technology which has a fairly good cost-effectiveness, has a low cost per QALY, might be associated with a negative decision from the committee. And it is possible that one which has got a higher cost per QALY might still be given a positive response. And I think, therefore, clinical need, patient

preference, the input from the professionals do hold sway.”

(NICE 6)

“I do sometimes have reservations about the figure of £30,000 per QALY. Where does the figure come from? Who determines where the cut-off point should be? ... This magic figure of £30,000 keeps popping up but I lack the underlying knowledge to be able to actually challenge a figure like that.”

(NICE 13)

“Why do people think so bloody categorically as if a threshold was a yes/no thing? Very few thresholds are yes/no things. They are things which go from zero to one and along that line somewhere there are lots of other influences coming in to affect you.”

(NICE 18)

“We don’t use threshold levels in NICE but if you get below that level [£30,000 per additional QALY] then usually we have a certain level of comfort.”

(NICE 27)

One of the interviewees made a strong call for the threshold, if it is to be used by NICE, to be more transparent.

“I find the £30,000 per QALY actually very frustrating simply because it’s what everybody uses as a benchmark. I think it is a key driver. Many people on the committee, certainly the people who’ve been there a long time and the more influential people on the committee, I think that’s what drives them but yet it’s not supposed to exist and I just think it ought to be bloody transparent.”

(NICE 2)

There was a suggestion that where the initial cost-effectiveness estimates are close to the threshold there tends to be further investigation of the data and the assumptions upon which the analysis is based.

“If it is closer to some unmentionable threshold then we might delve more into patient preference and so on.”

(NICE 25)

Opportunity costs

An important consequence of applying the current implied cost-effectiveness threshold range was thought by several interviewees to be that further pressure was being placed on the NHS at a local level to remain within budget.

“My biggest criticism of the approach used at NICE, in the technology appraisals, is basically we are funding things at a level that actually the NHS cannot

fund – that the [cost per] QALY figure is far too high, it should be much lower.”

(NICE 7)

The other repeated concern under this header was that the policy change to make the implementation of NICE guidance mandatory meant that there were real opportunity costs being incurred. This was thought to be compounded by the fact that, by definition, the main impact of the judgement is experienced at the local level and so is not seen by those making the decisions at NICE.

“I think NICE is a worthwhile enterprise, in principle, but the thing that worries me most about it is the fact that advice is, well it’s not advice anymore, it’s compulsory ... and it worries me because the opportunity cost notion that’s supposed to underlie economics doesn’t really bite at the NICE level.”

(NICE 30)

“There is no measure of opportunity cost in this at all because they’re not meant to look at affordability but actually when we were looking at the drugs for schizophrenia, for example, it would have been nice to have a series of cost per QALYs for intensive rehabilitation, for CPNs [community psychiatric nurses], because then you can actually reach a global view of what’s important. Now this isn’t a problem for NICE, this is partly a problem because of the way that the government has insisted that NICE recommendations are implemented but that is going to become unsustainable.”

(NICE 9)

Appraisal Committee composition and the roles of committee members

The committee as experts or representatives

Having looked at reflections on the evidence base for the decisions and how this is processed we now turn to interviewee comments regarding the roles they play in the appraisal process and the roles of other stakeholders.

Interviewees all indicated that committee members were selected as bearers of particular expertise and/or experience deemed relevant to the decision-making process. Within this there appear to be two identifiable roles which inform the selection of committee members: the ‘technical expert’ and the ‘advocate’ or ‘representative’.

“The range of skills that are on the committee are: health economics, clinical medicine and professions

allied to medicine – principally nursing, health management and finance and lay representation. That’s pretty much it.”

(NICE 1)

“Basically what they [NICE] do is they pick certain people who are technical experts.”

(NICE 20)

“Essentially the representation within the committee spans all of the disciplines that you would think impinge upon a decision about the use of a health care technology. We also have a couple of representatives from pharmaceutical companies and also the lay perspective.”

(NICE PD)

We haven’t made a point of selecting clinicians with a particular background ... We have principally gone for clinical individuals who have a wide variety of interests but who don’t necessarily represent a specific clinical discipline. It’s their expertise through coming from a background in hospitals or general practice that matters for the committee.

(NICE 6)

Some interviewees saw this as a strength of the committee because it enabled a range of perspectives to be brought to bear on appraisals and for different aspects of a decision scenario to be considered reasonably fully by different committee members.

“For people to work together as a team it’s important that people bring different approaches and different levels of knowledge and expertise.”

(NICE 15)

“What you have is people encountering perspectives that they otherwise wouldn’t encounter. So for example, people like myself who would take the individualistic perspective, encounter the health economic arguments and assimilate them. And equally, some people whose starting point was the utilitarian health economic perspective look at the human and at times temper what is otherwise purely cold numbers, if you like.”

(NICE 8)

“The health economists that we have are obviously a lot more involved and a lot more keen on that side of the information than perhaps other committee members and that’s good because it provides a balance ... We have people who are ... much more concerned with the financial impact. There will be clinicians who will be wrapped up in the evidence itself, GPs wrapped up in the practicalities of implementation and follow-up. So there’s actually a very good mix around the table of what people will concentrate on and everybody will pick out a different part.”

(NICE 3)

“Being a sort of general sceptic as an economist I came in here thinking ‘Are they biased in favour of industry? Are they lacking transparency?’ But I think ultimately they generally are a group of quite highly skilled people who genuinely are trying to get a decision that benefits the public. I’m convinced about that.”

(NICE 20)

Many interviewees bought into this model whereby the effectiveness as a decision-making committee was partly measured in terms of the breadth of expertise represented amongst them, to the extent that some identified areas of perceived under-representation.

“The committee is more represented by clinicians and health economists than it is by the people that actually are having to spend the money at the end of the day – the health service managers. If we had a few more of them on the committee saying ‘well how am I going to afford this?’ it would probably have a more curbing effect on the decisions.”

(NICE 14)

“I think it needs more people who are involved in commissioning services. So that would be PCTs, and I think people like clinical directors. There’s a finance director there. I think that’s quite a good person to have because they understand some of these issues.”

(NICE 7)

Clearly, there was a conception among some interviewees that the expertise of committee members provided added value to the process of considering new technologies. There was much discussion as to the ways in which these different skills and experiences combined to form a decision-making process. Most interviewees characterised the process as one of debate, usually leading to consensus:

“I think the strength of the committee is that we, insofar as I can remember, have always eventually reached a consensus despite having all those different people and those different viewpoints.”

(NICE 11)

“I think drawing on everybody’s expertise I think that’s where the consensus decisions come from.”

(NICE 13)

“I think it’s a value judgement as to how long you spend to enable a variety of discussion to be undertaken, a period of time to elapse during which people are able to express their views, to contradict each other, to counter each other. And then to try and abstract from that, if you like, a series of verbal bullet points upon which people have to make decisions.”

(NICE 6)

“Different people come from different places and do have different perspectives. They weren’t actually as polarised on this occasion as they have been on some other occasions.”

(NICE 18)

“I think one of the problems is it’s a very large committee and ... it’s difficult to get all the discussion one would want. Not everybody can say everything that they want to say because there’s so many people there. But I think the structure is pretty good.”

(NICE 7)

It was clear from interviews that there were occasions when a consensus position was not achieved. A committee member explained the likely surrounding circumstances.

“Resolving of conflicts internally is very important. And sometimes it reaches a point where it is not possible to do that and at which an internal vote has to be taken. We’d rather take a consensus but voting does occasionally occur ... My view of it has been and I think that the Institute supports this, that we cannot reach a point at which the committee say, ‘Well, it’s just too difficult for us to make up our mind.’ We have to be absolutely sure that we’ve explored all the possible avenues before we get there and we rarely do reach that point. The sort of times that we might reach the point at which a decision cannot be made may be when it becomes pretty obvious that further work needs to be done.”

(NICE 6)

It is clear from the views of committee members that the committee actively discusses the technology in question and members bring their expertise to bear upon the written evidence. The appraisal process also involves the co-opting of further expertise for specific technologies although in a strictly advisory capacity.

Role of committee members

Interviewees were aware of their own specialty or area of expertise, the exercising of which was cited as a major component of their role as committee members. This was particularly true for those designated as patient ‘advocates’ or ‘representatives’ but was also referred to by other interviewees. The following quotes are from committee members who see their role as representing the patient or lay person.

“Because I’m the lay representative and sort of patient advocate I pay particular attention to the submissions from any patient organisations. I try to look at those really carefully to make sure that I do fully understand all the points. I do feel a responsibility to pick those points up because I don’t necessarily see other people picking those points up.

I do feel a responsibility to that. I mean that's my understanding of why I'm there."

(NICE 2)

"Well as a lay representative right from the word go I have been looking hard at patient and carer and family issues – psychologically, physically, and socially although of course we're not really meant to look at non-health related costs and benefits."

(NICE 10)

"What I feel responsible for is ensuring that proper consideration is given to the user experience, the user perspective on the condition and on the technology. Because I don't believe that the methodologies that are used in trialling and researching treatments capture that information properly. I try to ensure that lay witnesses, those who are in a position to speak for the user, get a proper hearing and manage to fully convey that perspective."

(NICE 8)

The following quotes indicate that committee members with a range of backgrounds viewed their role as providing an informed expert opinion on the topic at hand. These areas of expertise included interpretation of the evidence (i.e. the clinical effectiveness review) and also implementation of the guidance (i.e. a management perspective).

"I always focus on the clinical effectiveness side of it first because that is more my area of expertise. I believe that's why I'm on the committee – to represent patients and healthcare in that capacity."

(NICE 5)

"I'm a pharmacist and so I guess I'm there to pick up details around medicines administration and I also work in both secondary and primary care so I tend to pick up issues about prescribing across the interface."

(NICE 3)

"I think I'm in an unusual role because I'm neither a clinical member of the committee, nor a health economist. I think nonetheless that there is an issue about implementation of guidance. And in terms of being realistic about how things can be implemented, particularly where there are supposed cost benefits of guidance – being clear about how realisable that is or isn't is quite important I think. So I think that's probably what I bring."

(NICE 15)

One interviewee suggested that, at the outset of his involvement in the committee, there was a lack of clarity in specifying the role committee members were expected to take on.

"I don't think it's an issue that's been fully addressed. I mean, I wonder how many people really understand

before they go on the Appraisal Committee what it's actually going to entail and what they're meant to be doing. And maybe that role hasn't been adequately defined either – if you're just there as a nurse, to give a nursing perspective, for example."

(NICE 7)

Interviewees consistently referred to the Chair's role in the process of reaching a decision. The Chair's role in facilitating the process was considered crucial and his influence on outcomes of discussion was widely seen as significant.

"I think that the committee is very well chaired. And I think that's an important part of it."

(NICE 15)

"I think [the Chair] is very good at trying to take everybody's point of view into consideration and I think he's got to drive it otherwise we'd never get to an answer but there are times when I feel if anything it gets driven a bit too much."

(NICE 2)

"[The Chair] makes sure it's not adversarial."

(NICE 20)

"The Chair is very different from the other committee members. He has to keep time, keep order, make the whole thing make sense and work to a conclusion ... As well as being the most active member of the whole procedure, the Chair has been devoting his life to reading the documents and he will be much more word perfect on the submissions than most committee members who will have done it in their spare time."

(NICE 1)

"If you want my opinion about decision-making in general it is that the Chairman has a very decisive role in leading the committee towards the decision which it takes ... and the considerations in his mind are obviously varied and fairly public."

(NICE 26)

"At the end of the day the thing that's often most influential is (the Chair) and his perspective on the thing. He's a very influential chair and he shapes the debate. And I suspect that mostly gets us through quite a difficult process."

(NICE 9)

Unsurprisingly, given the focus for this research exercise, the role of the health economists on the committee was a recurrent theme. They are clearly viewed as a distinct group of experts playing an important role in terms of advising others on the strengths and weaknesses in the economic analysis presented.

"Partly [my role is] to poke holes in the industry model and indeed the assessment model. It is a

model busting role I would call it – ‘What are the dodgy bits of this? What’s going on here?’”

(NICE 20)

“I think it is absolutely fundamental to have the health economists there, partly to explain but also to challenge.”

(NICE 9)

“I don’t think it would be possible to bring the health economic evidence into that decision-making if you didn’t have health economists there to interpret it and they have played an incredibly important part in helping the rest of the committee to deal with it in layman’s terms.”

(NICE 10)

“I do think it is helpful to have a variety of economists there to put different points of view.”

(NICE 11)

“Eventually the argument is dominated by those people who obviously have a very high knowledge of the health economics.”

(NICE 16)

A crucial area of input was the presentation of health economic evidence by the lead team.

“I find the presentations a useful check of ‘have I grasped the main points?’”

(NICE 2)

“I tend to get a much better understanding when it’s being discussed in the committee and when somebody’s doing the presentation up front.”

(NICE 2)

“It might have been quite useful if each of the economists had been assigned an appraisal to really focus on. I know that’s partly achieved through having these committee leads, but very often it isn’t an economist who’s actually assigned to one of them, and I just wonder if that’s something they could think about.”

(NICE 28)

The ability to take a detailed approach to the appreciation of economic analyses was seen as a further strength of the committee’s economists.

“There are a lot of health economists on the committee and I think I feel quite confident that they will pick up things and understand things from the assessment report.”

(NICE 2)

“I think those with more experience and skill in this area tend to look at things with a bit more scepticism and won’t just take things as read, and they obviously know what to look for in terms of spotting a gap and a weakness in an argument.”

(NICE 29)

Understanding of the economic evaluation by committee members

Interviewees unanimously felt that the committee included a sufficient number of professional health economists on each branch. There was less agreement concerning levels of expertise in health economics amongst the broader committee.

Although concerns have been expressed relating to the complexity of the economic analysis presented, many interviewees indicated that they spent time seeking to digest the analysis and its results. The view was also put forward that virtually all committee members do consider the economic analysis, although not everyone will focus primarily on that aspect of the assessment report. A number of interviewees indicated that they were concerned not only by their own personal lack of understanding of the economic analyses but also the level of understanding by others on the committee. In some instances this was expressed in stark terms and meant that there were parts of the assessment report that some committee members did not read because they knew that they would gain nothing from those sections. Levels of understanding were seen as more or less important by interviewees according to the extent to which they considered their role to involve the critical interpretation of the economic analyses.

Some believed there to be a good general level of understanding and expertise in this area by the non-economist members.

“The rest of the committee members who haven’t had formal training in economics, because its such an important part of the discussion have now, to my view, got a very, very good feel and understanding for what’s important in an economic evaluation and where some of the pitfalls are and where some of the discussion needs to take place about the robustness of whatever evaluation is taking place.”

(NICE PD)

“I think there’s an incredibly high level of understanding of health economics. Of any group of non-economists that I’ve ever sat with, that’s the highest level.”

(NICE 20)

“We do question it and we do analyse it very carefully. The non-experts – the ones who might be much more aligned to clinical need and patient acceptability and patient preference and so on – will question very carefully the economic analysis to such a degree until they come to the point where they say, ‘Well I now understand the principles here and I’m prepared to accept that what you tell me is correct’, as opposed to taking it on face value.

(NICE 1)

Other interviewees sounded a slightly more cautious note, suggesting that whilst a basic level of understanding existed, this might not be sufficient.

“I think it’s fair to claim that everyone on the committee has a basic understanding of QALYs, costs per QALYs, thresholds if you like and the cost-effectiveness acceptability curve and the ICER and so on. But clearly there would then be a range of understanding of the more complicated issues, and the more complicated the analysis, the more people will get lost on some of the issues.”

(NICE 25)

“I think I would say that two-thirds of the committee or possibly half of the committee fall into my sort of category of [low] understanding. And then perhaps a quarter have extremely detailed understanding and are perhaps the people who are at the forefront of research into health economics so they know everything that there is to know about it. And then there is about the 25% who know quite a lot, to be able to argue whether the models are right.”

(NICE 16)

A number of interviewees raised some more serious reservations concerning levels of understanding of the economic analyses. They questioned whether, for some members of the committee, there was any real understanding of the economic evaluation section of the assessment reports.

“Some of the people round the table I would think ... are probably not all that clear as to how it is done ... I think there are certainly a number [of committee members] who probably don’t understand a word of what is going on in the health economics bit. I’m in a worse position because I understand every second word (laughs) ... and some people do keep very quiet when the health economics is being talked about and that’s very noticeable.”

(NICE 17)

“I think my knowledge is poor and I know quite a number of other people on the committee feel theirs is poor as well, so I think the people representing sort of nursing, general practice and even quite a number of the medics would feel their understanding is poor.”

(NICE 2)

“There’s a belief, a sort of fuzzy belief that people do understand cost-effectiveness because it is so important we all understand it but the actual principles and so on are not well understood ... Everyone has attitudes to QALYs and think they know what they do but they couldn’t tell you the difference between an interval scale and a ratio scale or anything about the methodological issues underlying generic indexes, all that.”

(NICE 26)

Committee members were also asked to give an account of their own ability to understand the economic analyses submitted to them. A similar range of responses was received, ranging from those who felt that their understanding was poor, those who felt they had sufficient understanding to play a role in appraising economic analyses and those who felt confident that they understood all aspects of health economics evaluations. Examples of quotes indicating that members struggled with the economic aspects of the assessment reports are given below.

“I’m quite happy that the economic analysis which certainly is clearly very sophisticated and sometimes above my head, should remain sophisticated and a bit above my head.”

(NICE 19)

“Some of it is incredibly difficult. Some of the modelling, I mean good Lord, and the pictures we’re presented with: upside-down, back-to-front sort of graphs and everything. You’ve lost it after the first five minutes.”

(NICE 10)

“I make no bones about it, that’s not my strength. I understand it with a broad brush really. I don’t understand a lot of the details.”

(NICE 16)

“I do think that the assessment reports take a lot for granted from the committee members who are reading them. There are still a lot of terms which are very difficult to understand. We’ve had a number of tutorials on interpreting economic analysis. This is my fifth year on the committee now and I have to say that there are certain things I find very difficult to understand.”

(NICE 16)

“I always assume that everybody else’s understanding is far higher than mine.”

(NICE 22)

Below are examples of quotes indicating that some committee members were reasonably comfortable with the interpretation of the economic analyses but had problems with some technical aspects.

“I obviously am not an economist and I do not construct Markov models or any of the rest of it so obviously I couldn’t say that I have a deep understanding of it. I would hope that I would have enough to understand everything that is said in the committee, in other words everything that is relevant to the discussion. And I’m certainly very willing to admit my ignorance or ask questions if I feel really at sea.”

(NICE 11)

I understand most of it. Obviously there's certain technical sides of things which I do glaze over a bit."
(NICE 19)

"I feel I can understand most things. Obviously there's the varying amounts of detail about how things are done on the different reports. But I feel capable of understanding most things."
(NICE 24)

"I have an MSc in Health Economics so I'm not specifically a health economist but I think it probably helps. Sometimes when there's a really complex model it's quite difficult to get your head round."
(NICE 3)

Finally, the quotes below indicate that some committee members had no major problems with the economic aspects of the assessment reports.

"I think I do understand how they calculated it [the economic analysis]. Being a statistician I feel I should do."
(NICE 14)

"Personally I feel reasonably confident because I used to manage a health outcomes group a good few years ago and so I feel reasonably confident that I can interpret the models and if I can't then it's not usually my problem – it's the way it's either put together or presented."
(NICE 27)

One of the real dangers associated with low levels of understanding of the economic analysis that was highlighted is that too much faith might be placed in it.

"I think there's a real danger that the economic analysis gets taken as fact, and it's not fact. There are so many assumptions and judgements made that I think that makes it very difficult."
(NICE 2)

"The risk is that we are at the mercy of what is said by people in an expert position in the room."
(NICE 8)

"I'm not sure all the members of the committee really have a clear understanding of the strengths and weaknesses of the health economic analyses. I mean some people have a very, very good insight into them, and I think if you're a clinician and you don't understand that, you can just be taken in by the headline QALY number. And I think that is a big problem."
(NICE 7)

"I think they [committee members] feel their understanding [of economic analyses] is poor. I feel concerned that mine is poor. The attitude of [the Chair and Head of Appraisals] is it doesn't matter, they don't want everybody to be into the technical

detail, they want people to be able to stand back from it. I suppose the thing that worries me about that is I'm not convinced that I'm well enough informed to be able to objectively challenge the health economists."
(NICE 2)

The perceived need to increase committee expertise in health economics

One committee member questioned whether it was acceptable for some members of the committee to defer on the health economics aspects, suggesting that all members of the committee require an understanding of the decision model if they are to carry out their role adequately.

"I do think this is not the way a public decision body should operate in the sense that you have people proudly almost saying 'Oh well I'm not a health economist'. It seems to me that if you're in this position you jolly well ought to be pretty competent in these things that we're talking about."
(NICE 26)

There were two major areas discussed by interviewees when thinking about whether and how levels of understanding of health economics could and should be improved: (1) the extent to which simply being involved in the appraisal process itself brings about sufficient learning and (2) whether or not further training should be provided for committee members. Some quotes on the first point are given below.

"Everybody is gradually learning to be an amateur health economist as time goes on and it's become less important who is there on the day."
(NICE 1)

"I think we've all learnt as we've been on the committee and our understanding of those areas has improved."
(NICE 11)

"I think some are picked with expertise on management thinking about problems, management costs and so on and have some economics knowledge but basically the rest wouldn't necessarily have a great specialist knowledge of cost-effectiveness acceptability curves and so on. But I think once they've been there six months to a year, probably by osmosis they pick up some of these things."
(NICE 20)

"Absolutely no doubt that the more the committee meet and obviously with the appraisal process we meet very regularly the more refined their skills are becoming in that area and it's happening very quickly."
(NICE PD)

Below are some examples of comments from interviewees which indicate that further training in health economics would be welcomed.

“I think possibly the odd refresher course for everyone might be a good idea.”
(NICE 20)

“There’s a bit of a black box about which particular quality of life measure is used at different times and it might be useful if people had some sort of training in that and what to look for in terms of the advantages and disadvantages and where it’s weak.”
(NICE 17)

“I personally think that new people should receive at least a sort of induction explaining the process and just a bit of education.”
(NICE 5)

“I need to do some more reading around economic analysis.”
(NICE 30)

“I think more formal training on: ‘these are the principles of the economic analysis, these are the principles and the considerations that drive the committee’. I think that would be very useful.”
(NICE 2)

“I think having updates on things like the economic analysis and methods that are used is always very welcome. And other consideration about other issues like the ethical issues and affordability issues are always something that we ought to be reminded of and kept abreast of.”
(NICE 29)

“I think some basic education on how to interpret results would be useful.”
(NICE 4)

There was also the suggestion that some committee members, realising the importance of a good basic understanding of the economic analyses, have sought to overcome weaknesses in that area.

“I had really no health economics background, I suppose beyond any other physician interested in health care delivery. I realised very early on that that had to change.”
(NICE 18)

How the information is processed by the committee

Relationship between clinical effectiveness and cost-effectiveness evidence

Nearly everyone expressed the view that the economic evidence and evidence of clinical

effectiveness were given highest priority. However, there appeared to be a division between committee members who considered the economic evidence first and those who paid most attention to the clinical evidence.

“My first consideration when I look at this is ‘does this treatment actually work?’”
(NICE 10)

“Clearly it’s important we start off with clinical effectiveness but having established the clinical effectiveness we then have to look at the cost-effectiveness.”
(NICE 15)

“In a sense so much of this stuff does hinge on the clinical data that’s available, because that’s kind of the only factual stuff we have.”
(NICE 2)

“I have this little mantra in my mind and have done for years that if the clinical evidence doesn’t show efficacy then the economic evidence isn’t going to be helpful.”
(NICE 27)

Examples were cited when the economic analysis was not explored in detail and so was considered, in some situations, not to be such a dominant issue.

“I think for certain technologies, if the clinical evidence is very good as it is in this case then . . . I don’t think [the economic analysis] matters that much unless it’s a wildly expensive technique.”
(NICE 16)

There were, however, some forceful points made by those who felt that the economic analysis was sometimes used merely to support a position that had been adopted on other grounds, and ignored otherwise.

“While there would be no member of the committee who, in my experience, discounted the economic analysis, there are committee members whose primary interest is the economic analysis and there are other committee members whose primary interest is the clinical analysis, and only want to know that the economic analysis supports or not their view of the clinical analysis.”
(NICE 15)

Many of the interviewees expressed the view that the economic evidence and the clinical effectiveness evidence were inextricably woven together so it was difficult to weight the importance of the one over the other.

“Often the discussion centres around the clinical evidence but the particular arguments about the

clinical evidence are informed by the framework that the economic analysis has provided us.”
(NICE 12)

“I just think that if you’ve got the clinical effectiveness evidence and you’ve got the cost-effectiveness evidence you still have to balance between the two. I mean I do realise if something is very clinically effective it is usually cost effective anyway.”
(NICE 16)

“If you haven’t got good quality clinical evidence then your economic modelling is going to be equally poor.”
(NICE 6)

Many of the interviewees espoused the position that there was a strong ordinal approach to their consideration of the clinical evidence and economic analyses. That is, the first hurdle for the technology in question was that of effectiveness and a concern with cost-effectiveness was not appropriate unless the issue of effectiveness had an outcome that was positive for the technology.

“My first consideration when I look at this is ‘does this treatment actually work?’ ... obviously it has to appear to be clinically effective and to be shown to be clinically effective.”
(NICE 11)

“If it don’t work and it is not actually going to do much good to anyone then why know how much it costs? So I would stop at that point but we don’t and ... a lot of pressure is put on us to do economic appraisals no matter what. I would put the economics after the effectiveness bit and the economics simply says, given that it works, is it worthwhile for the amount of benefit it gives?”
(NICE 17)

“Once you’ve decided that something is effective or it isn’t effective, the decision on whether to recommend is an economic one.”
(NICE 18)

“If it doesn’t get through the clinical effectiveness hurdle then I’m not that interested in the economics. I’m quite comfortable with making hard nosed decisions that ‘Well it doesn’t really work very well so why bother with it?’”
(NICE 22)

“First of all it has to be clinically effective.”
(NICE 23)

A single interviewee appears to have gone further and suggested that an ordinal approach is to be supported but that in many situations the role of the economic analysis should really be limited to alerting the committee to possible very high cost technologies.

“I think for certain technologies if the clinical evidence is very good then I don’t think it matters that much unless it’s a wildly expensive technique. And I think the economic analysis should basically just be there to flag up something which says ‘Hey hang on a minute it’s actually far more expensive than we think it is’.”
(NICE 16)

One of the health economist interviewees acknowledged that this ordinal approach to decision-making was adopted by the committee but argued that this was wrong. Indeed, the respondent went further to suggest that this was something that should be addressed by NICE as a conceptual problem with the decision-making model being adopted by the committee. The ordinal approach implies that nothing can be deemed ‘cost-effective’ unless there is evidence of an improvement in effectiveness. However, an intervention that brought about large cost savings and was associated with a small reduction in effectiveness may have an incremental cost-effectiveness ratio below the relevant threshold.

“I don’t believe effectiveness should be a criterion for NICE decisions. Now that’s a fundamental conceptual problem with NICE that they require clinical effectiveness before we go on to examine cost-effectiveness.”
(NICE 26)

The economic analysis and its centrality to the decision-making process

Some interviewees argued that the economic analyses provided to the committee are in essence the central driving force behind the decisions that are taken.

“I’m conscious that what NICE is concerned about is cost-effectiveness because it is about deciding whether or not medication should be reimbursed or universally available on the NHS and so on ... It [the economic analysis] is only pivotal because it is what NICE brings that is new.”
(NICE 19)

“I think it [economic analysis] was regarded as being important from day one.”
(NICE 21)

“Well, it [economic analysis] has to be [important]. I mean that’s what NICE is about. At the end of the day, it’s not there to tell whether something is effective or not, it’s there to assess whether it’s cost effective in the current day’s circumstances ... In terms of its importance in the final decision, it’s critically important, it always was and always will be.”
(NICE 23)

It [the economic analysis] seems to me to be the clincher really. If it's too high then it's not going to get funded.

(NICE 30)

Others suggest that whilst it is clear that the economic analyses do have a key role in driving the decision process, they have some reservations about the appropriateness of this.

"It can feel sometimes like the cost-effectiveness does tend to dominate, maybe because we've not been able to voice our concerns within that arena."

(NICE 13)

"The whole tenor of the reviews and the lead presenters' reports and everything is about the economics, so you don't have much scope to dissent I would like to think in fact that as the members become more aware of the limitations of some of the health economics that actually some of the decisions that have been made have paid less credence to health economics. I'd like to think that was actually true."

(NICE 14)

"I have personal big reservations on [the economic analyses] because I see them as theoretical models ... which give a useful starting point and a useful baseline but I don't think they should be driving the ultimate decisions."

(NICE 2)

"I would say that it [the economic analysis] plays more of a part than I anticipated."

(NICE 25)

"Economic evaluation and the economic evidence is of paramount importance in the whole process. It is not possible for us to make a decision on clinical effectiveness alone. We do have to have cost-effectiveness factored into that ... but I think my view of it is that the economic evaluation must inform the debate as opposed to direct the debate."

(NICE 6)

"I have a fairly sceptical view of the application of health economics, which is not to say that I don't think that it is not a useful tool, but it ain't God ... You have this process where you collect data down to four decimal places of accuracy based on the crudest assumptions and then you get down to a number like £27,423 per QALY gained, which can only be a rough guide, and people treat it as though it came down from the mountains on tablets of stone."

(NICE 8)

Others express the view that over recent years there has been a distinct shift in the attitude of committee members towards the economic analysis, from a position of some scepticism to a

point of view that recognises the importance of the economic analysis.

"I think that's what's changed in my two years on the committee; that people have slowly realised that the only real way to make these decisions is on a cost-effectiveness basis using a generic index. Some positively accept that, some negatively accept it. They do it reluctantly mostly rather than enthusiastically. They've moved to saying 'God this is all complicated, for God's sake tell us what the ICER is!' because they've actually realised that it is a crucial issue."

(NICE 26)

"Since we've been given some training on that [economic evaluation] and as we've gone on, I think the true significance of the cost-effectiveness side of the equation has become more apparent."

(NICE 29)

Economic analyses as the framework for committee discussion

An opinion repeated by a number of respondents was that the main value of the economic evaluation was not limited solely to the fact that it provided an overall result (e.g. in terms of an ICER or CEAC), but that it allowed the discussion to be structured and focused on the most important aspects of the evidence (both clinical and economic).

"I go straight to that [the economic analysis]. In fact when I read the TAR report I go to the ICER in the summary first and then read backwards and forwards until I get to see how it was derived."

(NICE 1)

"[The economic analysis] is, if you like, the starting point, the bottom line from which you then say 'Yeah so that's it but what else do we need to think of?' The sensitivity analysis, the patient preference and those other issues."

(NICE 25)

"The reason why it [the economic evaluation] is important is not simply because all we talk about is cost per QALY or the only thing we look at is the economic model. It's the fact that it provides us with a framework to identify what we should be concerned about and where we should be pushing the argument in terms of, for example, interpretation of the clinical evidence The most useful thing about the economic analysis is it focuses the discussion on what actually matters: 'what is it that can actually switch a decision on this? And do we believe that there are plausible scenarios that could be run which might switch us?'"

(NICE 12)

A related issue raised by several interviewees was the importance placed on extensive sensitivity

analyses being included as part of the economic analysis.

“In this particular case they did a sensitivity analysis showing that whether you assume that there was about a 0.75 quality of life ... down to about 0.33 did not actually make that much difference as to whether it was cost-effective at that threshold level. And so we’re talking about quite large differences in the quality of life figure not actually changing our view on whether it is cost-effective.”

(NICE 20)

“The sensitivity analysis will determine the degree to which the committee can feel happy about recommending something.”

(NICE 6)

If the economic analysis, and particularly the sensitivity analysis aspect, is to be used effectively to provide the framework for the discussion then there is clearly a requirement that a minimum level of understanding of the analyses exists amongst committee members.

An iterative and participatory decision-making process

The tension and balance in the decision-making process between something that is highly evidence-based and something that involves participation and judgement by those on the committee was brought out by several interviewees.

“What happens in my experience is that no matter how much people read, new process happens in the committee. So most people, in my observation, enter the room in position A, and in light of what they hear, move to different positions and come out in position K, or wherever we end up.”

(NICE 8)

“When I started I naively assumed this would be a scientific process and I’ve been quite horrified by the quality of the evidence we usually have to look at. More often than not the proper comparisons haven’t been done, the studies are flawed, the economic models from the industry are increasingly reasonable but then they are all populated with the most favourable type of position, we often get bullied between the ACD and the FAD and I think all of those things are quite difficult in a process that tries to be engaging and inclusive. Having thought long and hard about whether this is a process to continue to be engaged in because of all these problems I’ve actually come to the conclusion that you can’t do this scientifically and that overall it is better to have a discussion and debate in this way than it would be to just do it based on a single assessment by an organisation externally. I think this feels more like a reasonable process.

(NICE 9)

“We’re taking a load of disparate elements at different levels of detail, some qualitative, some quantitative, and trying to reduce them to a single sentence, in effect. What we are doing is holistic. Ultimately, we’re synthesising fragments into one whole. I do think our society and particularly the whole world of health and medicine is obsessed with this concept of objective evidence which tends to be reductionist, linear and numerical. The other bit is that committees like this have real difficulty dealing with the fact that actually they make their judgements on the basis of emotion influenced by the rhetoric of the witnesses they’ve met. A lot of people are very uncomfortable about that but it’s a human reality.”

(NICE 8)

A health economist on the committee disagreed and felt that identifying and reaching agreement on more explicit decision criteria was required.

“I think the whole process is somewhat conceptually confused, so that there is a whole range of what is called clinical evidence, brought somehow into connection with what is called cost-effectiveness evidence. The implications of the latter are focused on but there is a very explicit refusal to say we’re guided only by that. There must be other considerations that enter into all our decisions. So NICE, to me, embodies all the best and the worst of the typical British case-by-case approach which refuses to say ‘our task here is to establish principles and settle questions and park them and not revisit them every time’.”

(NICE 26)

Conceptual issues concerning economic analyses

Strengths and limitations associated with the quality-adjusted life-year (QALY)

A particular issue brought up by many interviewees was the great benefit for a decision-making body like NICE of a single measure of benefit such as the QALY, in allowing comparison of very many disparate health interventions and in providing a benchmark for later decisions. It was also felt that the concept was broadly familiar to those in the health service and other NICE stakeholders.

“The ability to compare one treatment with another by using a QALY or a DALY [disability-adjusted life-year] or something like that is helpful because it does at least give you some sense of... a ball park.”

(NICE 10)

“What we’re looking for is consistency as much as possible in our judgements. If we can do it [make use

of cost/QALY] and if the information is available or it can be calculated then it is very useful for benchmarking.”

(NICE 11)

“The use of QALYs does seem to mean that at least there’s a currency that people are familiar with, generally. The key stakeholders, whether they be clinicians, economists, drug companies or manufacturers, all seem to have a certain familiarity and ability to understand and work with QALYs.”

(NICE 15)

“They really do allow us to begin to compare hearing aids to insulin pumps to MS drugs. Now there are a lot of problems with them, we all understand that, but without that it becomes very difficult to do anything meaningful in terms of decision-making or advising decision makers.”

(NICE 18)

The broad comparability facilitated by QALYs was not universally acknowledged.

“This is where I think the qualms about QALYs come in and the incommensurability of alleviating different kinds of woe. You’re comparing hip replacements with postponement of death and cancer and so on, which you can’t of course.”

(NICE 19)

A widely held view appears to be that despite the limitations and problems associated with QALYs, the advantage they bring in terms of comparability of technologies and the fact that there is no effective alternative makes them a valuable tool.

“It seems to me that it is a necessary part of the assessment but often is not sufficient. I mean certainly if you don’t do cost per QALY then you’re really not in the business of comparing your technologies with anything else ... the question is how you get from this necessary evaluation – cost per QALY – to a sufficient evaluation that makes everybody feel as if they’ve got the technology properly in focus, and that’s where I think we run into difficulty again and again.”

(NICE 19)

“I think they’re grossly flawed in hundreds of different ways but they’re the best we’ve got and what they allow us to do is to make a comparison.”

(NICE 9)

A theme relating to the limitations of QALYs identified by several interviewees was the concern that they fail to capture some important aspects of benefit. Using the example of patients with motor neurone disease, one committee member explored the weaknesses of QALYs in terms of their failure to incorporate issues of disease irreversibility.

“When it comes to something like motor neurone disease our measures of health outcome don’t capture everything of concern to us. For example, with motor neurone disease there is an issue of irreversibility, and if we could incorporate the value of the option of keeping somebody in a better state for a little bit longer with this disease then we’d be attaching greater weight to their health outcome without citing equity concerns.”

(NICE 12)

Using the same clinical example (motor neurone disease), the same interviewee moved on to consider the limitations of QALYs in assessing benefits in the situation of very severe conditions.

“The additivity assumption underlying QALYs may be really important when people are looking forward over that really quite dire prospect of health outcome that having a few weeks or a few months of better quality of life during that period might be valued much more highly than just assigning a QALY weight in the same way as you would do in any other profile.”

(NICE 12)

Similarly, another interviewee used the example of multiple sclerosis to consider the adequacy of the QALY measure.

“MS is a very good example ... the drug was supposed to limit the rate of relapse. And what patients would tell you is, ‘... it’s not the fact that I only had one relapse in the last two years, it’s the fact that I came to believe it and I had the confidence to go out and go on holiday for a week because I wasn’t scared of relapsing’. You try building that into a QALY!”

(NICE 23)

A general theme of interviewee comments appears to be that the patient experience is not captured fully in the QALY measure.

“The huge gaps are in the utility measurements – they [data on patient experience] are just never there. And the measurements that are being used for utility historically, and so far without exception, have nothing to do with patient experience.”

(NICE 8)

“It’s very easy for a group of people to sit around and assess life states and what they’re worth when they’re theoretical and they’re not the people who are ill. I mean in general we know that people who are ill tend to assess their quality of life as more valuable than the people who are not ill.”

(NICE 23)

Another potential objection to the use of QALYs was that the level of knowledge of QALYs by

committee members is limited and may cause problems in future.

“They [the committee members] either have a very sceptical view of QALYs and have little faith in them at all ... or they’re happy to sort of take the numbers as broad indicators and don’t really worry too much about the fact that these are societal views and not really the views of patients. I think if some of them did know a bit about it or thought a bit harder they might be uncomfortable so I think it’s potentially a source of problems down the line.”

(NICE 28)

Equity concerns

Many interviewees indicated that equity concerns tend not to be formally considered by the committee for a wide range of reasons. For example, one committee member indicated that he did not have a clear view on what the appropriate equity arguments are and, even if there was greater clarity on the nature of the arguments, there exists no agreement on how they might be included in the economic analysis.

“I’m not convinced of what the legitimate equity issues are, first off. So what it is that needs to be highlighted in the report in terms of equity I don’t exactly know. Even if we did know what it was it’s definitely not clear how those could be incorporated formally into the analysis.”

(NICE 12)

Support was given by another interviewee for the concern that robust methods for equity weighting are currently not available.

“I think there’s a sort of recognition at the moment, that we have no basis for doing the weighting.”

(NICE 28)

One committee member went further to suggest that the reason for equity issues not being considered was not a matter of methods not being available but rather a lack of concern for such issues in the committee and NICE more generally.

“I’ve raised the equity argument myself but it has fallen pretty much on deaf ears. Nobody seems to actually want to address or analyse whether what we’re recommending will particularly benefit a particular group. It seems to be a complete lack of concern. Which is interesting given the postcode prescribing background to the introduction of NICE.”

(NICE 21)

A line suggesting that in some circumstances other factors that might be considered under a broad header of equity concerns are taken into account was put forward by some of those we interviewed.

“What I do like is the fact that ... NICE doesn’t have a written constitution which is entirely proper because with say an orphan drug, for an orphan disease, you may be willing to spend more money per QALY simply because you’ll never ever get any drugs for that disease if you don’t.”

(NICE 19)

“The desire not to stifle the development of a technology which although it isn’t cost-effective now offers real prospects of being improved over time – the sort of not stifling innovation argument has been brought forward as well.”

(NICE 21)

These are all factors that might influence, for example, the extent to which the committee might not adhere rigidly to any suggested cost-effectiveness ‘threshold’. Inconsistency in the application of equity issues and variation in the circumstances in which equity arguments are evoked were concerns that were also raised. One interview commented on this in the context of endometrial ablation for menorrhagia.

“People didn’t say ‘these are women who have a hard time we should be giving them more ...’. Whereas when we’ve looked at particularly life-enhancing interventions say in cancer treatment where people have a very low life expectancy, quite a few people around the panel say ‘well we should be giving these people more weight. They only have six months to live so an extra month or two is going to be more important to them’.”

(NICE 28)

On a similar note concerning inconsistency in the application of equity principles, the issue of interventions targeted at children being given favourable consideration was also mentioned.

“At the end of each of these discussions people say, ‘well we have no basis for doing this so let’s just treat a QALY as a QALY regardless’. But where that isn’t true I think is in relation to children. In relation to children I think, although people don’t necessarily explicitly state it, I think everybody tends to give it more weight.”

(NICE 28)

Interviewees made the point that the type of decision being made could influence the process. For example, if it was a life-threatening condition then ethical considerations such as the ‘rule of rescue’ (giving priority to saving a person from an immediate risk of death) would come into the discussion:

“The fact that it is an important disease that causes death focuses the mind a little more than perhaps

some other technologies we've looked at where there may be good randomised clinical trials but sometimes it's difficult to judge the relative merits of the technology."

(NICE 27)

"People are often affected by the perceived seriousness of the disease, and therefore the advocacy of the patient groups."

(NICE 9)

"When we're looking at life extending technologies then that tends to raise different kinds of issues like rule of rescue."

(NICE 28)

Practical issues relating to the economic analyses received by the committee

Variation in methods and approaches to analysis by the assessment teams

The general lack of consistency in the methods employed by different assessment teams was highlighted by a small number of interviewees as a particular problem that hindered committee members in their interpretation of the economic analysis.

"You get quite different types of health economic evaluation from the different TARs. Some of them give you these Bayesian analyses with cost-effectiveness curves, and some don't. And some of them seem to have very back-of-the-envelope type calculations. I'm not saying you should ... make it more uniform. Short of throwing a lot more money at it, I don't know what you could do."

(NICE 14)

"So every time we get the assessment, at the end we could look at some sort of sensitivity and major determinants and the variation around the cost per QALY, in exactly the same format every time, because we'd learn to use it better."

(NICE 23)

Another committee member also highlighted the need for greater consistency, and called for the NICE committee to spend some of its time discussing, and coming to agreement on, principles concerning the methodology to be used.

"There should be a very standard way of doing something so that it will be feasible and justifiable to expect every member of the committee to understand what's happening in the presentation. At the moment from case to case it varies: what we get, how its presented, etc, so one standard form of presentation

of all the results will be a massive improvement ... I don't see why the analysis should be different from case to case. I mean you should have an agreed analysis which is for all cases, whatever it is, whatever the technology, and you should explain any deviation from that. The issue of extrapolation is a perfect example of the thing where we should take a principle decision which applies to all technologies. It is not something which you should decide on a case-by-case basis ... there are methodological issues here and they should be settled. ... Let's have a day or two on extrapolation rather than on say capacetabine.

(NICE 26)

The presentation of economic analyses

From many of the interviewees there was a call for much greater clarity in the economic analysis presented in the assessment report. The sensitivity analysis was highlighted in particular as a very useful aspect of the report and which needs to be made highly accessible. The use of summaries was promoted but the call was for overviews that do more than simply repeat what is in the report but are designed to be user-friendly and address the specific questions that committee members are likely to have. Graphical representations of the model were thought to be particularly helpful, where possible.

"A bit more simple and clear presentation of the sensitivity analysis and of the things that, with small changes, might make major differences to the model."

(NICE 23)

"I sometimes feel we're given stacks of stuff to read through with very little guidance. And although we're given overviews, the overviews are often just summaries, and what we really need is somebody to say, 'these are the key issues in relationship to the key studies, or key assumptions around health state values', or whatever, that could then help us be a bit more critical in how we read things."

(NICE 28)

"I think there should be a sort of summary document, describing in simple terms, that this is a model which includes the utility of the effect of the technology, the potential for adverse effects, the sorts of issues that have gone in making up this model, the principles behind it."

(NICE 6)

"I'm not sure if I wouldn't welcome a kind of summary of the model. A version of, how the model is constructed in very simple English on one side of a sheet of A4. 'And here are the assumptions that are in there, and the questions that you might want to ask' ... I would be more equipped I think if there was an intermediate step between the humungously

complicated, number populated thing we get, and the process in the room. ... If you could represent things visually you'd get further – a lot of us would comprehend quicker.”

(NICE 8)

The preference of some committee members was against the sole reliance on a single aggregated approach to presenting results of economic analyses, for example, QALYs. The presentation of information and/or results of analyses in a disaggregated manner was seen as appropriate, not necessarily as an alternative to a cost per QALY but as an adjunct.

“I think sometimes it doesn't need to be simplified down to the QALYs. I think if you gave people a sort of list and said ... 'this drug will cause you to have so much diarrhoea and vomiting for so long' and just give a list of the good and the bad points of the drug and then the cost, 'are you willing to take this on?' I think the committee themselves too could perhaps look at it in that way ... I mean the cost per QALY is a tremendous simplification of human life really – turning it all into one number at the end of the day is sometimes too simplistic, it seems to me.”

(NICE 17)

“Some people would consider that feeling sick all the time is pretty awful really and that might be more important than whether you live another three months.”

(NICE 19)

“When I'm making a decision myself, about a private thing, I tend to like to see things disaggregated, rather than all collected into one single – as it would be in the case of NICE – cost per QALY. I like to see them disaggregated ... Of course that then allows in perhaps more 'fudge factors' where any argument can carry any weight.”

(NICE 4)

Other weaknesses of the economic evaluations received

Committee members identified a number of areas that they felt were either routinely ignored by the assessment teams conducting the economic analyses or areas that could be dealt with in a fuller manner. These concerns particularly related to assessment of budget impact and issues concerning the implementation of the technology in practice.

“We tend to focus just on the ratios whereas sometimes it's worth taking a step back and looking at the total budget impact compared with the total QALY gain ... I don't think we spend enough time on the total budget impact, that's usually skirted over.”

(NICE 20)

“I tend to think a lot about implementation. If we're not specific about things, will PCTs, hospital trusts actually be able to implement what's happening?”

(NICE 3)

“I think the complexity of certain technologies and how long they may take to implement is something that we need to work out more as a committee and organisation.”

(NICE 29)

A weakness that was mentioned by many of the interviewees related to the common situation of poor-quality data being available for the economic analysis. The call from the committee members was for trialists to consider the needs of those conducting economic analyses in order to avoid, where possible, the need for model-based analyses to rely on assumptions and poor quality data.

“I think the message has to be stronger to the drug companies and to the clinicians that actually they need more good quality data.”

(NICE 24)

“The data are often not there or not the quality that one would like.”

(NICE 25)

“Sometimes the quality of the data isn't all that it should be. But that's just a consequence of the fact that sometimes the sort of trials that needed to be done have not been done so there are gaping holes and things that are incomplete. And that therefore requires the statisticians and the health economists to model things and having to make quite a few assumptions while they're doing that.”

(NICE 29)

An issue related to this was a widely held view that economic analyses tended not to reflect fully the uncertainties inherent in them, given the poor-quality data often feeding into the analysis.

“They [the economic analyses] don't take enough cognisance of uncertainty.”

(NICE 14)

Particularly in the context of model-based analyses, the importance of ensuring that committee members understand the limitations of the analysis was highlighted. The suggestion is that the results of model-based analyses are not interpreted with the caution they deserve. The potential for misleading results when inappropriate structural assumptions are made in modelling exercises was also indicated as a potentially serious problem.

“What worries me most about the whole process is all the assumptions that get built in to the economic

model. I think there's a real danger that the economic analysis gets taken as fact, and it is not fact. There are so many assumptions and judgements made that I think that makes it very difficult."

(NICE 2)

"The structural issues I think are more devastating because if the structure is wrong then it doesn't matter what you put in, it's going to be nonsense."

(NICE 12)

Summary of interview data

The information drawn upon by the committee

Interviewees unanimously emphasised the importance of the evidence base in the decision-making process. Within the written evidence the assessment report was generally considered to be of most importance. However, a small number of interviewees felt unable to digest fully the contents of the assessment report. Industry submissions were seen as a more contentious part of the evidence base. They appeared to be treated with differing degrees of scepticism by committee members. Despite these expressions of concern over the value and credibility of industry submissions, other interviewees appeared to treat the manufacturer's assessment as a counterweight to the academic review team's assessment. This approach was a source of concern to another interviewee. The role of experts who appear before the committee, and the need for experts to be informed about the model and economic analysis in order to play a supportive role, were also raised.

Appraisal Committee procedures and processes

Overall, interviewees praised the processes employed by NICE and indicated in general terms that the appraisal process worked very well. However, frustrations with the appraisal process were expressed in terms of the scope of the policy question sometimes being addressed. There was a repeated concern that the definition of the policy question, and the development of the appraisal scope, were not given sufficient time or resource and often led to problems in the committee meetings themselves. The suggestion was made that an opportunity to clarify and identify clearly the relevant policy question should more formally be part of the appraisal process.

Virtually all interviewees who spoke about the notion of using a cost-effectiveness threshold indicated that the NICE Appraisal Committee did make use of some form of threshold but also

expressed some concerns around both its basis (especially where the threshold in use currently might have come from) and its use as a basis for decision-making. An important consequence of applying the current implied cost-effectiveness threshold range was thought by several interviewees to be that further pressure was being placed on the NHS at a local level to remain within budget.

Appraisal Committee composition and the roles of committee members

All interviewees indicated that committee members were selected as bearers of particular expertise and/or experience deemed relevant to the decision-making process. Within this there appear to be two identifiable roles which inform the selection of committee members: the 'technical expert' and the 'advocate' or 'representative'. Many interviewees bought into this model whereby the effectiveness as a decision-making committee was partly measured in terms of the breadth of expertise represented amongst them, to the extent that some identified areas of perceived under-representation. Unsurprisingly, given the focus for this research exercise, the role of the health economists on the committee was a recurrent theme. They are clearly viewed as a distinct group of experts playing an important role in terms of advising others on the strengths and weaknesses in the economic analysis presented.

Interviewees unanimously felt that the committee included a sufficient number of professional health economists on each branch. There was less agreement concerning levels of expertise in health economics amongst the broader committee. A number of interviewees indicated that they were concerned both by their own personal lack of understanding of the economic analyses, but also the level of understanding by others on the committee. One of the real dangers associated with low levels of understanding of the economic analysis that was highlighted is that too much faith might be placed in it. There were two major areas discussed by interviewees when thinking about whether and how levels of understanding of health economics could and should be improved: (1) the extent to which simply being involved in the appraisal process itself brings about sufficient learning and (2) whether or not further training should be provided for committee members.

How the information is processed by the committee

Nearly everyone expressed the view that the economic evidence and evidence of clinical

effectiveness were given highest priority. However, there appeared to be a division between committee members who considered the economic evidence first and those who paid most attention to the clinical evidence. Many of the interviewees espoused the position that there was a strong ordinal approach to their consideration of the clinical evidence and economic analyses. That is, the first hurdle for the technology in question was that of effectiveness and a concern with cost-effectiveness was secondary. One of the health economist interviewees acknowledged that this ordinal approach to decision-making was adopted by the committee but argued that this was wrong. Indeed, the respondent went further to suggest that this was something that should be addressed by NICE as a conceptual problem with the decision-making model being adopted by the committee.

An opinion repeated by a number of respondents was that the main value of the economic evaluation was not limited solely to the fact that it provided an overall result but that it allowed the discussion to be structured and focused on the most important aspects of the evidence (both clinical and economic). If the economic analysis is to be used effectively to provide the framework for the discussion, then there is clearly a requirement that a minimum level of understanding of the analyses exists amongst committee members.

Conceptual issues concerning economic analyses

A particular issue brought up by many interviewees was the great benefit for a decision-making body such as NICE of a single measure of benefit such as the QALY, in allowing comparison of very many disparate health interventions and in providing a benchmark for later decisions. It was also felt that the concept was broadly familiar to those in the health service and other NICE stakeholders. However, the broad comparability facilitated by QALYs was not universally acknowledged. A theme relating to the limitations of QALYs identified by several interviewees was the concern that they fail to capture some important aspects of benefit, and that the patient

experience is not captured fully in the QALY measure. In addition, many interviewees indicated that equity concerns tend not to be formally considered by the committee for a wide range of reasons. For example, one committee member indicated that he did not have a clear view on what the appropriate equity arguments are and, even if there was greater clarity on the nature of the arguments, there exists no agreement on how they might be included in the economic analysis.

Practical issues relating to the economic analyses received by the committee

The general lack of consistency in the methods employed by different assessment teams was highlighted as a particular problem that hindered committee members in their interpretation of the economic analysis. There was a call for much greater clarity in the economic analysis presented in the assessment report. The sensitivity analysis was highlighted in particular as a very useful aspect of the report and which needs to be made highly accessible. The use of summaries was promoted.

The preference of some committee members was against the sole reliance on a single aggregated approach to presenting results of economic analyses, for example, QALYs. The presentation of information and/or results of analyses in a disaggregated manner was seen as appropriate. A number of areas were identified where the economic analyses tended not to be very full or detailed. These particularly related to assessment of budget impact and issues concerning the implementation of the technology in practice.

Particularly in the context of model-based analyses, the importance of ensuring that committee members understand the limitations of the analysis was highlighted. The suggestion is that the results of model-based analyses are not interpreted with the caution they deserve. The potential for misleading results when inappropriate structural assumptions are made in modelling exercises was also indicated as a potentially serious problem.

Appendix 12

Further details of the systematic review methods and results

Review of existing reviews in health care

Reviews were identified from sources listed in the ARIF Search Protocol for Reviews (see *Table 22*) plus handsearching of the *Journal of Health Services Research and Policy*, 2000–2. Search strategies for MEDLINE and EMBASE are given in *Tables 23* and *24*.

The following searches were also undertaken in order to inform all four stages of the review:

- Office of Health Economics – Health Economic Evaluations Digest (OHE HEED), October 2002 CD Rom. All data fields in the database were searched using textwords ‘decision-making’ or ‘policy making’ and combined with ‘cost effectiveness’ or ‘cost-benefit terms’ or ‘economic evaluation’.
- World Health Organization (WHO) library database. Searched on 7 November 2002 using textwords ‘economic evaluat\$’ or ‘cost benefit\$’ or ‘cost effectiveness’ and combined with ‘decision mak\$’ or ‘policy’.
- The World Bank. The information library was contacted by email on 6 November 2002. No information was forthcoming.
- Experts in health economics and those on the advisory group for this project within the UK were contacted by email (4 November 2002) for information on existing publications and ongoing and unpublished research.
- Additional experts were contacted for information within the Treasury Department of the UK Government.

TABLE 22 ARIF search strategy

Cochrane Library
 Cochrane Reviews
 Database of Abstracts of Reviews of Effectiveness (DARE)
 Cochrane Controlled Trials Register (CCTR)
 Health Technology Assessment (HTA) database
 ARIF Database (an in-house database of reviews compiled from DARE and scanning current journals and appropriate websites. Many reviews produced by the organisations listed below are included)
 NHSCRD (web access)
 DARE
 Health Technology Assessment Database
 Completed and ongoing CRD reviews
 Health Technology Assessments (web access)
 Office of Technology Assessment
 NHS Coordinating Centre for Health Technology Assessments
 Canadian Coordinating Office for Health Technology Assessment
 New Zealand Health Technology Assessment
 Wessex DEC Reports
 Trent Institute for Health and Related Research Reports
 NICE appraisals
 Agency for Healthcare Research and Quality (AHRQ)
 National Horizon Scanning Centre
 Bandolier (via the web)
 National Research Register (via the web)
 InterTasc database
 TRIP Database
 Drug and Therapeutics Bulletin
 Bibliographic databases
 MEDLINE – systematic reviews (suggested strategy from CRD)
 EMBASE – systematic reviews
 Other specialist databases, e.g. CINAHL, PsycLit

TABLE 23 MEDLINE and EMBASE search strategy (up to 2002)

Database: MEDLINE 1966 to April Week 1 2002

Search strategy:

- 1 economics/ (8872)
- 2 exp "costs and cost analysis"/ (94911)
- 3 cost of illness/ (4131)
- 4 exp health care costs/ (17125)
- 5 economic value of life/ (3926)
- 6 exp economics medical/ (9146)
- 7 exp economics hospital/ (11541)
- 8 economics pharmaceutical/ (1019)
- 9 exp "fees and charges"/ (18602)
- 10 (cost or costs or costed or costly or costing).tw. (111395)
- 11 (economic\$ or pharmaco-economic\$ or price\$ or pricing).tw. (53511)
- 12 or/1-11 (224870)
- 13 health policy/ (22287)
- 14 exp decision-making/ (41573)
- 15 decision-making organizational/ (5521)
- 16 health services research/ (15006)
- 17 (acceptab\$ or appropriat\$ or utilis\$ or utiliz\$).ti,ab. (311007)
- 18 diffusion of innovation/ (3658)
- 19 technology assessment biomedical/ (3981)
- 20 or/13-19 (393314)
- 21 12 and 20 (34718)
- 22 (systematic adj review\$).tw. (2724)
- 23 (data adj synthesis).tw. (2374)
- 24 (published adj studies).ab. (3271)
- 25 (data adj extraction).ab. (2050)
- 26 meta-analysis/ (4184)
- 27 meta-analysis.ti. (3494)
- 28 comment.pt. (191013)
- 29 letter.pt. (450290)
- 30 editorial.pt. (133399)
- 31 animal/ (3247184)
- 32 human/ (7520555)
- 33 31 not (31 and 32) (2541206)
- 34 21 not (33 or 28 or 29 or 30) (33011)
- 35 or/22-27 (14438)
- 36 34 and 35 (368)

Database: EMBASE 1980 to present

Search strategy:

- 1 cost benefit analysis/ (13679)
- 2 cost effectiveness analysis/ (25254)
- 3 cost minimization analysis/ (418)
- 4 cost utility analysis/ (624)
- 5 economic evaluation/ (1074)
- 6 medical decision-making/ (15995)
- 7 decision-making/ (15859)
- 8 health care management/ (7763)
- 9 health care policy/ (26068)
- 10 health care delivery/ (17353)
- 11 or/6-10 (75994)
- 12 (review\$ or overview).ti. (80350)
- 13 or/1-5 (38282)
- 14 11 and 13 and 12 (107)
- 15 (medline or embase or cinahl or scisearch or psycinfo or psyclit).ti,ab. (7130)
- 16 12 or 15 (85948)
- 17 16 and 11 and 13 (146)

TABLE 24 MEDLINE and EMBASE search strategy (2002 to 2004)

Database: Ovid MEDLINE 1966 to July Week 3 2004

Search strategy:

- 1 economics/ (23811)
- 2 exp "Costs and Cost Analysis"/ (110185)
- 3 cost of illness/ (6121)
- 4 exp health care costs/ (22284)
- 5 economic value of life/ (4345)
- 6 exp economics medical/ (9504)
- 7 exp economics hospital/ (12889)
- 8 economics pharmaceutical/ (1367)
- 9 exp "Fees and Charges"/ (20868)
- 10 (cost or costs or costed or costly or costing).tw. (136422)
- 11 (economic\$ or pharmaco-economic\$ or price\$ or pricing).tw. (68154)
- 12 or/1-11 (281615)
- 13 health policy/ (26658)
- 14 exp decision-making/ (54139)
- 15 decision-making organizational/ (6987)
- 16 health services research/ (19525)
- 17 (acceptab\$ or appropriat\$ or utilis\$ or utiliz\$).ti,ab. (375837)
- 18 diffusion of innovation/ (4761)
- 19 technology assessment biomedical/ (4701)
- 20 or/13-19 (479715)
- 21 12 and 20 (43443)
- 22 (systematic adj review\$).tw. (5556)
- 23 (data adj synthesis).tw. (3242)
- 24 (published adj studies).ab. (4423)
- 25 (data adj extraction).ab. (2999)
- 26 meta-analysis/ (5457)
- 27 meta-analysis.ti. (4915)
- 28 comment.pt. (253767)
- 29 letter.pt. (509370)
- 30 editorial.pt. (163392)
- 31 animal/ (3653674)
- 32 human/ (8547910)
- 33 31 not (31 and 32) (2808546)
- 34 21 not (33 or 28 or 29 or 30) (41277)
- 35 or/22-27 (21349)
- 36 34 and 35 (532)
- 37 limit 36 to yr=2002 - 2004 (152)
- 38 from 37 keep 1-152 (152)

Database: EMBASE 1980 to 2004 Week 30

Search strategy:

- 1 cost benefit analysis/ (18361)
- 2 cost effectiveness analysis/ (34179)
- 3 cost minimization analysis/ (678)
- 4 cost utility analysis/ (1103)
- 5 economic evaluation/ (1994)
- 6 medical decision-making/ (26452)
- 7 decision-making/ (23268)
- 8 health care management/ (9940)
- 9 health care policy/ (34711)
- 10 health care delivery/ (23845)
- 11 or/6-10 (107481)
- 12 (review\$ or overview).ti. (95482)
- 13 or/1-5 (51850)
- 14 11 and 13 and 12 (213)
- 15 (medline or embase or cinahl or scisearch or psycinfo or psyclit).ti,ab. (10850)
- 16 12 or 15 (103760)
- 17 16 and 11 and 13 (268)
- 18 limit 17 to yr=2002 - 2005 (133)
- 19 from 18 keep 1-133 (133)

The titles and abstracts of the results of these searches were also browsed for potentially relevant articles. The search hits are given in *Table 25*.

Hard copies of potentially relevant reports were obtained and where necessary translations were undertaken of part or all of foreign language articles to facilitate the selection process. Reviews to be included in this review were selected based on the following criteria:

1. study design:
 - (a) any review particularly those with a systematic approach
2. population in included studies in review:
 - (a) healthcare decision- and/or policy makers
3. focus of studies included in the review:
 - (a) evaluation of effectiveness of initiatives using economic evaluations OR
 - (b) studies attempting to assess the barriers to the use of economic evaluations OR
 - (c) studies attempting to assess how decision-making bodies make their decisions in relation to the use of economic evaluations.

Two reviewers independently applied the inclusion criteria (DM, IW) and disagreements were resolved by discussion. A third reviewer (C Hyde) was available to provide additional input if necessary. All decisions were recorded. All excluded articles were assessed for relevance to other sections of this review.

The quality of included reviews was assessed using a recognised critical appraisal tool (CASP). Two reviewers independently undertook quality assessment (DM, IW) and disagreements were resolved by discussion. A third reviewer (C Hyde) was available to provide additional input if necessary.

TABLE 25 Search hits for review of reviews in healthcare

MEDLINE (OVID)	366
EMBASE (OVID)	146
OHE HEED	32
National Coordinating Centre for HTA	2
National Research Register ^a	2
ISTAHC ^a	2
National Research Register ^a	2
Internet:	
WHO ^a	2
Other ^a	1
Total	555
Minus duplicates	506

^a Only relevant hits retrieved.

Formal data extraction was not planned for this stage of the review due to the perceived small number of included reviews and the likelihood that the reviews would not be directly comparable. The quality and findings of the included reviews were reported textually, highlighting important strengths and weakness of the review and commenting on the external validity with regard to the objectives of this review.

The one included review was:

Spath HM, Alleret B, Carrere MO. Using economic information in the health sector: the choice of which treatments to include in hospital treatment portfolios. *J Econ Méd* 2000;**18**:147–61 (in French).

The best near-miss reviews were:

Coyle D. *Increasing the Impact of Economic Evaluations on Health-care Decision-making*. Discussion Paper 108. York: Centre for Health Economics, University of York; 1993.

Drummond M. Evaluation of health technology: economic issues for health policy and policy issues for economic appraisal. *Soc Sci Med* 1994;**38**:1593–600.

McDonald R. *Using health economics in health services: rationing rationally?* Buckingham: Open University Press; 2002.

Prosser LA, Koplan J, Neumann P, Weinstein MC. Barriers to using cost-effectiveness analysis in managed care decision-making. *Am J Managed Care* 2000;**6**:173–9.

Studies excluded but marked as being of possible relevance to the wider review were:

Davies C, Walley P. Quality of care: replacing or removing ineffective services. *Int J Health Care Qual Assur* 2002;**15**:124–9.

Davies LM, Drummond MF, Coyle D. Do economic evaluations of health technologies have an impact in decision making? Results of an EC survey. *Int Soc Technol Assess Health Care Meeting* 1993;**9**:65.

Drummond M, Cooke J, Walley T. Cost-effectiveness guidelines for reimbursement of pharmaceuticals ... *Soc Sci Med* 1997;**45**:583–95.

Fahey T. Evidence based purchasing: understanding results of clinical trials ... *BMJ* 1995;**311**:1056–9.

Haines A, Jones R. Implementing findings of research. *BMJ* 1994;**308**:1488–92.

Henshall CD. Economic appraisal in the British National Health Service: implications ... *Soc Sci Med* 1994;**38**:1615–23.

Innavaer S. Health policy-makers' perceptions of their use of evidence: a systematic review. *J Health Serv Res Policy* 2002;**7**:239–44.

Ross J. The use of economic evaluation in health care: Australian decision makers' perceptions. *Health Policy* 1995;**31**:103–10.

Sassi F, Archard L, Le Grand J. Equity and the economic evaluation of health care. *Health Technol Assess* 2001;**5**(3).

Woolf SH. Evidence-based medicine – interpreting studies and setting policy. *Hematol Oncol Clinics North Am* 2000;**14**:761–84.

The totally excluded papers were:

Ament A, Baltussen R. The interpretation of results of economic evaluations: explicating the ... *Health Econ* 1997;**6**:625–35.

Balas EA, Rainer AC. Interpreting cost analyses of clinical interventions. *JAMA* 1998;**279**:54–7.

Baltussen RL. The impact of age on cost-effectiveness ratios and its control in decision-making. *Health Econ* 1996;**5**:227–39.

Banta DH. Strategies for successful evaluation and policy-making toward health ... *Soc Sci Med* 1994;**38**:1663–74.

Baram MS. The use of cost-benefit analysis in regulatory decision-making is proving ... *Ann NY Acad Sci* 1981;**363**:123–8.

Bernstein J. Current concepts review – decision analysis. *Ann Cases Inf Technol* 1997;**79**:1404–14.

Bloom BS. Usefulness of US cost-of-illness studies in health care. *Pharmacoeconomics* 2001;**19**:207–13.

Blumenschein KJ. Economic evaluation in health care: a brief history and future directions. *Pharmacoeconomics* 1996;**10**:114–22.

Buxton MJ. Heart transplantation in the UK: the decision-making context of an economic evaluation. In Stocking B, editor. *Expensive health technologies – regulatory and administrative mechanisms in Europe*. Oxford: Oxford University Press; 1988. pp. 36–48.

Craig NP. Clearing the fog on the Tyne: programme budgeting in Newcastle and North Tyneside. *Health Policy* 1995;**33**:107–25.

Crandall RW. The use of cost-benefit analysis in regulatory decision-making. *Ann NY Acad Sci* 1981;**363**:99–107.

Drummond M. Guidelines for reimbursement of pharmaceuticals: is economic evaluation ready for ... *Health Econ* 1992;**1**:85–92

Elsinga E, Rutten FH. Economic evaluation in support of national health policy: the case of The Netherlands. *Soc Sci Med* 1997;**45**:605–20

Epstein RSF. Intervention thresholds for the treatment of osteoporosis: comparison ... *Osteoporos Int* 1998; Suppl 1:S22–7.

Estabrooks C. Decisions aids – are they worth it? *J Health Serv Res Policy* 2001;**6**:170–82.

Garande-Kulis VG. Methods for systematic reviews of economic evaluations for the ... *Am J Prev Med* 2000; **18**:75–91.

Gerard K. Cost-utility in practice: a policymaker's guide to the state of the art. *Health Policy* 1992;**21**:249–79.

Glassman PAM. The role of the medical necessity and cost-effectiveness in making medical decisions. *Ann Intern Med* 1997;**126**:152–6.

Haily D. Australian economic evaluation and government decisions ... *Soc Sci Med* 1997;**45**:563–81.

Henry D. Economic analysis as an aid to subsidisation decisions – the development ... *Pharmacoeconomics* 1992;**1**:54–67.

Heyland KK. Economic evaluations in the critical care literature: do they help us ... *Crit Care Med* 1996;**24**: 1591–8.

Irwig L. A flow diagram to facilitate selection of interventions and ... *Bull World Health Organ* 1998;**76**: 17–24.

Jonsson B. Economic evaluation of medical technologies in Sweden. *Soc Sci Med* 1997;**45**:597–604.

Karlsson G. The decision rules of cost-effectiveness analysis. *Pharmacoeconomics* 1996;**9**:113–20.

Lipton JA. Research evaluation and policy in dental public health. *Curr Opin Dent* 1991;**1**:329–36.

Mandelblatt JS, Fryback DG, Weinstein MC, (1997) Assessing the effectiveness of health interventions for cost-effectiveness analysis. Panel on Cost-Effectiveness in Health and Medicine. *J Gen Intern Med* 1997; **12**:551–8.

Mason J. The generalisability of pharmacoeconomic studies. *Pharmacoeconomics* 1997;**11**:503–14.

Mason JM. Cost-per-QALY league tables: their role in pharmacoeconomic analysis. *Pharmacoeconomics* 1994;**5**:472–81.

McGettigan P, Sly K. The effects of information framing on the practices of physicians. *J Gen Intern Med* 1999;**14**:633–42.

Moatti JPC. Researcher-driven versus policy-driven economic appraisal of health technologies: the case of France. *Soc Sci Med* 1994;**38**:1625–33.

Muller C. Objective health care technology evaluation: it isn't easy. *Soc Work Health Care* 1991;**16**:119–32.

Murray CJL. Cost-effectiveness analysis and policy choices: investing in ... *Bull World Health Organ* 1994;**72**:663–74.

Neymark N. Critical reviews of economic analyses in order to make health care decisions for cancer. *Ann Oncol* 1998;**9**:1167–72.

Paalman M, Bekedam H. A critical review of priority setting in the health sector: the methodology of the 1993 World Development Report. *Health Policy Planning* 1998;**13**:13–31.

Pele A. Presenting economic information for decision-making. *Pharmacoeconomics* 1994;**6**:346–51.

Petrou S. A review of alternative approaches to health care resource allocation. *Pharmacoeconomics* 2000;**18**:33–43.

Saint S. The use of meta-analysis in cost-effectiveness analysis – issues and ... *Pharmacoeconomics* 1999;**15**:1–8.

Sanchez LA. Pharmacoeconomics and formulary decision-making. *Pharmacoeconomics* 1996;**9** (Suppl 1):16–25.

Sassi FM. Economic evaluation of diagnostic technology: methodological challenges ... *Int J Technol Assess Health Care* 1997;**13**:613–30.

Schmidt F. The impact of data-analysis methods on cumulative research knowledge ... *Evaluation and the Health Professions* 1995;**18**:408–27.

Stergachis A. Overview of cost-consequence modelling in outcomes ... *Pharmacotherapy* 1995;**15**(5 LL):40S–42S.

Vale L. Evidence-based medicine and health economics: a case study of end stage ... *Health Econ* 2000;**9**:337–51.

Walker D. Cost and cost-effectiveness guidelines: which ones to use? *Health Policy Planning* 2001;**16**:113–21.

Review of existing reviews in non-healthcare fields

The objective of this stage of the review was a systematic review of existing reviews on the use of economic evaluations in non-healthcare decision/policy making to test whether there was any useful literature outside the health sector. Given the breadth of this task, the review was limited to the following areas: social care, education, transport, environment and criminal justice areas. These were decided *a priori* by the consensus of the project steering group as those areas most likely to either contain reviews on use of economic information in decision/policy making and/or be most relevant to healthcare decision/policy making.

Difficulties in undertaking the reviews of non-healthcare studies include the relative lack of electronic databases compared with healthcare and the unsophisticated nature of those databases that are available. As such, searching the databases is cruder due to the absence of or limited indexing terms and unsophisticated search engines with which to probe the databases. In addition, in the absence of databases, the most accessible compendium of literature is usually found as lists of reports or pages on topic specific websites, but the ability to search these websites in a structured way is limited. Searching is often restricted to the use of single keywords and/or to the title of articles/

pages due to the provision of only basic search engines with which to probe the website. Many sites have no means of searching them at all and the identification of items of interest is restricted to browsing undertaken as systematically as possible.

Taking all the above together, the identification of relevant articles is less precise and more subjective searching than in healthcare. With regard to this review, in order to overcome the limitation a pragmatic approach to searching was undertaken. Databases were searched with a trade-off of high sensitivity against poor specificity such that as far as possible any relevant articles were captured but not at the expense of having to sift through unmanageable quantities of search results. Websites were searched where possible using supplied search facilities and using the most appropriate text term(s). Where no search facility was provided on the website or that provided appeared imprecise, websites were systematically browsed targeting the pages most likely to contain relevant sources of information.

Searches were primarily undertaken in Autumn 2002.

Social care

After consultation with colleagues undertaking reviews in social care at the Centre for Evidence Based Policy and Practice (University of London) and the Campbell Collaboration Social Welfare Coordinating Group, the key online databases of key organisations were searched using terms relevant to economic evaluations and social care singularly or in combination. The sources were:

- MEDLINE
- EMBASE
- CareData [Electronic Library for Social Care (UK)]
- Correspondence with the Chairperson of the Campbell Collaboration Social Welfare Coordinating Group for identification of published, unpublished or ongoing reviews.

We would have liked to have searched the Campbell Collaboration Database of Systematic Reviews of Interventions and Policy Evaluations (C2-RIPE), but at the time of undertaking this review the database was still under development.

Education

The websites and online databases of key organisations were searched using terms relevant to economic evaluations and education singularly or in combination. The sources were:

- Education Resources Information Center (ERIC)
- Correspondence with the Chairperson of the Campbell Collaboration Education Coordinating Group for identification of published, unpublished or ongoing reviews.

As with the searches for social care reviews, we would have liked to have searched the Campbell Collaboration database of systematic Reviews of Interventions and Policy Evaluations (C2-RIPE), but at the time of undertaking this review the database was still under development.

Transport

The websites and online databases of key organisations were searched using terms relevant to economic evaluations and transport singularly or in combination. The sources were:

- Transport Research Laboratory (UK)
- Highways Agency (UK)
- National Transportation Library (USA)
- Planning and Transport Research and Computation (UK)
- US Department of Transportation – Transport Research Information Services.

Environment

The websites and online databases of key organisations were searched using terms relevant to economic evaluations and environment singularly or in combination. The sources were:

- International Bibliography of Social Sciences
- The Environment Agency (UK)
- Department for Environment Food and Rural Affairs
- United Nations Environment and Human Settlements Division
- European Union Online
- Friends of the Earth and Greenpeace websites.

In addition, information was available from searches undertaken for other stages of the review and those searches undertaken to inform the whole review.

Search strategies

Full search strategies for all sectors and an indication of the number of hits are recorded in *Tables 26–30*.

A record was kept of the search terms used, the date the searches were executed and the quantity of results from each search. Articles identified through websites were browsed online for relevancy (SB/DM). Hard copies of potentially relevant articles were obtained for formal application of the inclusion/exclusion criteria. The criteria for each subject area were similar and analogous to those used in healthcare.

Quantity of literature identified

The yield of articles from the searches varied dependent on the database/website and the non-healthcare area searched. The greatest number of search results came from the social care area, primarily because of the more extensive coverage of the topic by available databases and more sophisticated search engines associated with these databases. Furthermore, social care feels as if it has a more active research profile than some of the other non-healthcare areas.

Scanning the search results revealed very few articles of sufficient relevance to be applied to the formal inclusion/exclusion process. Most of these articles came from the social care field and do not necessarily note more relevant research being undertaken in this field but might be the result of a greater number of search hits from a relatively

TABLE 26 Search strategy and results for identifying reviews on the use of economic evaluations in the field of social care

Database/website	Search terms	No. of hits
MEDLINE (Ovid)	Similar to EMBASE search shown below	
EMBASE (Ovid)	See below	494
CareData [Electronic Library for Social Care (UK)]	(Home care or community health care or foster care or nursing homes or residential care) AND (economics or cost effectiveness or cost benefit)	
Campbell Collaboration Social Welfare Coordinating Group	Request for information on published, unpublished or ongoing reviews on use of economic evaluations in decision/policy making in social care.	NA
NA, not applicable.		

TABLE 27 Search strategy and results for identifying reviews on the use of economic evaluations in the field of education

Database/website	Search terms	No. of hits
ERIC (Ovid)	Economic evaluation or cost effectiveness or economic factors or cost benefit AND decision-making or policy formation	438
	Title search using economic or cost or information or evaluation AND decision or policy	181
British Education Index (BEI)	Economic evaluation	1
	Policy making or policy formation	68
	Cost effectiveness	160
	Decision-making and cost effectiveness	0
	Decision-making or policy formation and economic or economics	4
	Cost effectiveness or cost benefit and policy making or decision-making	0
Campbell Collaboration Education Coordinating Group	Request for information on published, unpublished or ongoing reviews on use of economic evaluations in decision/policy making in education	NA

more comprehensive collation of research in the databases searched. Furthermore, many of the articles for which hard copies were obtained and thus to which the inclusion/exclusion criteria were applied were only obtained due to lack of information with which to exclude them from the title/abstract alone.

On application of the inclusion/exclusion criteria, no articles were subsequently included in the review. A list of studies identified and excluded is available on request from the authors of this report as space does not permit printing them here. The primary reasons for exclusion were that articles did not address the use of economics in the context of the decision-making process.

Overall, this review identified no reviews on the use of economic evaluations in the non-healthcare fields assessed. This suggests that no such reviews have been undertaken in this area, or that reviews have been undertaken but the available bibliographic databases that were searched are not extensive/comprehensive enough to catalogue them. It is interesting to speculate why there appears to be no such literature. A further option is that reviews have been undertaken but that the findings are nested within larger reports and thus not easily identified. However, it is our feeling that reviews on the use of economic evaluations in decision-making in these areas are unlikely to have been undertaken. Therefore, as with the healthcare area, there appears to have been no robust evaluation and summary of the research on the use of economic evaluations in decision-making. On this basis, we decided it would not be efficient to extend the searches for primary

literature on stages 3 and 4 outside healthcare databases.

Review of empirical studies in healthcare

Searches were under taken of the following sources:

- Electronic databases: MEDLINE, EMBASE, EconLit, Social Science Citation Index, the NHS Economic Evaluation Database (NHS EED), the Office for Health Economics Health Economic Evaluation Database (OHE HEED), Health Management Information Consortium (HMIC) database.
- Handsearching of key methods journals: *Health Economics* (1997–2002), *Journal of Health Economics* (1997–2002), *Pharmacoeconomics* (1998–2002), *Milbank Quarterly* (1997–2002).
- Bibliographies of all reviews and provisionally included articles retrieved were scrutinised.
- Research Registers.
- The Project Advisory Group were asked if they were aware of any relevant studies.

Searches of electronic databases used free-text terms and keywords (and where appropriate MESH headings) for decision/policy making and economic evaluations. Electronic searches were conducted from inception of the database to the end of 2002 in the first instance. No language restrictions were applied. The search strategies for electronic databases are given in *Tables 31–33*.

The search results are given in *Table 34*.

TABLE 28 Search strategy and results for identifying reviews on the use of economic evaluations in the field of transportation

Database/website	Search terms	No. of hits
TRL (Transport Research Laboratory), UK http://www.trl.co.uk/1024/search.asp	Policy	8
	Decision	5
	Cost	88
	Cost effectiveness	0
	Economic	19
	Economic evaluation	0
Highways Agency, UK http://www.highways.gov.uk/	Policy	5
	Policy-making	0
	Decision-making	5
	Decision	15
	Cost effectiveness	18
	Cost benefit	57
	Evaluation	37
National Transportation Library, USA http://search.bts.gov/ntlsearch/	Cost benefit & policy-making	14
	Cost benefit & decision-making	110
	Economic evaluation	57
Planning and Transport Research and Computation, UK http://www.ptrc-training.co.uk/shop/PTRCStore.asp	Policy-making, decision-making, cost effectiveness, cost benefit, economic evaluation, economic information	0
Transport Research Information Services Online (TRIS), US Department of Transportation http://199.79.179.82/sundev/search.cfm	Economic & decision-making	15
	Cost effectiveness & decision	17
	Cost effectiveness & policy	13
	Cost & policy making	2
	Cost & decision	48
	Cost & policy	37
	Economic evaluation & decision	1
	Economic evaluation & policy	0
International Bibliography of Social Sciences (IBSS) via BIDS	Transport & economic & decision	16
	Transport & economic & policy	274
	Economic & evaluation & transport	28
	Cost & effect & transport	19
	Cost & benefit & transport	50
	Transport & decision-making	55
	Policy making and transport	77
Institution of Civil Engineering (ICE) database http://www.ice.org.uk/	Cost, economic and transport	
World Bank Transport Economics Section http://www.worldbank.org	Economic evaluation, decision-making	Limited to specific economic evaluations

The numbers in *Table 34* represent the number of articles in addition to those already identified from the all the databases high up the list (i.e. EconLit searches identified 406 references not found in either MEDLINE or EMBASE). In addition, there were 12 articles in the book reporting the EuroMet studies which were already familiar to the authors of this report. Searches of HMIC identified 86 articles in the Kings Fund Library and Department of Health Data sections and 63 articles in HELMIS. The titles/abstracts were scanned for relevance and duplication of

previously identified articles. No new relevant studies were identified.

Given the difficulty with the way in which the literature in this field is poorly served by keyword indexing and the broad spectrum of possible search terms, once developed the search strategies were piloted to ensure that they were able to identify relevant studies/articles that were already known to the authors. If not, minor modifications were made but care was taken to ensure that sensitivity of the searches was not lost. In addition,

TABLE 29 Search strategy and results for identifying reviews on the use of economic evaluations in the field of environmental research

Database/website	Search terms	No. of hits
International Bibliography of Social Sciences (IBSS) via BIDS	Environment & economic & decision	74 (20 marked)
	Economic evaluation & environment*	9 (7 marked)
	Cost benefit & environment* & policy	2 (2 marked)
	Cost effectiveness and environment*	1 (1 marked)
	Cost & environment & decision	18 (4 marked)
	Decision-making & environment & economic	37 (3 marked)
Environment Agency http://www.environment-agency.gov.uk/search/?lang=_e		0
DEFRA (Department of Environment Food and Rural Affairs) http://www.defra.gov.uk	Economic evaluation & decision	122
	Economic evaluation	288
	Cost effectiveness & decision	106
	Economic evaluation & policy	193
Environment Agency and DETR (Department of the Environment Transport and the Regions) http://www.environment-agency.gov.uk	Decision-making	0
	Economic evaluation	
	Economic information	
UN website Environment and Human Settlements Division http://www.un.org/env/eia/	Decision-making & economic evaluation	1
	Economic information	
European Union Online website http://europa.eu.int	Economic evaluation & environment	422
	Policy & economic information	365
Science Direct	Economic evaluation & environment	32 (15 marked)
	Economic decision & environment	12 (3 saved)

TABLE 30 Search strategy and results for identifying reviews on the use of economic evaluations in the field of criminal justice

Database/website	Search terms	No. of hits
Home Office website http://www.homeoffice.gov.uk	Various combinations of usual search terms	Numerous but little of relevance (see comments)
	Economic evaluation decision-making cost effectiveness cost benefit and crime or criminal justice or law or legal	
RAND http://www.rand.org/publications	Evaluation	83
	Cost & benefit	27
National Criminal Justice Reference Service database http://abstractsdb.ncjrs.org/content/AbstractsDB_Search.asp	Cost effectiveness & decision	18
	Cost benefit & decision	38
	Economic evaluation & decision	4
	Economic evaluation & policy	16

relevant articles were identified from searches undertaken to inform all stages of the review.

Given the large volume of search results, a pragmatic approach was taken to focus on the most relevant studies. The titles of the results were browsed from the database on-screen by one reviewer for potential relevance to the review using criteria for the population and the intervention.

Inclusion criteria

Hard copies of potentially relevant studies were obtained and where necessary translations were undertaken of part or all of foreign language

articles to facilitate the selection process. Studies to be included in this review were selected based on the criteria below:

A. Study design

1. Does the study adopt a research design (including surveys and case studies) that assesses the use of economic evaluations by healthcare decision- and/or policy makers?
2. Is it an experimental or quasi-experimental study which utilises a control/comparator group to assess the use of economic evaluations by healthcare decision- and/or policy makers?

TABLE 31 MEDLINE and EMBASE search strategies (up to 2002)

Database: MEDLINE 1966 to December Week 3 2002	
Search strategy:	
1	economics/ (25869)
2	exp "costs and cost analysis"/ (101664)
3	cost of illness/ (4806)
4	exp health care costs/ (18881)
5	economic value of life/ (6949)
6	exp economics medical/ (9495)
7	exp economics hospital/ (11968)
8	economics pharmaceutical/ (1107)
9	exp "fees and charges"/ (20461)
10	(cost or costs or costed or costly or costing).tw. (119947)
11	(economic\$ or pharmaco-economic\$ or price\$ or pricing).tw. (59771)
12	or/1-11 (260253)
13	health policy/ (24673)
14	exp decision-making/ (52766)
15	decision-making organizational/ (6104)
16	health services research/ (16912)
17	diffusion of innovation/ (4009)
18	technology assessment biomedical/ (4403)
19	or/13-18 (104373)
20	12 and 19 (19132)
Database: EMBASE 1980 to 2003 Week 5	
Search strategy:	
1	health economics/ (5526)
2	exp economic evaluation/ (50955)
3	exp health care cost/ (53451)
4	pharmacoeconomics/ (731)
5	resource allocation/ (3875)
6	(cost or costs or costed or costly or costing).tw. (99300)
7	(economic\$ or pharmaco-economic\$ or price\$ or pricing).tw. (46236)
8	or/1-7 (177679)
9	health care policy/ (28662)
10	decision-making/ (18052)
11	health services research/ (1462)
12	biomedical technology assessment/ (2936)
13	or/9-12 (49764)
14	8 and 13 (12368)

B. Population

Healthcare decision- and/or policy makers.

C. Intervention

Using economic evaluations.

D. Outcomes

Any considered.

E. Exclusion

Any article that is solely a literature review or discussion piece.

If a study met all of the criteria A–D and not E it was included in the review of experimental/quasi-experimental studies (stage 3). If a study met the criteria except A2 and E it was included in the review of non-experimental studies (stage 4). If a

study met criteria B–E but not A1 it was marked for assessment for inclusion in the review of reviews in healthcare (stage 1). These criteria were applied by one reviewer (DM) and independently checked by a second (IW). Any disagreements were resolved by discussion and involving a third reviewer (SB) if required.

Excluded empirical health care studies were:

Alban A. The role of economic appraisal in Denmark. *Soc Sci Med* 1994;**38**:1647–52.

Anderson SE, Chen YK. Applying economic analysis to the decision-making process. *Cost Qual QJ* 1997;**3**:9–10.

Anell A. Priority setting for pharmaceuticals. The use of health economic evidence by reimbursement and clinical guidance committees. *Eur J Health Econ* 2004;**5**:28–35.

TABLE 32 MEDLINE and EMBASE search strategies (2002 to 2004)

Database: Ovid MEDLINE 1966 to June Week 2 2004

Search strategy:

- 1 exp "Costs and Cost Analysis"/ (109584)
- 2 cost of illness/ (6032)
- 3 exp Health Care Costs/ (22085)
- 4 economic value of life/ (4327)
- 5 exp Economics, Medical/ (9490)
- 6 exp Economics, Hospital/ (12830)
- 7 economics pharmaceutical/ (1355)
- 8 exp "Fees and Charges"/ (20781)
- 9 (cost or costs or costed or costly or costing).tw. (135374)
- 10 (economic\$ or pharmaco-economic\$ or price\$ or pricing).tw. (67610)
- 11 economics/ (23801)
- 12 or/1-11 (279871)
- 13 health policy/ (26471)
- 14 exp decision-making/ (53647)
- 15 decision-making organizational/ (6936)
- 16 health services research/ (19373)
- 17 (acceptab\$ or appropriat\$ or utilis\$ or utiliz\$).ti,ab. (372375)
- 18 diffusion of innovation/ (4707)
- 19 technology assessment biomedical/ (4628)
- 20 or/13-19 (475386)
- 21 12 and 20 (43129)
- 22 (systematic adj review\$).tw. (5409)
- 23 (data adj synthesis).tw. (3218)
- 24 (published adj studies).ab. (4373)
- 25 (data adj extraction).ab. (2939)
- 26 meta-analysis/ (5394)
- 27 meta-analysis.ti. (4830)
- 28 comment.pt. (251303)
- 29 letter.pt. (506648)
- 30 editorial.pt. (162193)
- 31 animal/ (3626177)
- 32 human/ (8494073)
- 33 31 not (31 and 32) (2791062)
- 34 21 not (33 or 28 or 29 or 30) (40977)
- 35 or/22-27 (20988)
- 36 34 and 35 (527)
- 37 limit 36 to yr=2002 - 2004 (148)
- 38 from 37 keep 1-148 (148)

Database: EMBASE 1996 to 2004 Week 25

Search strategy:

- 1 cost benefit analysis/ (12510)
- 2 cost effectiveness analysis/ (25642)
- 3 cost minimization analysis/ (663)
- 4 cost utility analysis/ (1075)
- 5 economic evaluation/ (1927)
- 6 medical decision-making/ (21729)
- 7 decision-making/ (16607)
- 8 health care management/ (6491)
- 9 health care policy/ (23239)
- 10 health care delivery/ (17516)
- 11 or/6-10 (77344)
- 12 (review\$ or overview).ti. (46115)
- 13 or/1-5 (37942)
- 14 11 and 13 and 12 (183)
- 15 (medline or embase or cinahl or scisearch or psycinfo or psyclit).ti,ab. (9300)
- 16 12 or 15 (53114)
- 17 16 and 11 and 13 (231)
- 18 limit 17 to yr=2002 - 2004 (125)
- 19 from 18 keep 1-125 (125)

TABLE 33 HMIC, HELMIS and EconLit search strategies

HMIC searches

- #1 RESEARCH-AND-DEVELOPMENT in DE:HMIC (1149 records)
- #2 HEALTH-SERVICES-RESEARCH in DE:HMIC (143 records)
- #3 QUALITATIVE-RESEARCH in DE:HMIC (141 records)
- #4 QUANTITATIVE-RESEARCH in DE:HMIC (16 records)
- #5 (RESEARCH in DE:HMIC) or (RESEARCH- in DE:HMIC) (8190 records)
- #6 #1 or #2 or #3 or #4 or #5 (8190 records)
- #7 HEALTH-POLICY in DE:HMIC (1280 records)
- #8 HEALTH-ECONOMICS in DE:HMIC (1814 records)
- #9 (ECONOMICS in DE:HMIC) or (ECONOMICS- in DE:HMIC) (2776 records)
- #10 ECONOMIC-EVALUATION in DE:HMIC (571 records)
- #11 COST in DE:HMIC (3301 records)
- #12 #7 or #8 or #9 or #10 or #11 (7255 records)
- #13 (EVALUATION in DE:HMIC) or (EVALUATION- in DE:HMIC) (9428 records)
- #14 UTILISATION in DE:HMIC (951 records)
- #15 (IMPLEMENTATION in DE:HMIC) or (IMPLEMENTATION- in DE:HMIC) (1914 records)
- #16 DISSEMINATION-OF-INFORMATION in DE:HMIC (282 records)
- #17 RESEARCH-IMPLEMENTATION in DE:HMIC (142 records)
- #18 RESEARCH-UTILISATION in DE:HMIC (1 record)
- #19 DECISION-MAKING in DE:HMIC (2263 records)
- #20 ACCEPTABLE in DE:HMIC (44 records)
- #21 APPROPRIATE in DE:HMIC (5 records)
- #22 #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 (14362 records)
- #23 #6 and #12 and #22 (87 records)
- * #24 #23 and (PY=1984-2002) (86 records)

HELMIS searches:

- #1 (RESEARCH-AND-DEVELOPEMTS in DE:HQ) or (RESEARCH-AND-DEVELOPMENT in DE:HQ) (302 records)
- #2 HEALTH-RESEARCH in DE:HQ (38 records)
- #3 HEALTH-SERVICES-RESEARCH in DE:HQ (213 records)
- #4 QUALITATIVE-RESEARCH in DE:HQ (99 records)
- #5 QUANTITATIVE-RESEARCH in DE:HQ (7 records)
- #6 (RESEARCH in DE:HQ) or (RESEARCH- in DE:HQ) (2356 records)
- #7 #1 or #2 or #3 or #4 or #5 or #6 (2356 records)
- #8 HEALTH-POLICY in DE:HQ (2459 records)
- #9 HEALTH-ECONOMICS in DE:HQ (884 records)
- #10 (ECONOMICS in DE:HQ) or (ECONOMICS- in DE:HQ) (1200 records)
- #11 ECONOMIC-EVALUATION in DE:HQ (279 records)
- #12 COST in DE:HQ (1760 records)
- #13 #8 or #9 or #10 or #11 or #12 (5079 records)
- #14 (EVALUATION- in DE:HQ) or (EVALUATION in DE:HQ) (2216 records)
- #15 (UTILISATION in DE:HQ) or (UTILISATION- in DE:HQ) or (UTILIZATION in DE:HQ) (788 records)
- #16 (IMPLEMENTATION in DE:HQ) or (IMPLEMENTATION- in DE:HQ) (609 records)
- #17 DISSEMINATION-OF-INFORMATION in DE:HQ (74 records)
- #18 DECISION-MAKING in DE:HQ (650 records)
- #19 (APPROPRIATE in DE:HQ) or (APPROPRIATENESS in DE:HQ) or (APPROPRIATENESS- in DE:HQ) (45 records)
- #20 #14 or #15 or #16 or #17 or #18 or #19 (4207 records)
- * #21 #7 and #13 and #20 (63 records)

Database: EconLit 1969 to June 2003

Search strategy:

- 1 health economics.sh. (3)
- 2 health economics general.sh. (2)
- 3 cost benefit analysis.kw. (18)
- 4 cost effectiveness.kw. (62)
- 5 cost utility analysis.kw. (1)
- 6 (cost or costs or costed or costly or costing).tw. (39622)
- 7 (economic\$ or pharmaco-economic\$ or price\$ or pricing).tw. (138620)
- 8 or/1-2 (5)
- 9 or/3-7 (163011)

continued

TABLE 33 HMIC, HELMIS and EconLit search strategies (cont'd)

10	health policy.sh. (1)
11	health.tw. (9715)
12	or/10-11 (9715)
13	9 and 12 (3601)
14	8 and 12 (4)
15	implement\$.tw. (9906)
16	utilis\$.tw. (528)
17	utiliz\$.tw. (4042)
18	(decision adj making).tw. (4191)
19	or/15-18 (18178)
20	11 and 19 and 9 (406)
21	from 20 keep 1-199 (199)

TABLE 34 Search results

MEDLINE (OVID)	173,77
Plus the following additional references:	
EMBASE (OVID)	110,22
EconLit	406
Social Sciences Citation Index	299
OHE HEED	21
Handsearching ^a	2
National Research Register ^a	2
Internet:	
WHO ^a	2
Other ^a	1
Citation checking ^a	1

^a Only relevant hits retrieved.

American Journal of Managed Care. Using pharmaco-economic studies for decision-making. *Am J Managed Care* 2000;**6** (7 Suppl):S388-92.

Anis AH, Gagnon Y. Using economic evaluations to make formulary coverage decisions: so much for guidelines. *Pharmacoeconomics* 2000;**18**:55-62.

Atfield R. An analysis of how economic decisions regarding purchasing are made in the N.H.S. *J Sterile Serv Manage* 1987;**5**:2-5.

Baltussen R, Ament A, Leidl R. Making cost assessments based on RCTs more useful to decision-makers. *Health Policy* 1996;**37**:163-83.

Baram MS. The use of cost-benefit analysis in regulatory decision-making is proving harmful to public health (Abstract). *Ann NY Acad Sci* 1981;**363**:123-28.

Bloom BS. Cost-benefit and cost-effectiveness analysis in policymaking: cimetidine as a model (Abstract). New York: Biomedical Information Corp. Publications. Data not available.

Buxton MJ. Heart transplantation in the UK: the decision-making context of an economic evaluation. In Stocking B, editor. *Expensive health technologies – regulatory and administrative mechanisms in Europe*. 1988. pp. 36-48.

Buxton MJ. Managing new technology: economics research and practical decisions. *Health Serv Manage Res* 1988;**1**:43-50.

Crandall RW. The use of cost-benefit analysis in regulatory decision-making (Abstract). *Ann NY Acad Sci* 1981;**363**:99-107.

Dahlqvist G. Evaluation of process economics is not a sufficient basis for decision on health policy. *Lakartidningen* 1995;**92**:2211 (in Swedish).

Davies L, Coyle D, Drummond M. Current status of economic appraisal of health technology in the European Community: report of the network. The EC Network on the Methodology of Economic Appraisal of Health Technology. *Soc Sci Med* 1994;**38**:1601-7.

Davies L, Coyle D, Drummond M, Alban A, Henke KD, Moatti JP, et al. Current status of economic appraisal of health technology in the European community: report of the network. *Soc Sci Med* 1994;**38**:1601-7.

Davies LM, Drummond MF, Coyle D. Do economic evaluations of health technologies have an impact in decision making? Results of an EC survey. *Int Soc Technol Assess Health Care Meeting* 1993;**9**:65.

Dixon S, Coleman P, Nicholl J, Brennan A, Touch S. Evaluation of the impact of a technology appraisal process in England: the south and west development and evaluation committee. *J Health Serv Res Policy* 2003;**8**:18-24.

Drummond M. Using economic studies to make cost-effective decisions in the NHS (focus groups). Unpublished.

Drummond M. Cost-effectiveness guidelines for reimbursement of pharmaceuticals: is economic evaluation ready for its enhanced status? (Abstract). *Health Econ* 1992;**1**:85-92

Drummond M, Cooke J, Walley T. *Economic evaluation in health care decision-making: evidence from the UK*. Report No. 148. York: Centre for Health Economics, University of York; 1996.

Drummond M, Cooke J, Walley T. Economic evaluation under managed competition: evidence from the UK. *Soc Sci Med* 1997;**45**:583-95.

- Drummond M, Weatherly H. Implementing the findings of health technology assessments. If the cat got out of the bag, can the tail wag the dog? *Int J Technol Assess Health Care* 2000;**16**:1–12.
- Drummond MF. Economic appraisal and health service decision-making. *Effective Health Care* 1983;**1**:25–33.
- Drummond MF. Survey of cost-effectiveness and cost-benefit analyses in industrialized countries. *World Health Statistics Quarterly – Rapport Trimestriel de Statistiques Sanitaires Mondiales* 1985;**38**:383–401.
- Drummond MF. Economic evaluation and the rational diffusion and use of health technology. *Health Policy* 1987;**7**:309–24.
- Elliott H, Popay J. How are policy makers using evidence? Models of research utilisation and local NHS policy making. *J Epidemiol Commun Health* 2000;**54**:461–8.
- Elsinga E, Rutten FF. Economic evaluation in support of national health policy: the case of The Netherlands. *Soc Sci Med* 1997;**45**:605–20.
- Epstein RS, Feng W, Hirsch LJ, Kelly M. Intervention thresholds for the treatment of osteoporosis: comparison of different approaches to decision-making (Abstract). *Osteoporos Int* 1998;Suppl 1:S22–7.
- Feldman R, Morrisey MA. Health economics: a report on the field. *J Health Politics Policy Law* 1990;**15**:627–46.
- Graf von der Schulenburg JM. Economic evaluation of medical technologies: from theory to practice – the German perspective. *Soc Sci Med* 1997;**45**:621–33.
- Granados A, Jonsson E, Banta HD, Bero L, Bonair A, Cochet C, *et al.* Eur-Assess project subgroup report on dissemination and impact. *Int J Technol Assess Health Care* 1997;**13**:220–86.
- Griffiths A. Evaluation and decision-making. The economist's point of view (author's translation). *Rev Epidemiol Santé Publique* 1981;**29**:363–70 (in French).
- Grund J, Husbyn H. The role of pharmacoeconomics in health policy and management in Norway. *Pharmacoeconomics* 1995;**7**:475–83.
- Hailey D. Australian economic evaluation and government decisions on pharmaceuticals, compared to assessment of other health technologies. *Soc Sci Med* 1997;**45**:563–81.
- Harris A, Buxton M, O'Brien B, Rutten F, Drummond M. Using economic evidence in reimbursement decisions for health technologies: experience of 4 countries. *Expert Rev Pharmacoecon Outcomes Res* 2001;**1**:7–12.
- Henry D. Economic analysis as an aid to subsidisation decisions – the development of Australian guidelines for pharmaceuticals (Abstract). *Pharmacoeconomics* 1992;**1**:54–67.
- Henry D, Lopert R. Pharmacoeconomics and policy decisions: the Australian health care system. *Clin Ther* 1999;**21**:909–15.
- Hoffmann C, van der Graf SJM, Hoffmann C, Rutten F, Van Rijkdom J, Leidl R, *et al.* The influence of economic evaluation studies on decision-making. A European survey. *Health Policy* 2000;**52**:179–92.
- Hoffman, C, von der Schulenburg JMG. The use of economic evaluation studies in health care decision-making – summary report. In von der Schulenburg JMG ed. *The influence of economic evaluation studies on health care decision-making. A European survey*. Washington, DC: IOS Press, 2000. pp. 3–16.
- Hoffmann C, Stoykova B, Nixon J, Glanville J, Misso K, Drummond M. Re: Hutton J, Brown R. Use of economic evaluation in decision-making: what needs to change? (Editorial) *Value Health* 2002;**5**:65–6 [comment]. *Value Health* 2002;**5**:114.
- Hoffmann C, Stoykova BA, Nixon J, Glanville JM, Misso K, Drummond MF. Do health-care decision makers find economic evaluations useful? The findings of focus group research in UK health authorities. *Value Health* 2002;**5**:71–8.
- Hurst J. The impact of health economics on health policy in England, and the impact of health policy on health economics, 1972–1997. *Health Econ* 1998;**7** Suppl 1:S47–61.
- Hutton J, Brown RE. Use of economic evaluation in decision-making: what needs to change? [comment]. *Value Health* 2002;**5**:65–6.
- Johannesson M. Economic evaluation of health care and policymaking. *Health Policy* 1995;**33**:179–90.
- Johnson JA, Friesen E. Reassessing the relevance of pharmacoeconomic analyses in formulary decisions. *Pharmacoeconomics* 1998;**13**:479–85.
- Johnstone P, Lacey P. Are decisions by purchasers in an English health district evidence based? *J Health Serv Res* 2002;**7**:166–9.
- Jonsson B. Economic evaluation of medical technologies in Sweden. *Soc Sci Med* 1997;**45**:597–604.
- Kanavos P, Trueman P, Bosilevac A. Can economic evaluation guidelines improve efficiency in resource allocation? The cases of Portugal, The Netherlands, Finland, and the United Kingdom. *Int J Technol Assess Health Care* 2000;**16**:1179–92.
- Kernick D. The impact of health economics on health care delivery: a health economist's perspective: a primary care response [1]. *Pharmacoeconomics* 2002;**20**:785–7.
- Kristen MM. Using cost-effectiveness and cost-benefit analysis for health care policy making. *Adv Health Econ Health Serv Res* 1983;**4**:199–224.
- Leidl R, Hoffman C, König HH, von der Schulenburg JMG. Do physicians accept quality of life and utility measurement? Results from a survey among German

physicians. In von der Schulenburg ed. *The influence of economic evaluation studies on health care decision-making. A European survey*. Washington, DC: IOS Press; 2000. pp. 109–15.

Luce BR, Brown RE. The use of technology assessment by hospitals, health maintenance organizations, and third-party payers in the United States. *Int J Technol Assess Health Care* 1995;**11**:79–92.

Luft HS. Benefit–cost analysis and public policy implementation: from normative to positive analysis. *Public Policy* 1976;**24**:437–62.

Mandelblatt JS, Fryback DG, Weinstein MC. Assessing the effectiveness of health interventions for cost-effectiveness analysis. Panel on Cost-Effectiveness in Health and Medicine. *J Gen Intern Med* 1997;**12**:551–8.

Martin DK, Pater JL, Singer PA. Priority-setting decisions for new cancer drugs: a qualitative case study [comment]. *Lancet* 2001;**358**:1676–81.

Mason J. The generalisability of pharmacoeconomic studies (Abstract). *Pharmacoeconomics* 2006;**11**:503–14.

Mason JM. Cost-per-QALY league tables: their role in pharmacoeconomic analysis (Abstract). *Pharmacoeconomics* 1994;**5**:472–81.

Miller DW. The impact of methodological and drug development issues on the use of economic data generated by clinical trials. *Pharm Pract Manage Q* 1997;**17**:75–86.

Mitton C, Donaldson C. Setting priorities in Canadian regional health authorities: a survey of key decision makers. *Health Policy* 2002;**60**:39–58.

Mooney G, Drummond M. Economic appraisal in health care 2. Economic appraisal and health service decision-making. *Hosp Health Serv Rev* 1981;**77**:308–13.

Mullins CD, Wang J. Pharmacy benefit management: enhancing the applicability of pharmacoeconomics for optimal decision-making. *Pharmacoeconomics* 2002;**20**:9–21.

Neumann PJ. The quality and usefulness of pharmacoeconomic studies for drug coverage decisions. *Pharm News* 2002;**9**:15–20.

Pelc A. Presenting economic information for decision-making. *Pharmacoeconomics* 1994;**6**:346–51.

Popper C. Using cost-effectiveness analysis to weigh testing decisions. *Mlo: Medical Laboratory Observer* 1992;**24** (9S Suppl):29–35.

Prosser LA, Koplan JP, Neumann PJ, Weinstein MC. Barriers to using cost-effectiveness analysis in managed care decision-making. *Am J Managed Care* 2000;**6**:173–9.

Reinhardt UE. Making economic evaluations respectable. *Soc Sci Med* 1997;**45**:555–62.

Rosen R. Applying research to health care policy and practice: medical and managerial views on effectiveness and the role of research. *J Health Serv Res Policy* 2000;**5**:103–8.

Rutten F. Economic evaluation and health care decision-making. *Health Policy* 1996;**36**:215–29.

Rutten F. The impact of health economics on health policy and practice. *J Health Serv Res Policy* 1996;**1**:62–3.

Salkeld G, Davey P, Arnolda G. A critical review of health-related economic evaluations in Australia: implications for health policy. *Health Policy* 1995;**31**:111–25.

Sanchez LA. Pharmacoeconomics and formulary decision-making. *Pharmacoeconomics* 1996;**9** Suppl 1:16–25.

Segal R, Pathak DS. Formulary decision-making: identifying factors that influence P&T committee drug evaluations. *Hosp Formulary* 1988;**23**:174–8.

Selby-Smith C, Hailey D, Drummond M. The role of economic appraisal in health technology assessment: the Australian case. *Soc Sci Med* 1994;**38**:1653–62.

Singer P, Martin D, Giacomini, Purdy L. Priority setting for new technologies in medicine: qualitative case study. *BMJ* 2000;**321**:1316–19.

Spath HM, Carrere MO, Fervers B, Philip T. Analysis of the eligibility of published economic evaluations for transfer to a given health care system. Methodological approach and application to the French health care system. *Health Policy* 1999;**49**:161–77.

Thwaites R, Anderson PM. Health care decision-making: health economics research and the pharmaceutical/biotechnology industry. *J Biolaw Bus* 1999;**2**:30–7.

Tolpin HG, Bentkover JD. Economic cost of illness: decision-making applications and practical considerations. *Adv Health Econ Health Serv Res* 1983;**4**:165–98.

Warner KE. Health policy uses and usefulness of cost–benefit and cost-effectiveness analysis. *Mead Johnson Symposium on Perinatal and Developmental Medicine* 1982;(20):53–69.

Weatherly H, Drummond M, Smith D. Using evidence in the development of local health policies. *Int J Technol Assess Health Care* 2002;**18**:771–81.

WHO-FICOSSER. Use of health economics for decision-making in complex emergencies. Report of a WHO-FICOSSER meeting, Paris, 16–18 December, 1999. *Cah Sociol Demogr Med* 2000;**40**:159–88.

Quality of included articles

For experimental and quasi-experimental studies, the methodological quality was to be assessed utilising the framework employed by the Cochrane Library, which aims to assess threats to validity in the areas of selection, performance, attrition and detection bias. For non-experimental studies, the potential value of quality assessment for this component of the review was less clear. After deliberation and consultation, the research team

decided against formal quality assessment of included studies, opting instead to present a detailed account of methods used by studies and to identify potential areas for further improvement in the literature, for example, through the use of different methodological approaches.

Data extraction and reporting

Formal data extraction was likely to be possible only for studies included in the review of experimental and quasi-experimental studies, and a data extraction pro forma was constructed *a priori* for this purpose. All relevant data for studies included in this component of the review were to be recorded and tabulated. For the review of non-experimental

studies, only basic key study characteristics were to be tabulated. Analysis for both stages was qualitative, based on patterns of results revealed in the tabulated data. *A priori* we believed that a quantitative summary is unlikely to be helpful even in attempting to assess the effectiveness of initiatives to use economic evaluations.

The research team agreed on the basic study characteristics to be tabulated. These were study aims, methods, the study population, the types of economic evaluation included in the study and the study results, including reported barriers to use of economic evaluation and strategies for improving its use.



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We look forward to hearing from you.